

## **Distribution Agreement**

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

---

Erica Modeste

---

Date

**Proteomic profiling of the cerebrospinal fluid of African Americans and Caucasians  
reveals common and unique biomarkers of Alzheimer's disease**

By  
Erica Modeste  
Doctor of Philosophy

Graduate Division of Biological and Biomedical Sciences  
Molecular and Systems Pharmacology

---

Nicholas Seyfried  
Advisor

---

David Weinshenker  
Committee Member

---

Ellen Hess  
Committee Member

---

John Hepler  
Committee Member

Accepted:

---

Kimberley Jacob Arriola, PhD  
Dean of the James T. Laney School of Graduate School

---

Date



**Proteomic profiling of the cerebrospinal fluid of African Americans and Caucasians  
reveals common and unique biomarkers of Alzheimer's disease**

By

Erica Modeste  
B.S. University of Richmond, 2015

Advisor: Nicholas Seyfried, Ph.D.

An abstract of  
a dissertation submitted to the faculty of the  
James T. Laney School of Graduate Studies of Emory University  
in partial fulfillment of the requirements for the degree of Doctor of Philosophy  
in the Graduate Division of Biological and Biomedical Sciences  
Molecular and Systems Pharmacology

2024

## **ABSTRACT**

### **Proteomic profiling of the cerebrospinal fluid of African Americans and Caucasians reveals common and unique biomarkers of Alzheimer's disease**

By Erica Modeste

Despite being twice as likely to get Alzheimer's disease (AD), African Americans have been grossly underrepresented in AD research. While emerging evidence indicates that African Americans with AD have lower cerebrospinal fluid (CSF) levels of Tau compared to Caucasians, other differences in AD CSF biomarkers have not been fully elucidated. In this thesis, we performed unbiased proteomic profiling of CSF from African Americans and Caucasians with and without AD to identify both common and divergent AD CSF biomarkers. Multiplex tandem mass tag-based mass spectrometry (TMT-MS) quantified 1,840 proteins from 105 control and 98 AD patients of which 100 identified as Caucasian and 103 identified as African American. Differential protein expression and co-expression approaches were then utilized to assess how changes in the CSF proteome were related to race and AD. Co-expression network analysis organized the CSF proteome into 14 modules associated with brain cell-types and biological pathways. Consistent with previous findings, the increase of Tau levels in AD was greater in Caucasians than in African Americans by both immunoassay and TMT-MS measurements. Similarly, modules enriched with proteins involved with glycolysis and neuronal/cytoskeletal proteins were more increased in Caucasians than in African Americans with AD. In contrast, a module enriched with synaptic proteins including VGF, SCG2, and NPTX2 was significantly lower in African Americans than Caucasians with AD. CSF modules which included 14-3-3 proteins (YWHAZ and YWHAG) demonstrated equivalent disease-related elevations in both African Americans and Caucasians with AD. A targeted mass spectrometry method, selected reaction monitoring (SRM), with heavy labeled internal standards was then used to measure a subset of CSF module proteins and a receiver operating characteristic (ROC) curve analysis assessed the performance of each protein biomarker in differentiating controls and AD by race. Following SRM and ROC analysis, VGF, SCG2, and NPTX2 were significantly better at classifying African Americans than Caucasians with AD. In total, these findings provide insight into additional protein biomarkers and pathways reflecting underlying brain pathology that are shared or differ by race.

**Proteomic profiling of the cerebrospinal fluid of African Americans and Caucasians  
reveals common and unique biomarkers of Alzheimer's disease**

By

Erica Modeste  
B.S. University of Richmond, 2015

Advisor: Nicholas Seyfried, Ph.D.

A dissertation submitted to the faculty of the  
James T. Laney School of Graduate Studies of Emory University  
in partial fulfillment of the requirements for the degree of Doctor of Philosophy  
in the Graduate Division of Biological and Biomedical Sciences  
Molecular and Systems Pharmacology

2024

## **TABLE OF CONTENTS**

<b>LIST OF FIGURES.....</b>	<b>9</b>
<b>LIST OF TABLES.....</b>	<b>10</b>
<b>LIST OF ABBREVIATIONS.....</b>	<b>11</b>
<b>LIST OF PROTEINS.....</b>	<b>13</b>
<b>CHAPTER 1: INTRODUCTION.....</b>	<b>18</b>
<b>1.1 The increasing burden of Alzheimer’s disease (AD).....</b>	<b>19</b>
<b>1.2 Monitoring memory loss in those with AD.....</b>	<b>22</b>
<b>1.3 The initial discovery of AD.....</b>	<b>27</b>
<b>1.4 Neuropathological hallmarks of AD.....</b>	<b>28</b>
1.4.1 <i>Amyloid cascade.....</i>	<i>28</i>
1.4.2 <i>Pathologic Tau.....</i>	<i>31</i>
<b>1.5 The ATN network for staging AD progression.....</b>	<b>35</b>
<b>1.6 Early-onset AD versus late-onset AD.....</b>	<b>36</b>
1.6.1 <i>Early-onset AD.....</i>	<i>36</i>
1.6.2 <i>Late-onset AD.....</i>	<i>36</i>
<b>1.7. Risk factors for AD.....</b>	<b>37</b>
1.7.1. <i>Age.....</i>	<i>37</i>
1.7.2 <i>Sex.....</i>	<i>38</i>
<b>1.8 Modifiable risk factors for AD.....</b>	<b>38</b>
1.8.1 <i>Role of modifiable risk factors in AD.....</i>	<i>38</i>
1.8.2 <i>Cardiovascular health.....</i>	<i>39</i>
1.8.3 <i>Smoking / physical activity / diet.....</i>	<i>40</i>
<b>1.9 Social determinants of health.....</b>	<b>40</b>
1.9.1 <i>Education.....</i>	<i>40</i>
1.9.2 <i>Employment.....</i>	<i>41</i>
1.9.3 <i>Environment.....</i>	<i>42</i>
1.9.4 <i>Stress.....</i>	<i>43</i>
1.9.5 <i>Discrimination and social exclusion.....</i>	<i>44</i>
1.9.6 <i>Final conclusions.....</i>	<i>44</i>
<b>1.10 Therapeutic attempts to slow the progression of AD.....</b>	<b>45</b>
<b>1.11 Cerebrospinal fluid (CSF) as a gateway to neuropathological changes in AD..</b>	<b>46</b>
<b>1.12 African Americans: the most at risk racial group for AD.....</b>	<b>51</b>
<b>1.13 The utility of mass spectrometry (MS)-based proteomics in identifying novel</b>	

<b>protein signatures in AD.....</b>	<b>52</b>
1.13.1 Strategies for MS-based quantification of proteomes.....	52
1.13.2 Fundamentals of network construction and module identification.....	53
1.13.3 Why prioritize the study of the proteome over the genome?.....	54
1.13.4 Core modules of the AD brain network proteome.....	55
1.13.5 The CSF proteome as a reflection of AD brain changes.....	56
<b>1.14 Summary.....</b>	<b>56</b>
<b>CHAPTER 2: MATERIALS AND METHODS.....</b>	<b>58</b>
2.1 CSF samples.....	59
2.2 Protein digestion of CSF.....	60
2.3 Tandem mass tag labeling of CSF peptides.....	60
2.4 High-pH fractionation.....	61
2.5 Mass spectrometry analysis and data acquisition.....	62
2.6 Database search and protein quantification.....	62
2.7 Adjustment for batch and other sources of variance.....	63
2.8 Differential expression analysis.....	66
2.9 Weighted Gene Co-expression Network Analysis.....	66
2.10 Gene ontology and cell type enrichment analysis.....	66
2.11 Selected Reaction Monitoring.....	67
<b>CHAPTER 3: RESULTS.....</b>	<b>69</b>
3.1 CSF Cohort characteristics.....	70
3.2 Discovery tandem mass spectrometry analysis of CSF from African Americans and Caucasians reveals unique and shared changes in Alzheimer's disease.....	72
3.2.1 Correlation analysis uncovers a strong relationship between mass spectrometry and immunoassay measurements of Tau.....	72
3.2.2 Differential expression analysis of African American and Caucasian CSF proteome reveals unique and shared changes in AD.....	72
3.2.3 Network analysis of the CSF proteome reveals modules related to pathways and brain cell-types.....	75
3.2.4 CSF protein modules correlate to race and clinicopathological phenotypes of AD.....	81

3.3 Selected reaction monitoring validates protein alterations across Alzheimer's disease and race.....	89
CHAPTER 4: DISCUSSION.....	98
4.1 Protein co-expression between the brain and CSF reflects the crucial role of CSF in brain function and health.....	99
4.2 CSF network analysis indicated differences in endothelial markers across race, irrespective of disease, yet there is insufficient evidence to indicate that these differences stem from variations in endothelial damage.....	101
4.3 Unveiling the interplay between neuronal alterations in AD and the role of the CSF in mirroring cognitive decline.....	103
4.4 Future directions.....	107
CHAPTER 5: REFERENCES.....	110
CHAPTER 6: APPENDIX.....	126

## LIST OF FIGURES

<b>Figure 1.1:</b> Projected number of people in the United States with Alzheimer's disease (AD) in millions from 2010 to 2050.....	20
<b>Figure 1.2:</b> Healthy brain compared to a brain affected by Alzheimer's disease.....	23
<b>Figure 1.3:</b> A comparison of the scoring patterns of the Mini-Mental State Examination (MMSE) with the Montreal Cognitive Assessment (MoCA).....	25
<b>Figure 1.4:</b> The amyloidogenic and non-amyloidogenic pathways of amyloid precursor protein (APP) processing.....	29
<b>Figure 1.5:</b> Hypothesized time course of neuropathological and clinical changes in Alzheimer's disease based on biomarker alterations.....	32
<b>Figure 1.6:</b> Cerebrospinal fluid (CSF) creation and flow alongside sample immunoassay measurements of Amyloid-beta <sub>1-42</sub> (A $\beta$ <sub>42</sub> ) and Tau from 105 controls and 98 Alzheimer's disease (AD) samples.....	47
<b>Figure 1.7:</b> Methods by which pathological Tau can be secreted or released into extracellular space.....	49
<b>Figure 2.1:</b> Batch correction, outlier removal and bootstrap regression.....	65
<b>Figure 3.1:</b> Schematic of experimental workflow and correlation between proteomic Tau and total Tau immunoassay measurements.....	73
<b>Figure 3.2:</b> Differential expression of Caucasian and African American CSF proteomes in AD...	76
<b>Figure 3.3:</b> Network analysis classifies the CSF proteome into modules associated with specific brain cell-types and gene ontologies.....	79
<b>Figure 3.4:</b> Protein overlap between modules in CSF network and modules in a human AD brain network.....	82
<b>Figure 3.5:</b> CSF protein modules correlate to race and clinicopathological phenotypes of AD....	84
<b>Figure 3.6:</b> Additional CSF network protein modules.....	87
<b>Figure 3.7:</b> Validation of shared and divergent CSF protein levels across AD and race.....	90
<b>Figure 3.8:</b> Stratification of SRM CSF protein measurements in by APOE genotype and comorbidity.....	93
<b>Figure 3.9:</b> ROC analysis to evaluate CSF protein classification of AD by race.....	96
<b>Figure 4.1:</b> Hypothesized time course differences in neuropathological and clinical changes based on biomarker alterations between Caucasians and African Americans with AD.....	104

## LIST OF TABLES

<b>Table 3.1:</b> Cohort characteristics.....	71
---	----



## LIST OF ABBREVIATIONS

**A $\beta$** : Amyloid beta peptides

**A $\beta$ <sub>42</sub>**: Amyloid beta peptide<sub>1-42</sub>

**ACh**: Acetylcholine

**ACN**: Acetonitrile

**AD**: Alzheimer's disease

**ADRC**: Alzheimer's Disease Research Center

**BBB**: Blood brain barrier

**BICOR**: Biweight midcorrelation coefficient

**CBF**: cerebral blood flow

**CDR**: Clinical Dementia Rating

**CSF**: Cerebrospinal fluid

**CV**: Coefficient of variation

**$\epsilon$** : epsilon

**EOAD**: Early-onset Alzheimer's disease

**FAIMS**: High-field asymmetric waveform ion mobility spectrometry

**FDR**: False discovery rate

**GIS**: Global internal standards

**GO**: Gene ontology

**GWAS**: Genome Wide Association Studies

**LC**: Liquid chromatography

**LC-MS/MS**: Liquid chromatography tandem mass spectrometry

**LOAD**: Late-onset Alzheimer's disease

**LFQ**: Label-free quantification

**LysC**: Lysyl endopeptidase

**MCI**: Mild cognitive impairment

**MDS:** Multidimensional scaling plots

**MoCA:** Montreal Cognitive Assessment

**MMSE:** Mini-Mental Status Examination

**MS:** Mass spectrometry

**NFT:** Neurofibrillary tangles

**NIA-AA:** National Institute on Aging and Alzheimer's Association

**PC:** Principal component

**PET:** Positron emission tomography

**PHF:** Paired helical filaments

**pTau<sub>181</sub>:** Phosphorylated Tau<sub>181</sub>

**QC:** Quality controls

**ROC:** Receiver operating characteristic

**SRM:** Selected reaction monitoring

**TMT:** Tandem Mass Tag

**tTau:** Total Tau

**WGCNA:** Weighted Gene Co-expression Network Analysis

## LIST OF PROTEINS

**ADAM10:** ADAM Metallopeptidase Domain 10

**ADAM17:** ADAM Metallopeptidase Domain 17

**ADM:** Adrenomedullin

**AICD:** Amyloid Precursor Protein Intracellular Domain

**ALB:** Albumin

**ALDOA:** Aldolase

**ANG:** Angiogenin

**ANG1:** Angiopoietin-1

**ANP:** Atrial Natriuretic Peptide

**ANXA5:** Annexin A5

**APLP1:** Amyloid Beta Precursor Like Protein 1

**APOE:** Apolipoprotein E

**APP:** Amyloid Precursor Protein

**BASP1:** Brain Abundant Membrane Attached Signal Protein 1

**BGN:** Biglycan

**BIN1:** Bridging Integrator 1

**BNP:** B-Type Natriuretic

**CACNA2D:** Calcium Voltage-Gated Channel Auxiliary Subunit Alpha 2/Delta

**CADM3:** Cell Adhesion Molecule 3

**CAMK2A:** Calcium / Calmodulin Dependent Protein Kinase II alpha

**CD33:** CD33 Molecule

**CTF83:** C-terminal Fragment 83

**CTF99:** C-terminal Fragment 99

**CTSB:** Cathepsin B

**CTSH:** Cathepsin H

**CTSZ:** Cathepsin Z

**C1QA:** Complement C1q A Chain

**C1QB:** Complement C1q B Chain

**C1QC:** Complement C1q C Chain

**C1RL:** Complement C1r Subcomponent Like

**C2:** Complement C2

**C3:** Complement C3

**ECM2:** Extracellular Matrix Protein 2

**ENO2:** Enolase 2

**F5:** Coagulation Factor V

**FGB:** Fibrinogen

**FLNA:** Filamin A

**GAPDH:** Glyceraldehyde-3-Phosphate Dehydrogenase

**GAP43:** Growth Associated Protein 43

**GDA:** Guanine Deaminase

**GOT1:** Glutamic-Oxaloacetic Transaminase 1

**HEXA:** Hexosaminidase Subunit Alpha

**HEXB:** Hexosaminidase Subunit Beta

**ICAM1:** Intracellular adhesion molecule 1

**IDUA:** Alpha-L-iduronidase

**IGFBP7:** Insulin Like Growth Factor Binding Protein 7

**IGSF8:** Immunoglobulin Superfamily Member 8

**LAMA5:** Laminin Subunit Alpha 5

**LAMC1:** Laminin Subunit Gamma 1

**LCP1:** Lymphocyte Cytosolic Protein 1

**LDHB:** Lactate Dehydrogenase B

**LINGO2:** Leucine Rich Repeat and Ig Domain Containing 2

**LTBP4:** Latent Transforming Growth Factor Beta Binding Protein 4

**L1CAM:** L1 Cell Adhesion Molecule

**MAPT:** Microtubule Associated Protein Tau

**MYL6:** Myosin Light Chain 6

**NBL1:** Neuroblastoma Suppressor Of Tumorigenicity 1

**NID2:** Nidogen 2

**NPTXR:** Neuronal Pentraxin Receptor

**NPTX1:** Neuronal Pentraxin 1

**NPTX2:** Neuronal Pentraxin 2

**NEFL:** Neurofilament Light Chain

**NEFM:** Neurofilament Medium Chain

**NEGR:** Neuronal Growth Regulator 1

**NEO1:** Neogenin 1

**NRGN:** Neurogranin

**NRN1:** Neuritin 1

**OLFM1:** Olfactomedin 1

**OPN:** Osteopontin

**PAI1:** plasminogen activator inhibitor-1

**PAM:** Peptidylglycine Alpha-Amidating Monooxygenase

**PARK7:** Parkinsonism Associated Deglycase

**PCSK1:** Proprotein Convertase Subtilisin/Kexin Type 1

**PICALM:** Phosphatidylinositol Binding Clathrin Assembly Protein

**PKM:** Pyruvate Kinase M1

**PLXNA2:** Plexin A2

**PPIA:** Peptidylprolyl Isomerase A

**PSEN1:** Presenilin 1

**PSEN2:** Presenilin 2

**PTPRN:** Protein Tyrosine Phosphatase Receptor Type N

**RTN4R1:** Reticulon 4 Receptor

**S100A11:** S100 Calcium Binding Protein A11

**SCG2:** Secretogranin II

**SDCBP:** Syndecan Binding Protein

**SHARPIN:** Shank Associated RH Domain Interactor

**SLIT1:** Slit Guidance Ligand 1

**SMOC1:** Secreted Modular Calcium-binding Protein I

**SNCB:** Synuclein Beta

**SNX1:** Sorting Nexin 1

**SORL1:** Sortilin Related Receptor 1

**SORT1:** Sortilin 1

**SPDGFRB:** Soluble Platelet-Derived Growth Factor Receptor-Beta

**SYN1:** Synapsin 1

**SYT1:** Synaptotagmin 1

**TMEM106B:** Transmembrane Protein 106B

**TPI1:** Triosephosphate Isomerase 1

**TREM2:** Triggering Receptor Expressed on Myeloid Cells 2

**TSPAN14:** Tetraspanin 14

**VCAM1:** vascular cell adhesion molecule 1

**VCAN:** Versican

**VEGFA:** Vascular Endothelial Growth Factor A

**VGEF:** Vascular Endothelial Cadherin

**VGF:** VGF Nerve Growth Factor Inducible

**VSTM2A:** V-set and Transmembrane Domain Containing 2a

**WDR81:** WD Repeat Domain 81

**YWAHB:** Tyrosine 3-Monooxygenase/Tryptophan 5-Monooxygenase Activation Protein Beta

**YWHAE:** Tyrosine 3-Monooxygenase/Tryptophan 5-Monooxygenase Activation Protein Epsilon

**YWHAG:** Tyrosine 3-Monooxygenase/Tryptophan 5-Monooxygenase Activation Protein Gamma

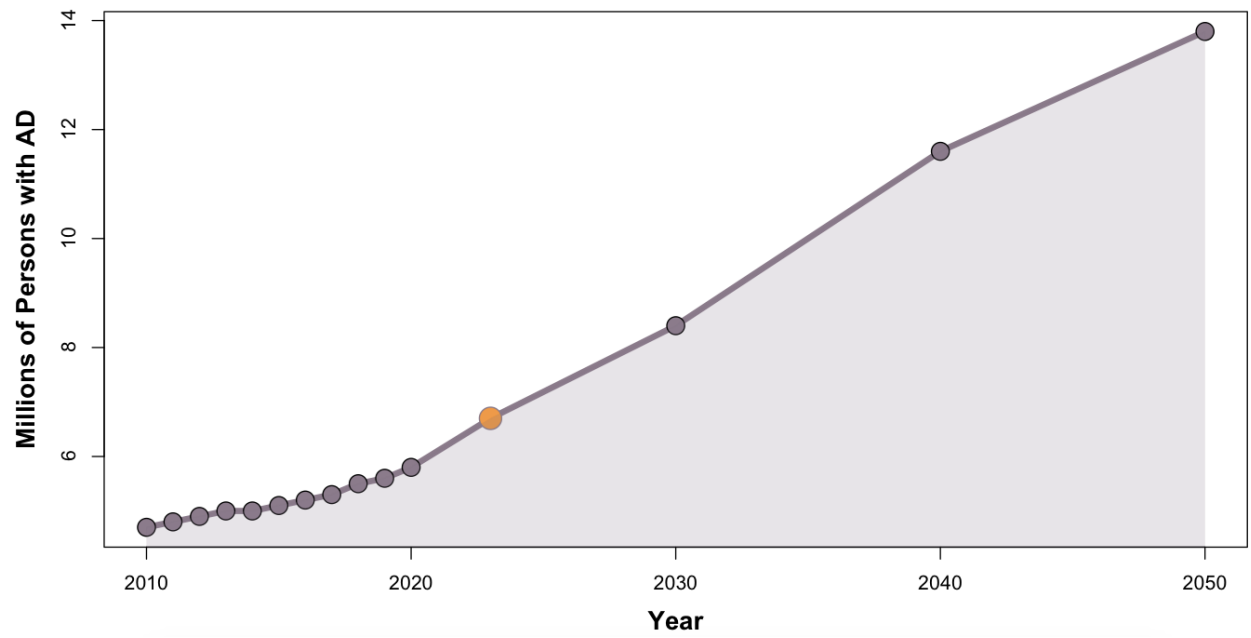
**YWHAZ:** Tyrosine 3-Monooxygenase/Tryptophan 5-Monooxygenase Activation Protein Zeta

**CHAPTER 1:**  
**INTRODUCTION**



## 1.1 The increasing burden of Alzheimer's disease (AD)

Alzheimer's disease (AD) is a progressive and irreversible disorder of the brain that affects memory, thinking, and behavior (1). It is the most common form of dementia, accounting for approximately 60 to 80 % of all dementia cases (2). AD primarily affects older adults, typically starting in individuals over the age of 65 years old (2-6). Notably, the elderly population in the United States has been undergoing rapid expansion since 2011 as the first wave of baby boomers transitioned into the age of 65 (7). The baby boom era, which spanned from 1946 to 1964, marked a distinctive phase in American history characterized by a surge in birth rates following World War II (7). Consequently, with the progression of the baby boomer population from middle to older ages, there has also been a substantial increase in the incidence of AD (7; 8). Up from approximately 4.7 million people in 2010, an estimated 6.7 million people in the United States are currently affected by this disease, and this number is only expected to double by the year 2050 (2; 7; 8) (**Figure 1.1**). Alongside this rise, there also comes the substantial burden the disease places on caregivers and society (2; 8). In 2022 alone, over 11 million Americans selflessly provided 18 billion hours of unpaid care to older adults afflicted with dementia; a collective contribution valued at nearly \$340 billion (2). Furthermore, total annual payments for healthcare and long-term care for people with AD and other dementias are expected to increase from \$345 billion in 2023 to just under \$1 trillion by 2050, exceeding the costs of treatments for cancer and cardiovascular disease (2; 9). This projection includes three-fold increases in government spending in Medicare and Medicaid, as well as out-of-pocket expenditures (2). Taking into account all of these factors, if there is no progress made in preventing or delaying the onset of AD, coupled with the substantial rise in the number of individuals affected by AD, the proportion of the population impacted by the disease will also increase. This, in turn, will escalate the overall societal burden of AD.

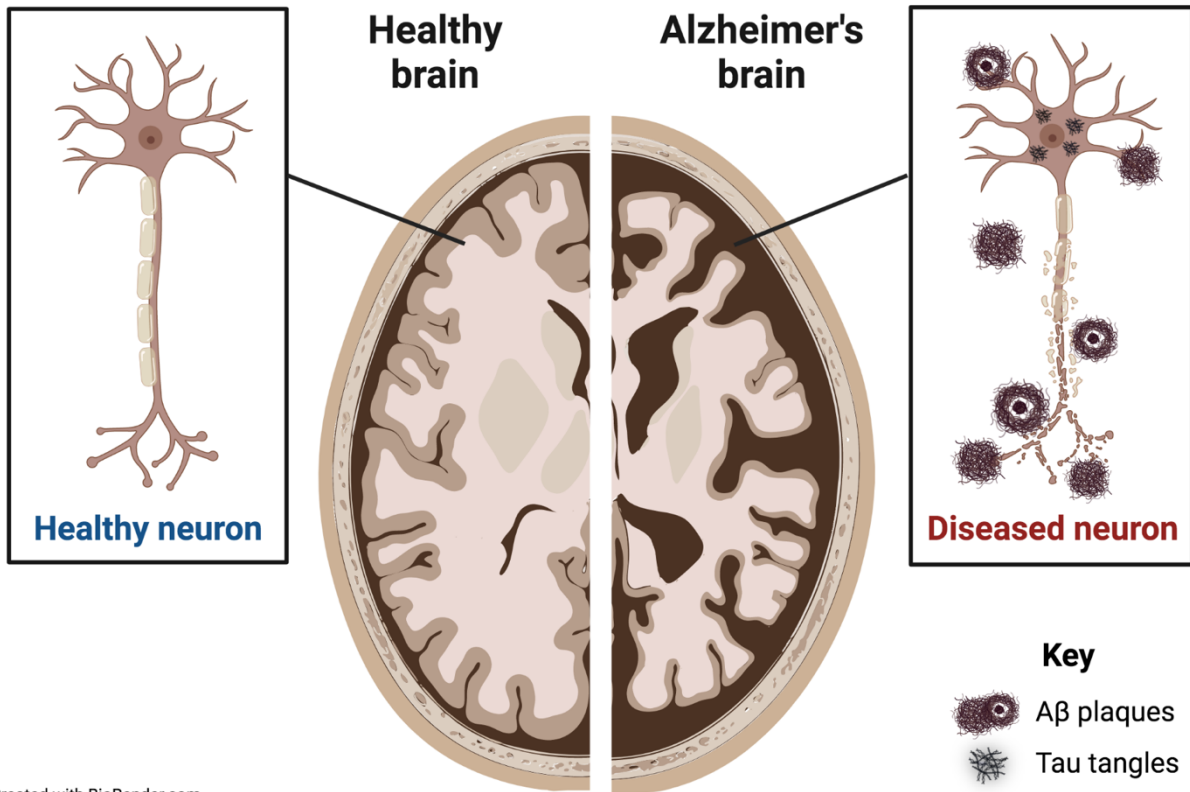


**Figure 1.1: Projected number of people in the United States with Alzheimer's disease (AD) in millions from 2010 to 2050.** The estimated number of people with AD in the United States in 2023 (orange circle) is predicted to nearly double by 2050.

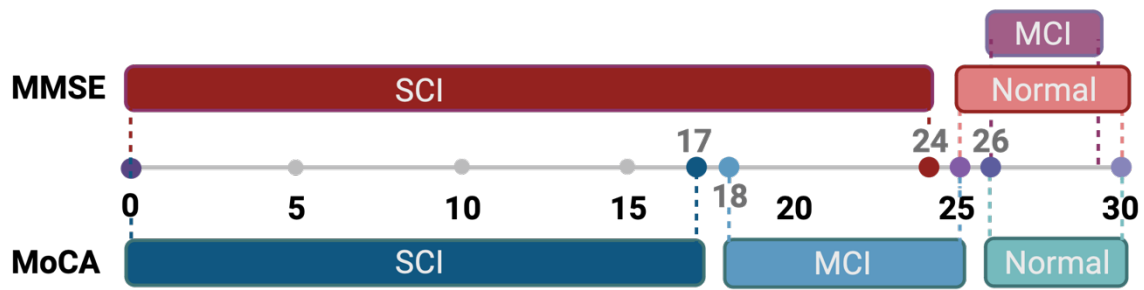
## 1.2 Monitoring memory loss in those with AD

AD can be most notably recognized by its incapacitating and progressive memory loss. This gradual decline in memory with disease progression is a consequence of spreading neuronal damage across the brain (**Figure 1.2**) (1; 2). Common early signs of memory loss in AD include forgetfulness, difficulty in finding words, misplacing items, and struggling with familiar tasks like tying a shoe (1; 2). As the disease progresses, individuals may begin to experience confusion, mood swings, disorientation, and difficulties in communication and decision-making (1; 2). Ultimately, in the later stages, individuals often require full time care, as they lose the ability to recognize love ones, communicate, and perform basic activities of daily living (1; 2). In the clinic, patients undergo cognitive exams such as the Mini-Mental Status Examination (MMSE) and the Montreal Cognitive Assessment (MoCA). These assessments serve as crucial clinical diagnostic tools for evaluating and monitoring cognitive impairment. (10-12). While the MoCA test is the preferred test for the early detection of dementia such as in cases of mild cognitive impairment (MCI), MMSE is often used for monitoring cognitive decline over time (11; 13).

MCI is an intermediate stage between typical cognitive aging and dementia (11). In the beginning, physicians heavily depended on the MMSE to gauge cognitive impairment in individuals (12). The MMSE was found to be effective in distinguishing cognitively normal individuals from those with cognitive impairment with significant specificity, where a score below 25 on the MMSE was indicative of impairment (12) (**Figure 1.3**). Its efficacy declined, however, when attempting to identify those with MCI, as individuals with MCI could score between 26 and 29, falling within the range for cognitively normal individuals (14-16) (**Figure 1.3**). This highlighted a significant limitation of the test: its difficulty in detecting early dementia-related changes (17). Consequently, the MoCA test was developed with a heightened emphasis on MCI, while maintaining the scoring ranges of the MMSE (11). Aligned with this, the generally accepted optimal threshold for discerning between individuals with typical cognitive function and those with



**Figure 1.2: Healthy brain compared to a brain affected by Alzheimer's disease.** In comparison to a healthy brain, brain changes observed in Alzheimer's disease include injured neuronal cells that are accompanied by abnormal accumulations of amyloid beta ( $A\beta$ ) plaques and tangles of hyperphosphorylated Tau.



Created with BioRender.com

**Figure 1.3: A comparison of the scoring patterns of the Mini-Mental State Examination (MMSE) with the Montreal Cognitive Assessment (MoCA).**



MCI in the MoCA test was determined to be 26 (11) (**Figure 1.3**). Though, more recent meta-analysis has suggested that a cutoff score of 23 may be better (18). Moreover, individuals with MCI may score between 18 and 25, while those with dementia typically scored below 18 with significant specificity (**Figure 1.3**). Overall, the MoCA test has demonstrated superior effectiveness compared to the MMSE in monitoring the progression from MCI to severe dementia in clinical settings involving living patients (19-22).

There are various factors to consider when utilizing the specified scores mentioned above. Firstly, studies have indicated that education can significantly impact overall MoCA score (11; 23). It was found that persons with 12 years of education or less tended to have worse performance on the MoCA (11). To mitigate this, it has become common practice to add 1 point to the final score for individuals with 12 years or less of education (11). There is debate, however, as to whether this adjustment adequately addresses education-related disparities (24). In some cases, it has been observed that this adjustment may in fact reduce the test's sensitivity (25). Besides education, age can also impact the score (23; 26; 27). This places older individuals with lower levels of education as the group most vulnerable to obtaining false positive results (24). Finally, studies have revealed that MoCA performance can also be influenced by racial background (26; 28; 29). Including minority participants in a study led to lower cutoffs for distinguishing between normal cognition and MCI (26; 28; 29). In addition, when directly comparing optimal MoCA score cutoffs across multiple races, it was found that the optimal cutoff for both African Americans and Hispanics was lower than that of Caucasians (30). This implies that lower MoCA cutoffs may be more appropriate when assessing the MoCA score of minority individuals (26; 28-30). In conclusion, considering factors such as education, age, and racial background is essential for accurately interpreting and applying MoCA scores in clinical settings.

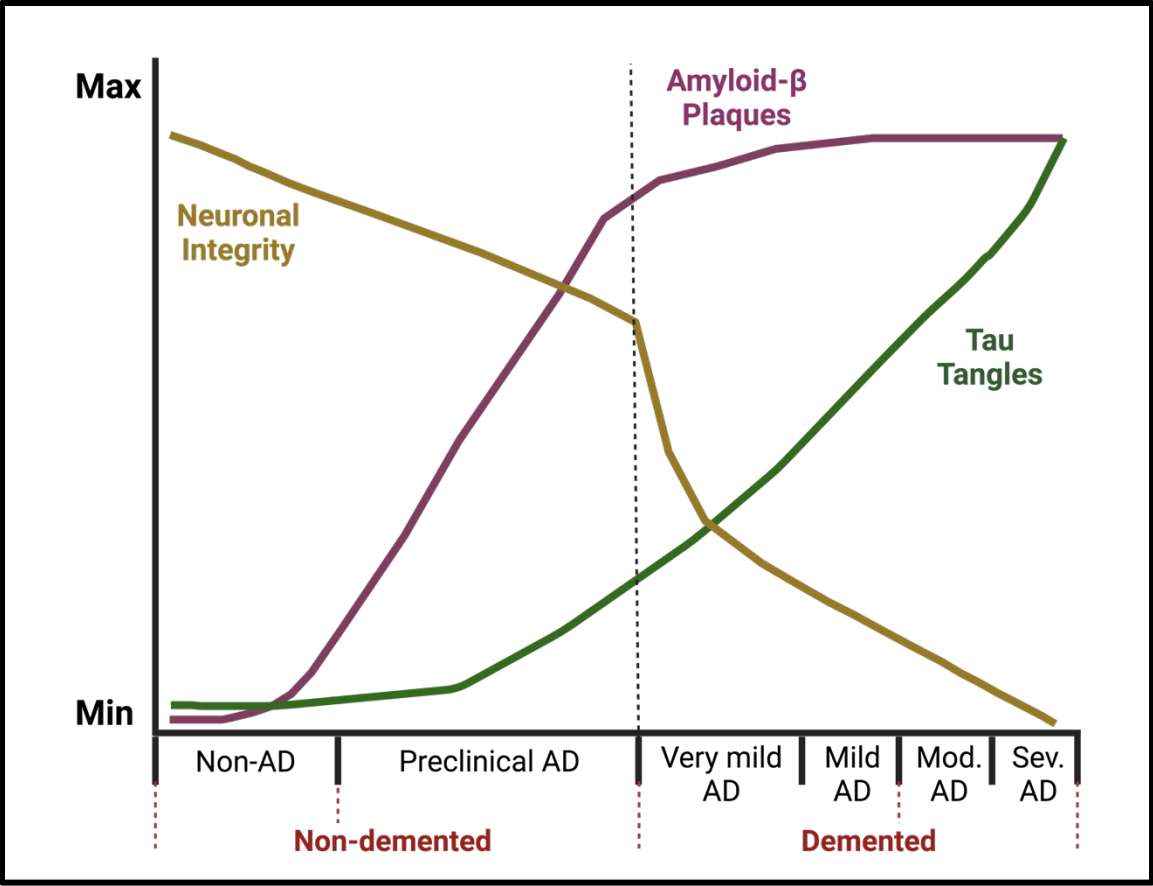
### **1.3 The initial discovery of AD**

Alois Alzheimer was a German psychiatrist and neuropathologist who discovered AD through his work with a patient named Auguste Deter. In 1901, Deter, who was in her early 50s,

was admitted to the mental asylum where Alzheimer worked for exhibiting symptoms of memory loss, confusion, and hallucinations (31). Intrigued by her condition, Alzheimer meticulously documented the continued progression of her disease up until her death on April 6, 1906. Following her death, Alzheimer was able to investigate the brain of Auguste both morphologically and histologically. During the autopsy, Alzheimer noted significant abnormalities in her brain, including unusual protein deposits (now identified as amyloid plaques) and tangled nerve fibers (now known as neurofibrillary tangles) (31; 32). These observations led him to hypothesize that Deter's symptoms stemmed from physical changes in her brain (31). Shortly thereafter, Alzheimer published his findings, presenting the case as a distinct form of dementia that differed from the typical symptoms associated with aging (31). His work laid the groundwork for understanding Alzheimer's disease as a progressive neurodegenerative disorder characterized by cognitive decline and distinct brain pathology. Today, the disease bears Alois Alzheimer's name in recognition of his pioneering research.

## **1.4 Neuropathological hallmarks of AD**

*1.4.1 Amyloid Cascade:* The amyloid cascade hypothesis is a central theory in AD research that proposes that the deposition of amyloid-beta ( $A\beta$ ) peptides in the brain occurs prior to and initiates a series of events that culminate in neurodegeneration and the distinctive symptoms of AD (**Figure 1.4**). More specifically, according to this hypothesis, the abnormal accumulation of  $A\beta$  peptides leads to the formation of amyloid plaques, which disrupt neuronal function and activate inflammatory responses (33). As a consequence, a cascade of subsequent events is initiated, including the hyperphosphorylation of Tau protein, the formation of neurofibrillary tangles, synaptic dysfunction, and ultimately neuronal death (32). Given its crucial role, the formation and inhibition of  $A\beta$  has profoundly shaped investigations into the underlying mechanisms of AD and the creation of potential therapeutic approaches, which primarily focused on  $A\beta$  pathways (32; 33). The abnormal accumulation of insoluble  $A\beta$  plaques in the extracellular space surrounding neurons has become a hallmark pathology of AD (34; 35) (**Figure 1.2**).  $A\beta$  is

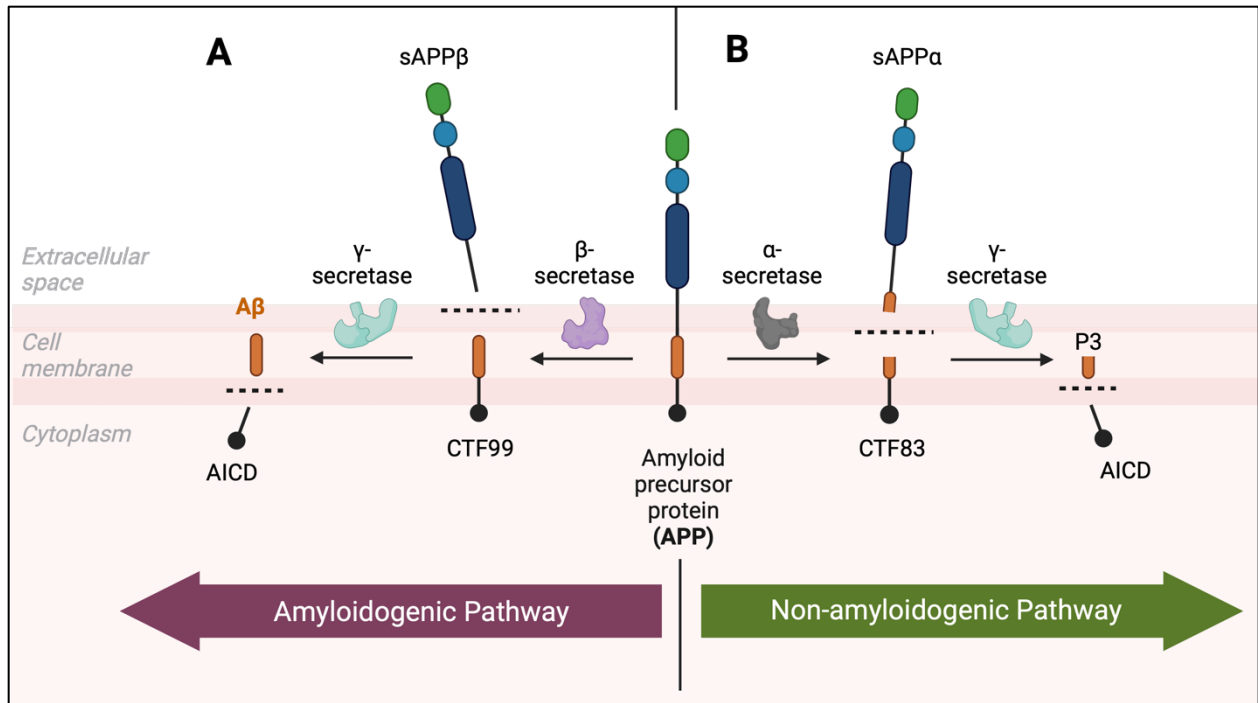


Created with BioRender.com

**Figure 1.4: Hypothesized time course of neuropathological and clinical changes in Alzheimer's disease based on biomarker alterations.** In Alzheimer's disease (AD), the conversion from a non-demented to demented state is associated with a buildup of amyloid beta ( $A\beta$ ) plaques (purple line), a more gradual accumulation of neurofibrillary Tau tangles (green line), and neuronal and synaptic loss (yellow line). Modified from Craig-Schapiro, R., Fagan, A. M., and Holtzman, D. M. (2009) Biomarkers of Alzheimer's disease. *Neurobiol Dis* 35, 128-140.

a peptide ranging from 38-43 amino acids long and is the result of sequential cleavages on amyloid precursor protein (APP) by  $\beta$ -secretase and  $\gamma$ -secretase (36) (**Figure 1.5A**). Initially, APP is cleaved by  $\beta$ -secretase producing a long soluble secreted form of APP (sAPP $\beta$ ) and a C-terminal fragment 99 (CTF99) (37) (**Figure 1.5A**). Subsequently, CTF99 is cleaved by  $\gamma$ -secretase complex to form A $\beta$  and an intracellular amyloid precursor protein intracellular domain (AICD) (38) (**Figure 1.5A**). This cleavage can produce peptides of 43, 45, 46, 48, 49, or 51 amino acids, which are subsequently processed to generate two forms of A $\beta$ , A $\beta_{40}$  or A $\beta_{42}$  (39). While A $\beta_{40}$  is the most prevalent form, A $\beta_{42}$  has been noted to be more prominently present in amyloid plaques (40). Because this pathway leads to the formation of the A $\beta$  peptides that make up the plaques found in AD, its considered amyloidogenic and is associated with the pathological changes observed in AD. The accumulation of A $\beta$  peptides in the brain is central to the amyloid cascade hypothesis, even though A $\beta$  can be extensively present in the human brain without AD symptoms (36; 41-43) (**Figure 1.4, purple line**). The production of A $\beta$  peptides is not the sole outcome of APP processing. Alternatively, APP can also undergo cleavages that diverts the protein toward a non-amyloidogenic pathway (**Figure 1.5B**). Here,  $\alpha$ -secretase cleaves APP to release soluble APP $\alpha$  (sAPP $\alpha$ ) and CTF83 (**Figure 1.5B**). Importantly, this pathway prevents the generation of A $\beta$  as the cleavage site for  $\alpha$ -secretase is within the A $\beta$  domain (37).  $\gamma$ -secretase then cleaves CTF83 to form AICD and p3. This neuroprotective pathway promotes neuronal survival, neurite outgrowth and neural stem cell proliferation, providing an avenue for mitigating AD (44-47). Under typical circumstances, these two pathways operate in equilibrium, permitting neurons to remove unnecessary A $\beta$  as required. Nevertheless, in AD, the balance shifts towards heightened A $\beta$  formation, triggering the cascading events described earlier.

*1.4.2 Pathologic Tau:* The next hallmark of AD is the formation of neurofibrillary tangles (NFT) that consist of hyperphosphorylated microtubule-associated protein Tau (MAPT). Tau is primarily located intracellularly within neurons, but it can also be found in other cell types of the



Created with BioRender.com

**Figure 1.5: The amyloidogenic and non-amyloidogenic pathways for processing the amyloid precursor protein (APP).** **(A)** The amyloidogenic pathway involves cleavages by  $\beta$ -secretase and  $\gamma$ -secretase resulting in the generation of a long-secreted form of APP (sAPP $\beta$ ), and C-terminal fragments, CTF99, amyloid precursor protein intracellular domain (AICD), and A $\beta$ . **(B)** The nonamyloidogenic pathway involves cleavages by  $\alpha$ -secretase and  $\gamma$ -secretase resulting the generation of a long-secreted form of APP, sAPP $\alpha$ , and C-terminal fragments, CTF83, AICD, and P3.

brain, such as microglia (34; 35). In the brain, normal Tau protein plays a crucial role in promoting tubulin assembly and microtubule stabilization. Microtubules are essential structures for maintaining the structural integrity of neurons and facilitating intracellular transport, acting like highways within neurons, allowing molecules and organelles to move to different parts of the cell. Tau protein binds to and stabilizes these microtubules, helping to maintain their structure and function. In addition to this, Tau is also involved in regulating synaptic function, which is essential for communication between neurons. It interacts with various proteins involved in synaptic transmission, contributing to the proper functioning of synapses. Overall, normal Tau protein in the brain is involved in maintaining the structural integrity of neurons by stabilizing microtubules and regulating synaptic function; both of which are critical for normal brain function.

The distinction between normal Tau and pathologic Tau primarily lies in several structural and functional characteristics: conformation, phosphorylation, and aggregation (1). Normal Tau protein is typically structured in a way that allows it to bind and stabilize microtubules within neurons. In contrast, pathological Tau undergoes conformational changes, leading to the formation of abnormal Tau aggregates, such as NFTs (48). In addition to conformational changes, phosphorylation, which is the addition of phosphate groups to proteins, plays a crucial role in deciphering Tau's normal function from that of pathologic Tau. Under normal conditions, Tau is moderately phosphorylated, allowing it to bind and unbind to microtubules effectively. However, in AD, Tau becomes hyperphosphorylated, leading to its detachment from microtubules and the formation of insoluble aggregates (3). Under normal conditions, Tau remains soluble and distributed throughout the neuron, and primarily associated with microtubules. Pathological tau, on the other hand, aggregates into insoluble structures, such as paired helical filaments (PHFs) and NFTs which disrupt neuronal function. These insoluble structures then obstruct transport of essential nutrients and molecules vital for the regular function and survival of neurons (1), making it a more immediate precursor to neurodegeneration (**Figure 1.4, green and yellow lines**) (49-51).



## 1.5 The ATN framework for staging AD progression

As defining features of AD, A $\beta$  deposition (A), Tau tangle formation (T), and neurodegeneration (N) make up the basis of the ATN framework (52). Essentially, this framework proposes different sets of biomarkers to represent hallmark pathological features (A $\beta$  and Tau) and cognitive aspects (neurodegeneration) of AD, utilizing them to categorize patients along the AD continuum (52). In this framework, amyloid biomarkers represent the earliest indicators of AD neuropathological changes in living persons (53-57). Given this, A $\beta$  biomarkers help determine whether an individual falls within the AD continuum (52). Examples of biomarkers indicative of A $\beta$  plaques include amyloid positron emission tomography (PET) imaging of radiolabeled ligands binding to A $\beta$  plaques in the brain and reduced levels of A $\beta_{42}$  in cerebrospinal fluid (CSF) (58-62). The quantification of both A $\beta$  and Tau are required for the diagnosis of AD. Therefore, the presence of pathologic Tau biomarkers is what ultimately determines whether an individual within the AD continuum truly has AD (52). Examples of Tau biomarkers include monitoring elevations in the phosphorylation of Tau at residues Thr181, Thr217, and among other sites (59) within the CSF and PET scans of cortical Tau using radiolabeled ligands that bind to Tau tangles (59; 63-65). Finally, biomarkers of neurodegeneration gauge the severity of neuronal injury. However, these markers do not strictly contribute to the understanding of where a person lies along the AD continuum (52). This is because these markers are not specific to neurodegeneration induced by AD, making it difficult to determine whether neuronal injury is directly attributed to disease or some other comorbid condition (52). Despite this, indicators of neurodegeneration still provide vital staging information when combined with measures of pathologic biomarkers for A $\beta$  and Tau (52). Biomarkers of neurodegeneration include total Tau levels in the CSF, cortical PET scans measuring diminished glucose metabolism, and indicators of brain atrophy detected through magnetic resonance imaging (66-73).

## 1.6 Early-onset AD versus late-onset AD

The majority of people who develop AD are 65 and older. The presentation of AD at older ages is referred to as late-onset AD (LOAD). It is believed that LOAD, like other chronic diseases, is brought on as result of multiple factors, i.e. environmental and genetics, rather than a single genetic cause. The exception to these would-be cases of AD related to uncommon genetic changes that greatly affect risk. In those cases, the person typically develops AD before the age of 65. This presentation of AD at younger ages is referred to as early-onset AD (EOAD). While the greatest risk factors for LOAD are older age, environmental exposures (i.e lifestyle, education, financial attainment), and genetics, EOAD is primarily caused by genetics alone (74-80).

*1.6.1 Early-onset AD:* EOAD accounts for only ~2 percent of all cases. Individuals who experience familial AD experience rapid decline and die within several years of symptom onset (81). EOAD has been most notably tied to gene mutations that affect the processing or production of A $\beta$ , whose abnormal accumulation contributes to disease. For this reason, despite being on different chromosomes, mutations in *APP*, *PSEN1*, or *PSEN2* are known to cause AD (5; 82-85). Remarkably, both *PSEN1* and *PSEN2* make up the catalytic components of  $\gamma$ -secretase which assists in the cleavage of APP into A $\beta$ . In addition to these three genetic variants that are known to cause AD, individuals with Down syndrome are often at high risk for developing EOAD (2). This is because they possess an extra chromosome 21, which carries the *APP* gene. Estimates suggests that nearly 50% or more of individuals living with Down syndrome will develop symptoms of AD by their 50s or 60s (86; 87).

*1.6.2. Late-onset AD:* Contrary to EOAD, LOAD is the most common form of AD, mainly occurring in individuals over 65 (3-6). Also known as sporadic AD, LOAD accounts for the remaining 98% of cases (2; 81). Multiple gene loci have been implicated in LOAD. As a result, LOAD is often considered a polygenic disorder (2). One of the most impactful genetic susceptibilities to LOAD involves the Apolipoprotein E gene (5; 88; 89). Apolipoprotein E (APOE) epsilon ( $\epsilon$ ) protein has three different variants that differ at residues 112 and 158: APOE  $\epsilon$ 2

contains a cysteine at both residues 112 and 158 while APOE  $\epsilon$ 3 contains a cysteine at residue 112 but an arginine at residue 158. Lastly, APOE  $\epsilon$ 4 has two arginine residues that occupy position 112 and 158 in the full-length protein. Those who inherit a copy of the APOE  $\epsilon$ 4 allele have three times the risk of developing AD while those who inherit two copies have an eight- to 12-fold risk (90-92). Contrastingly, the inheritance of the APOE  $\epsilon$ 3 allele has no risk of developing AD while the APOE  $\epsilon$ 2 offers some protection. Although genetic studies support that APOE is the largest modifier of an individual's risk of developing LOAD, half of the individuals with LOAD do not possess an APOE  $\epsilon$ 4 allele indicating that other loci influence LOAD development. Innovations in genomic sequencing technology have allowed for the identification of other genetic polymorphisms linked to AD through genome wide association studies (GWAS). Such genes include genes that encode for proteins involved in the dysregulation of microglia (CD33, SHARPIN, TREM2),  $\alpha$ -secretase (ADAM10, ADAM17, TSPAN14), endocytosis (BIN1, PICALM, WDR81), the lysosome (CTSB, CTSH, IDUA, TMEM106B), and sorting receptors (SORL1, SORT1, SNX1) (93; 94). More genes are expected to be revealed as genomic studies continue to expand and grow in sample size and ethnic background.

## **1.7 Risk factors for AD**

**1.7.1 Age:** The most significant contributor to AD risk is age (2; 74). This is evident by the steep increases in the percentage of people with AD with advancing age. For example, five percent of individuals between 65 and 74 years old have AD which then increases to 13.1 % for those aged from 75 to 84 (95). By the time one reaches 85, this number doubles, affecting 33.3% of this population range (95). It is worth highlighting again that these prevalence statistics are projected to steadily increase as the baby-boom generation continues to move throughout these age ranges (8; 95). Although age plays a major role in risk, AD is not a natural outcome of the aging process; in other words, simply reaching an older age is not adequate enough to trigger the onset of AD (96).

**1.7.2 Sex:** Approximately two-thirds of AD patients are women (97). While men have only a 1 in 10 chance of developing AD, women's likelihood is twice as high, 1 in 5 (95). Although it has been speculated that women's heightened risk of developing AD could be due to their longer lifespan, studies indicate that differences in several biological factors such as sex hormones, immune response, and metabolic regulation can modulate risk (98). One significant factor affecting risk is the sex hormone, estrogen. Estrogen receptors are distributed throughout the brain, regulating various physiological processes, some of which exert protection against AD pathology. Studies show that estrogen achieves this protective effect by stimulating the generation of vesicles containing APP from the Golgi network (99; 100). This mechanism then facilitates the transport of APP to the cell surface where, it either undergoes cleavage by  $\alpha$ -secretase, yielding the soluble and neuroprotective molecule, sAPP $\alpha$ , or is re-internalized through an endosomal/lysosomal degradation pathway (101-103). Both of which precludes the production of insoluble A $\beta$  peptide (99-104). Additionally, estrogen has been shown to decrease the presence of hyperphosphorylated Tau and increase the presence of dephosphorylated of Tau (105). In the perimenopausal phase, however, which occurs 1-4 years prior to menopause, estrogen levels fluctuate significantly. This variability contributes to dysfunction in metabolic, inflammatory, and sensory-processing pathways associated with estrogen (106; 107). Consequently, the eventual loss of estrogen during menopause contributes to females' susceptibility to AD (108; 109). In contrast, men do not undergo an equivalent of perimenopause. Instead, they experience a gradual decline in testosterone (110). This gradual transition elucidates the age-related dysfunction in male hormonal pathways compared to those in females (110).

## **1.8 Modifiable risk factors for AD**

**1.8.1 Role of modifiable risk factors in AD:** Although age and sex cannot be changed, some risk factors can be modified to reduce the risk of cognitive decline and dementia without relying on a cure or medicine (111). In fact, studies suggest that addressing modifiable risk factors may prevent or delay up to 40% of all dementia cases (112). Notably, nearly a third of cases of

AD and other dementias in the United States are associated with at least one of eight modifiable risk factors: physical activity, smoking, depression, low education, diabetes, midlife obesity, midlife hypertension, and hearing loss (113). Of these, the greatest factors to AD risk have been shown to be midlife obesity, physical inactivity, and low educational attainment (113).

Timing also holds significant importance in relation to modifiable risk factors in that the age in which these risk factors develop affects the impact on AD risk. For example, developing obesity, hypertension, and high cholesterol during midlife can elevate one's risk of dementia in later stages of life (114-120). For example, those between 40 and 79 years old lacking a number of modifiable risk factors (low education, hypertension, hearing loss, traumatic brain injury, alcohol or substance abuse, diabetes, smoking and depression) have been shown to exhibit cognitive performance akin to individuals 10-20 years younger with multiple modifiable risk factors (121). Conversely, the onset of obesity and hypertension in late life, after the age of 80, is associated with a reduced risk in dementia (122; 123). Moreover, addressing modifiable risk factors during midlife was connected to decreased dementia risk, even among individuals with a heightened genetic predisposition to dementia (124). In essence, while genetic inheritance is unalterable, exerting an influence on cognitive function becomes feasible by avoiding modifiable risk factors.

*1.8.2 Cardiovascular health:* The interdependence between brain health and cardiovascular health has been recognized for a considerable time. This connection is likely rooted in the fact that, despite accounting for just 2% of the body's weight, the brain utilizes approximately 20% of the body's oxygen and energy resources. In this context, a healthy heart is crucial for facilitating adequate blood supply to the brain, while healthy blood vessels ensure the delivery of oxygen and nutrient-rich blood to this vital organ. As a result of this intricate relationship between brain and cardiovascular health, many factors that increase the risk of cardiovascular disease are also associated with a higher risk of dementia (125). Notably, these factors encompass conditions such as hypertension and diabetes (114; 116; 118; 119).

*1.8.3 Smoking / physical activity / diet:* Due to the close relationship between cardiovascular health and brain function, behaviors that impact the heart's well-being can also influence the brain, thereby affecting the risk of developing dementia. Not surprisingly, smoking has been associated with an elevated risk of dementia (126), whereas engaging in physical activity has been shown to decrease risk (127-136). Now despite extensive exploration into various forms of physical activity, determining the specific types, frequencies, and durations that yield the most significant reduction in risk remains an ongoing challenge. In addition to physical activity, emerging evidence suggest that adhering to a heart-healthy diet could decrease one's risk of dementia (137-142). A heart-healthy diet places emphasis on fruits, vegetables, whole grains, fish, poultry, nuts, legumes, and beneficial fats such as olive oil while simultaneously limiting the intake of saturated fats, red meat, and sugar (2).

## **1.9 Social determinants of health**

Historically, the healthcare sector bore the primary responsibility for addressing health and disease concerns, as it was widely recognized for its role in delivering care to those most in need (143). However, it's increasingly evident that medical care alone is not sufficient to improve health outcome or mitigate health disparities (144). In fact, research suggests that differences in life expectancy and disease prevalence among various demographics are largely shaped by the conditions in which individuals are raised, live, work, and age (143). These nonmedical factors, encompassing socioeconomic status, educational attainment, job opportunities, social support networks, healthcare accessibility, and the quality of the physical environment, profoundly influence health outcomes and overall well-being, and are collectively referred to, today, as social determinants of health (143). Some of these factors that most notably affect disease risk include education, employment, income, environment, discrimination and exposure to stress.

*1.9.1. Education:* Education can improve health by increasing health knowledge and healthy behaviors (144). In support of this, higher educational attainment has been linked to engaging in health-promoting behaviors and adopting health-related recommendations earlier

(145; 146). This could partially be attributed to literacy (147; 148). It is believed that literacy enables individuals with higher education levels to make more informed health-related decisions for themselves and their families (147; 148). Education also holds significance in health by influencing employment opportunities (144). Higher levels of education are associated with reduced unemployment rates, a factor strongly correlated with poorer health and increased mortality (149). Similarly, individuals with higher educational attainment are more inclined to hold positions offering healthier physical working environments, superior health-related benefits, and higher compensation (150; 151). Lastly, education may also affect health by influencing social and psychological factors where higher education levels have been correlated with heightened perceived personal control, a factor frequently associated with improved health outcomes and health-related behaviors (145; 147). In summary, higher levels of education are associated with improved health outcomes because education equips individuals with the knowledge and ability to make healthier choices, to obtain secure employment conducive to better access to healthcare, and to exercise greater personal control over their health.

*1.9.2. Employment:* The physical aspects of work can have clear impacts on health (144). For instance, occupations involving repetitive movements and/or high physical demands increase the likelihood of workers experiencing muscular or skeletal injuries and disorders (152). Similarly, individuals with sedentary jobs who are physically inactive face elevated risks of obesity and chronic diseases such as diabetes and heart disease (153). Besides physical factors, the psychosocial aspects of work also have an impact on health (144). Psychosocial factors refer to the circumstances wherein a person's social environment, cultural norms, interpersonal relationships, and overall well-being shapes their mindset and behavior. For instance, employees in roles marked by high demands coupled with low control or perceived imbalance of efforts and rewards face an increased risk of experiencing poor health (154; 155). Those who are socially disadvantaged frequently contend with lower wages or income and are typically the ones most likely to confront these health-harming physical and psychosocial conditions in their workplaces

(156). In conclusion, both the physical and psychosocial aspects of work play crucial roles in determining individuals' health outcomes, with socially disadvantaged groups often bearing a disproportionate burden of these adverse conditions, further exacerbating health disparities.

Work can also affect health through the opportunities and resources it provides (144). In general, for most Americans, earnings from employment constitute their primary economic resource. Consequently, health can be influenced by employment-related benefits such as medical insurance, paid leave, flexible scheduling, workplace wellness initiatives, resources for child and elder care, and retirement benefits (144). Positions with higher salaries are likelier to provide benefits, increased financial security, and the means to afford healthier living environments (144). On the flip side, those categorized as the working poor generally earn inadequate income to meet basic needs and are less likely to have access to health-related benefits (157; 158). In summary, the opportunities and resources available through employment significantly impact health outcomes. While higher salaries often come with benefits and financial security conducive to healthier living, those who are poor often face challenges accessing basic necessities and health-related benefits. This underscores how the socioeconomic impacts of employment can contribute to disparities in health.

*1.9.3 Environment:* There are many characteristics of one's environment and neighborhood that can influence health (144). Regarding physical characteristics, the quality of air and water, along with the accessibility of nutritious foods and safe exercise spaces, can collectively influence an individual's health (159-165). For example, exposure to pollutants, unsafe living conditions, and limited access to green spaces can contribute to respiratory problems, injuries, and chronic diseases such as cardiovascular diseases. In addition to the physical characteristics, the availability and quality of the services a neighborhood offers could also influence health. Services such as schools, transportation, medical care and employment resources can influence health by shaping individuals' opportunities to earn a living (166-168). Interestingly, neighborhood features can be linked to health even when considering individuals



within the same neighborhood (169). Remarkably, some researchers have found poorer health among disadvantaged individuals living in relatively advantaged neighborhoods (170-172). This could be largely due to the adverse psychological effects of feeling worse off than one's neighbors, the perception of having weaker social ties to other residents in the neighborhood, or even having increased exposure to discrimination (173). In conclusion, the environment, or neighborhood, in which one lives plays a significant role in shaping an individual's health outcomes. Beyond the physical aspects such as air and water quality and access to nutritious foods and safe exercise spaces, the availability and quality of neighborhood services also exert considerable influence. Surprisingly, even within the same neighborhood, disparities in health outcomes can persist, highlighting the complex interplay of social and psychological factors. As we continue to explore these dynamics, it becomes increasingly clear that addressing health disparities requires a multifaceted approach that considers not only physical environments but also social and economic factors.

*1.9.4 Stress:* Coping with daily challenges can be particularly taxing, especially when an individual's financial and social resources are restricted (144). Recent evidence suggests that, in fact, chronic stress connects many social determinants of health and likely plays a causal role in their effects on health (174; 175). Stressful experiences, such as those associated with social disadvantage, like economic hardship and racial discrimination, triggers the release of cortisol, cytokines, and other substances that can damage immune defenses, vital organs, and physiologic systems (174; 176-179). Subsequently, this harm contributes to the accelerated onset or advancement of chronic conditions, such as cardiovascular disease, and the physical toll from chronic stress may hasten the aging process (175; 180-182). In fact, evidence suggest that the accumulated strain from repeatedly attempting to cope with daily challenges, especially with limited resources, may actually cause more physiological damage than a single significantly stressful event would (180). In conclusion, the intricate relationship between chronic stress and health emphasizes the urgent need for comprehensive interventions that address the systemic

inequities contributing to daily challenges. This highlights the increased significance of allocating resources and establishing support systems to address health disparities.

*1.9.5 Discrimination and social exclusion:* In the United States and many other societies, race or ethnic group is another important social factor that influences health, primarily because of racism (144). It's important to note that the associations between discrimination and health are not uniquely observed in the United States and has been also observed in other countries (178). Racism encompasses not only explicit, intentional acts and beliefs of discrimination, but also entrenched societal systems that, even without explicit discriminatory intent, systematically limit the opportunities and resources available to certain individuals based on their race or ethnic background (144). Racial segregation in residential areas is a critical mechanism by which racism generates and sustains social disadvantage (168; 183). African American and Hispanic individuals are more prone to living in underprivileged neighborhoods characterized by poorly equipped schools, leading to lower educational achievement and quality, which can result in health consequences through the pathways outlined earlier (184). Racism can also have a more direct impact on health by triggering chronic stress. Persistent stress resulting from encounters with racial or ethnic bias, including subtle instances lacking overt prejudicial intent, can potentially contribute to health inequalities based on race or ethnicity, regardless of one's neighborhood, income, or educational attainment (178; 185). In fact, research suggests that African Americans and Hispanic Americans with more education or income are exposed to more discrimination than those who are disadvantaged (144). Acknowledging the widespread impact of racial or ethnic bias on health outcomes underscores the imperative of addressing systemic inequities to achieve genuine health equity.

*1.9.6 Final conclusions:* Ultimately, insufficient and unequal living conditions arise from flawed social policies, unfair economic structures, and ineffective governance (143). As a result, tackling the social determinants of health necessitates a holistic approach involving government at various levels, civil society, local communities, businesses, international organizations, and

global initiatives (143). Consequently, policies and programs designed to enhance health outcomes must encompass all sectors of society, rather than solely concentrating on healthcare (143). Collaboration among these sectors is crucial for implementing policies and programs that address the root causes of health disparities, especially across racial and ethnic background.

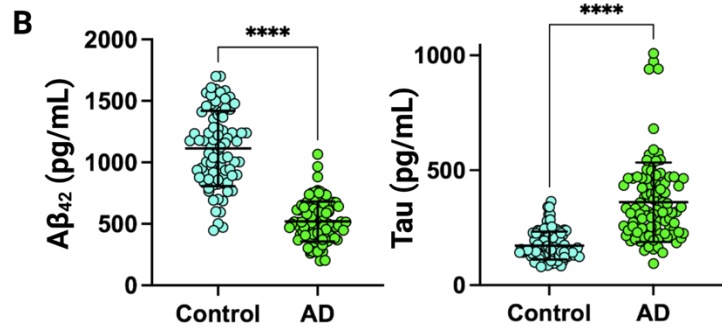
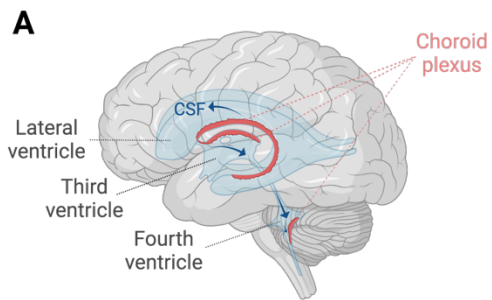
### **1.10 Therapeutic attempts to slow the progression of AD**

Despite decades of research, we still have no disease modifying treatment and no cure. Although the clinical symptoms of AD are frequently diagnosed in older age, the degenerative process of AD can begin many years prior to disease onset where individuals can remain cognitively normal for 10-20 years despite accumulating pathology (**Figure 1.4**) (186-188). Given this, AD has remained an elusive disease to treat and cure. Current treatments available mainly alleviate the cognitive deficits associated with AD. Cholinesterase inhibitors, such as galantamine, rivastigmine, donepezil, and memantine, have remained routine treatment options for the symptomatic relief of mild to moderate AD. Drugs such as these were first implemented to combat the theory that the loss of acetylcholine (ACh) neurons is to blame for the cognitive deficits observed in AD (189). Similarly, declines in nicotinic ACh receptors and M2 muscarinic ACh receptors have been shown to be responsible for AD progression (190; 191). Overall, these treatments have remained ineffective in removing the root of AD pathogenesis, merely targeting symptoms so as to only temporarily improve a patient's cognitive outcome. Consequently, it has become a critical goal of AD research to develop drugs that target the underlying mechanisms and processes involved in the progression of AD. Such therapies would aim to modify the course of the disease by reducing the build-up of A $\beta$  plaques and Tau tangles, which are hallmarks of AD pathology. For this reason, immunotherapeutic strategies such as A $\beta$ -directed immunotherapy dominated the AD research for its potential to directly target the plaques associated with disease. Passive immunotherapies, such as bapineuzumab and ALZ 801, relied on the direct injection of monoclonal antibodies into the patient's body, utilizing the immune system to increase clearance of pathologic A $\beta$  fragments (192). Remarkably, recent amyloid immunotherapy treatments

lacanemab and donanemab were found to not only reduce amyloid burden in the brain but also moderately slow cognitive decline (193; 194). Despite this, however, they were unable to reverse the neuronal loss and cognitive impairments observed in advanced stages of AD (193-196). This failure has been attributed to the initial treatment being administered at too advanced stage of AD in which neuronal damage is severe (195; 197; 198). Thus, it has become a prioritization of AD research to shift towards the early detection and or prevention of AD (52).

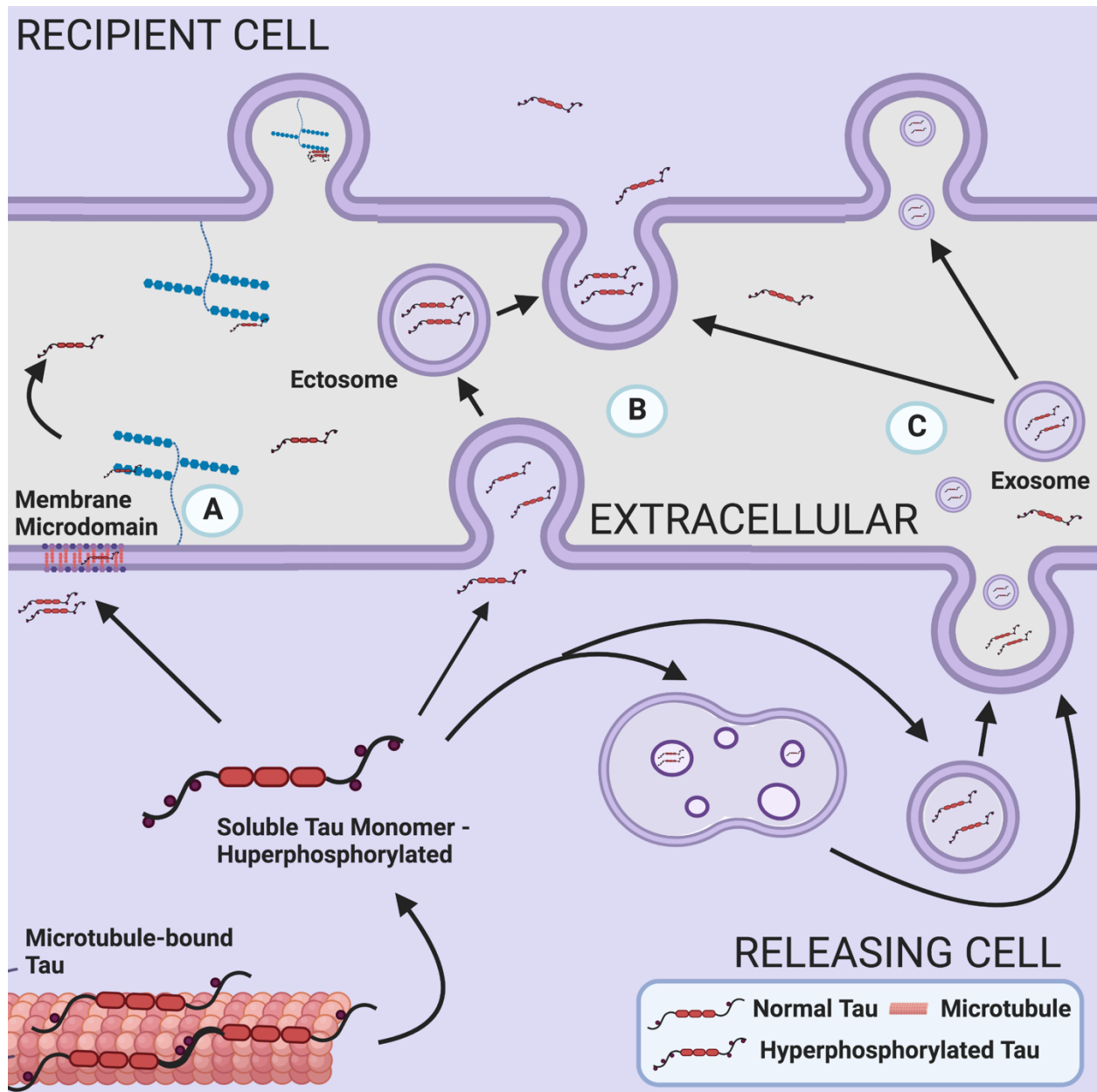
### **1.11 Cerebrospinal fluid (CSF) as a gateway to neuropathological changes in AD**

CSF has become a promising source of biomarkers for the early detection and monitoring of AD in living patients. CSF is made by highly vascularized tissue within the ventricles of the brain called choroid plexus (199). Once created, CSF flows from the lateral ventricles to the third and fourth ventricles, and then into the subarachnoid space and spinal cord (**Figure 1.6A**). This direct contact with the brain gives CSF, removed via lumbar puncture from the spinal cord, the ability to reflect neuropathological changes in the brain of living patients (200). More specifically, decreases in A $\beta$  and elevations in Tau in the CSF have been shown to distinguish healthy controls from AD (201) (**Figure 1.6B**). Decreases in A $\beta$  in the CSF is thought to be the result of increases in accumulations of A $\beta$  into plaques in the brain which have been largely found to be the result of the impaired clearance of A $\beta$  out of neurons during disease (202). Interestingly, only a fraction of Tau found in the CSF is due to the passive release of Tau from dying cells (203). Markedly, increasing levels of Tau in the CSF are predominantly the result of the enhanced secretion or release of Tau from the intracellular regions of neurons into the extracellular space. In fact, studies have shown that Tau hyperphosphorylation may be critical for its secretion (**Figure 1.7**). For example, studies have shown that Tau can be secreted at the synaptic terminal during normal synaptic activity (204; 205). Tau hyperphosphorylation, however, can enhance its secretion at the synaptic terminal as hyperphosphorylated Tau has been shown to be preferentially secreted during both ectosome shedding and exosome fusion (**Figure 1.7B & C**) (204; 206). Moreover, unlike normal physiological Tau, hyperphosphorylated Tau can also be secreted directly across



Part A of this figure was created with BioRender.com

**Figure 1.6. Cerebrospinal fluid (CSF) creation and flow alongside sample immunoassay measurements of Amyloid beta<sub>1-42</sub> (A $\beta$ <sub>42</sub>) and Tau from 105 controls and 98 AD cases. (A)** CSF is created by and secreted from highly vascularized tissue called the choroid plexus located within each ventricle of the brain. The CSF flows from the lateral ventricles to the the third and fourth ventricles and then into the subarachnoid space and spinal cord. **(B)** A $\beta$ <sub>42</sub> and total Tau levels as measured by Roche Elecsys Platform between 105 control and 98 AD cases. T-test determined significance and A $\beta$ <sub>42</sub> values that reached saturation (1700 pg/mL) were excluded.



Created with BioRender.com

**Figure 1.7. Methods by which pathological Tau can be secreted or released into extracellular space.** (A) Tau can be actively secreted through the plasma membrane. (B) Tau can be released by ectosome shedding from the plasma membrane. (C) Tau can be packed into exosomes by inward budding and become secreted by of multivesicular bodies along the plasma membrane. Modified from Brunello, C. A, Merezko, M., Uronen, R., and Huttunen, H. J. (2019) Mechanisms of secretion and spreading of pathological tau protein. *Cellular and Molecular Life Sciences*. <https://doi.org/10.1007/s00018-019-03349-1>



the plasma membrane (**Figure 1.7A**) (207; 208). While the exact mechanism by which Tau is secreted into the CSF is unclear, it remains evident that the CSF of AD patients displays changes in Tau composition and that these changes, particularly that of phosphorylated Tau species, significantly correlate with neocortical NFT pathology in the brain (209). Together, these changes observed in CSF biomarkers, A $\beta$  and Tau, give physicians the ability to determine individuals at risk of developing AD and researchers the ability to use CSF as a tool for assessing biological processes reflective of early disease stages (210).

### **1.12 African Americans: the most at-risk racial group for AD**

African Americans are almost twice as likely to have AD compared to Caucasians (211-213). Current evidence suggests that this difference in risk could be explained by a multitude of factors including genetic ancestry and disparities in health, socioeconomic and environmental conditions (214-217). For example, GWAS show that the *ABCA7* gene has stronger associations with AD risk in individuals with African ancestry than in individuals with European ancestry (216; 217). *ABCA7* also has a stronger effect size in African Americans than even the strongest genetic risk factor gene for AD, the *APOE*  $\epsilon$ 4 allele (216). Yet, despite the *APOE*  $\epsilon$ 4 allele being more prevalent amongst African Americans, *APOE*  $\epsilon$ 4 confers a lower risk for AD compared to Caucasians (76). Beyond genetic ancestry, chronic health conditions associated with higher risk for dementia, such as cardiovascular disease and diabetes, also disproportionately affect African Americans (214; 215). Furthermore, societal and environmental disparities that disproportionately affect African Americans, including lower levels and quality of education, higher rates of poverty, and greater exposure to adversity and discrimination, increase risk for both chronic diseases and dementia (214; 215). This highlights how racial differences in AD risk cannot be explained by genetics alone (214). Currently there is a gap in knowledge of the racial differences in underlying pathophysiology related to AD. Therefore, a better understanding of these mechanisms can help move towards a more precise definition of AD across diverse racial, ethnic, and genetic

backgrounds. An unbiased analysis into the CSF proteome of African Americans could provide insight into additional biomarkers reflecting underlying brain pathology that differ by race in AD.

### **1.13 The utility of mass spectrometry (MS)-based proteomics in identifying novel protein signatures in AD**

*1.13.1 Strategies for MS-based quantification of proteomes:* Proteomic analyses of AD brain have predominantly utilized "bottom-up" mass spectrometry (MS) for protein identification and quantification. This workflow generally involved enzymatic digestion of proteins with trypsin, followed by protein separation via liquid chromatography (LC), and subsequent measurement of protein peptides using tandem mass spectrometry (MS/MS) (218). The first stage of measurement (MS1) involves the selection of several precursor peptides for fragmentation. The fragmented peptides are then identified through spectral matching and quantified using well-established statistical and informatic methods during the second stage of tandem MS (219-224). In summary, the "bottom up" approach to MS has become a cornerstone in the comprehensive analysis of proteomic profiles in AD research. Since then, significant advancements have been made to enhance protein identification and quantification, resulting in more detailed proteomic profiles.

Over the years technological strategies have further improved this workflow by enhancing the quantification and depth of proteomic datasets. Initially, label-free quantification (LFQ) was the preferred technique. Using this technique, each sample is individually prepared and analyzed using LC-MS/MS. Since each sample is analyzed individually, a limitation of this technique is that the peptides selected and analyzed can vary significantly between samples. This is due to the inherent nature of MS1 where peptide selection is biased toward the most intense signals (225). When trying to quantify proteins that are lost in a disease, this means that a protein quantified in a healthy state may be completely absent in the disease state and therefore not quantified. This results in a well-documented "missing value" problem, ultimately reducing the number of proteins retained in an LFQ dataset (225-228). Multiplex isobaric peptide labeling with tandem mass tags (TMTs) helps address the issue of missing values by allowing the simultaneous analysis of

multiple samples within a single LC-MS/MS run, currently accommodating up to 16 samples per run (229; 230). When combined with off-line fractionation, this strategy can quantify thousands of additional proteins compared to LFQ, which has enabled remarkably deep proteomic analysis of AD brain tissue (227; 228; 231; 232). A study that came out of the Seyfried Lab, Johnson et al., demonstrated this advantage in one of the first TMT-MS network proteome studies of the AD brain. This study quantified 6,533 proteins across 47 brain tissues compared to just 2,736 proteins quantified by LFQ-MS using the same samples (227). Despite these advancements in quantification, TMT-MS may still produce missing values across multiple batches which occurs when analyzing large numbers of samples (233). Targeted approaches such as selected reaction monitoring (SRM) can serve as a mitigate for the limitation of “missing values” by utilizing its ability to identify nearly all detectable peptides within a selected mass range. This allows for comprehensive and accurate quantification of the identified proteins in the sample with minimal to no missing values. This method is often used in research settings for more robust quantification of pre-specified individual peptides (234). Utilizing a targeted approach like this can be useful in validating discovery-driven data that results from tandem MS, as it requires specifying a target beforehand. In conclusion, the evolution of technological strategies, from LFQ to multiplex isobaric peptide labeling and targeted approaches like SRM, has significantly enhanced proteomic workflows, enabling comprehensive and accurate quantification of proteins.

*1.13.2 Fundamentals of network construction and module identification:* Unbiased proteomics of human brain coupled with network analysis has emerged as a valuable approach for organizing complex proteomic data into groups or “modules” of co-expressed proteins that reflect various biological functions (227; 235-237). Co-expression network analysis operates on the premise that proteins react to biological stimuli as a “system,” altering expression collectively within groups or “modules” of a network. Effectively organizing proteomic datasets into the described co-expression protein modules requires a thoroughly validated statistical algorithm. One such extensively validated algorithm, commonly employed in transcriptomic studies, is

Weighted Gene Co-expression Network Analysis (WGCNA) (235; 238-241). This algorithm applies graph theory principles to detect modules of proteins exhibiting highly correlated abundance levels across samples. Through evaluating the connectivity of each protein within a module, researchers can identify module-specific hubs or proteins that play central roles in module function. Typically, the most centrally connected proteins in a module serve as key drivers (238; 240; 242). Module-level abundance profiles can then be correlated with various phenotypic traits of the disease, such as amyloid burden, tangle deposition, and cognitive decline (243). These module-trait correlations reveal protein groups with strong positive or inverse relationships to the disease. In addition to module-trait correlations, module enrichment profiles can also provide important insights into proteomic composition. This analysis seeks to identify the over-representation of module proteins linked to specific cell types, biological functions, or genetic risk factors. It accomplishes this by cross-referencing the proteins within a module with well-validated databases. For instance, cell type enrichment is usually conducted by comparing module proteins with marker lists from established reference proteomes or transcriptomes of purified murine brain cells (218; 227; 228). In addition to cell enrichment lists, numerous resources are available for pathway and ontology analysis. Go Elite is a versatile analytical tool that enables users to incorporate both reference and custom databases to investigate ontological over-representation at biological, molecular, and organellar levels (244). Altogether, network analysis offers the ability to resolve the complex nature of disease by utilizing mathematical and computational tenets of system biology which results in the formation of communities (modules) of proteins, which can be representative of phenotypes that arise out of the molecular pathophysiology of disease.

*1.13.3 Why prioritize the study of the proteome over the genome:* Proteins are the ideal markers for understanding diseases such as AD because they are most proximal to the phenotypic changes seen in AD. Protein-level analysis offers the advantage of revealing disease-related changes that are not easily detectable in transcriptomic networks. Notably, only 30-40% of the modules in the AD brain network proteome overlap with those in the network transcriptome.

(235; 245). Furthermore, despite the fact that differential protein expression within these overlapping modules has been found to exhibit a reasonable degree of concordance, with a correlation coefficient of approximately 0.5, it has been repeatedly observed that the targets within the most concordant modules across transcriptomics and proteomics exhibit highly discordant changes at the protein and RNA levels (235; 245; 246). These discrepancies highlight the complexity and non-linear relationship between the transcriptome and proteome, stressing the importance of the numerous events that occur from the initial transcription of DNA to the point when a protein performs its function. This also aligns with the observation that only half of the disease-related variance in the AD network proteome is mirrored in transcriptome-level gene expression, while the remaining 50% results from transcriptional and post-translational effects (246). These findings align with previous comparisons of protein and mRNA data (237), and strongly supports the value of protein profiling in AD research, highlighting the unique aspects of proteomic changes that can only be achieved through protein analysis.

*1.13.4 Core modules of the AD brain network proteome:* Nearly a dozen comprehensive network-based analyses of the AD proteome in the human brain have led to the identification of six highly conserved modules, each with reproducible associations to specific cell types, organelles, and biological functions (217; 221; 225; 226; 235-241). Several modules, such as inflammatory, myelination, and RNA binding/splicing, consistently showed increases in the AD brain network proteome, while others, like synaptic, mitochondrial, and cytoskeleton, displayed consistent decreases. Notably, some of these modules (inflammatory, myelination, synaptic, and mitochondrial) appear to be driven by cell-type-specific perturbations (226), while those lacking such enrichment (RNA binding/splicing and cytoskeleton) represented underlying biochemical changes associated with the disease. The complexity of the modules preserved in AD confirms the multifactorial nature of the condition, which has led to inherent challenges in understanding AD and, consequently, in developing effective interventions.

*1.13.5 The CSF proteome as a reflection of AD brain changes:* The close proximity of CSF to the brain, along with its ability to reflect changes in amyloid burden and neurodegeneration through markers like A $\beta$  and Tau, provides a compelling rationale for integrating the CSF proteome with the brain proteome. Furthermore, the reflection of other AD pathophysiologies in the CSF would provide additional avenues for detecting and monitoring treatment responses, especially at earlier stages of disease. Our first attempt to validate this interaction via proteomics was based on findings by Johnson et al., which identified that approximately 20 proteins from the highly conserved microglial module showed significant elevations in AD CSF (237). This provided the initial evidence necessary to explore this interaction more deeply. In another large-scale study by the Seyfried lab, Higginbotham et al. used a similar integrative proteomic approach to examine the statistical overlap between the entire AD brain network proteome and differentially expressed proteins in the AD CSF proteome (245). Notably, fifteen of the 44 brain modules identified in this study showed a strong overlap with the markers differentially expressed in AD CSF. Collectively, those 15 modules from the brain were being represented by 300 proteins that were significantly altered in AD CSF compared to controls. Based on their corresponding brain modules, these approximately 300 CSF AD targets were then segregated into five biomarker panels that represented a wide range of brain pathophysiology. These panels included synaptic transmission, vascular biology, myelination, glial-mediated inflammation, and energy metabolism. The panels highlighting brain changes in AD that could potentially be monitored through CSF. This comprehensive approach highlights the potential of CSF proteomics to uncover diverse aspects of AD pathology and to enhance the precision of biomarker-based diagnosis and therapeutic monitoring.

## **1.14 Summary**

Evidence of differences in AD biomarkers between African Americans and Caucasians exists yet the underrepresentation of African Americans in research means data to support such alterations is lacking. This demonstrates a greater need for broad investigations into the

underlying biological differences of AD in African Americans as a means to identify AD biomarkers that are representative of and generalizable across diverse racial, ethnic, and genetic backgrounds. Including participants from diverse racial backgrounds ensures that research findings are more representative of the entire population and can be generalized to different racial and ethnic groups. Without this, there lies a risk of bias and limited applicability of research outcomes to specific populations. The following research will demonstrate how an integrated proteomic and network approach can be utilized to comprehensively define the proteomic profiles of AD within individuals of African American or Caucasian background. We hypothesize that the biological pathways most relevant or impacted by changes in Tau burden will demonstrate varying expression levels in the CSF of African Americans and Caucasians with AD. Through a combination of unbiased system level and target approaches, I have been able to (i) directly characterize CSF within a large cohort of individuals (ii) gain insight into race-specific molecular signatures of AD and (iii) validate novel race-dependent signatures for AD pathogenesis using an independent mass spectrometry technique. In total, there is a significant gap in our knowledge of the racial differences underlying molecular mechanisms of AD biology. A better understanding of these mechanisms is critical to move the field towards clearer biological methodologies for the early detection of AD across a diverse population of people.

## CHAPTER 2:

### MATERIALS AND METHODS

This Materials and Methods was originally published in *Molecular Neurodegeneration*:

Modeste, E.S., Ping, L., Watson, C.M. *et al.* Quantitative proteomics of cerebrospinal fluid from African Americans and Caucasians reveals shared and divergent changes in Alzheimer's disease. *Mol Neurodegeneration* **18**, 48 (2023). <https://doi.org/10.1186/s13024-023-00638-z>

A full list of tables can be accessed at the following link:

<https://molecularneurodegeneration.biomedcentral.com/articles/10.1186/s13024-023-00638-z>



## 2.1 CSF samples

All cerebrospinal fluid (CSF) samples were collected as part of ongoing studies at Emory's Goizueta Alzheimer's Disease Research Center (ADRC) including participants in the ADRC Clinical Core, the Emory Healthy Brain Study, and the ADRC-affiliated Emory Cognitive Neurology Clinic. All participants provided informed consent under protocols approved by Emory University's Institutional Review Board. Clinical diagnosis of AD as well as classification as cognitively normal controls was based on review of clinical history, neurological examination, detailed cognitive testing, and diagnostic studies including Magnetic Resonance Imaging and CSF AD biomarker testing. Diagnosis of AD was made by subspecialty certified Cognitive and Behavioral Neurologists with additional input from Neuropsychologists based on current NIA-AA criteria (247; 248). A consensus clinical diagnosis of controls was made without consideration of CSF biomarkers by a panel of experts at the Emory Goizueta ADRC. Criteria for assigning diagnosis are provided in the National Alzheimer Coordination Center coding guidelines, form D1, based on clinician judgment. The basis for this judgment includes many metrics, with controls considered to have normal cognition and normal behavior after reviewing all testing including Montreal Cognitive Assessment (MoCA), Clinical Dementia Rating (CDR) score, and detailed neuropsychological testing. Hence, control participants may have MoCA scores that are lower than traditional cut points for impairment on this screening test. CSF was collected by lumbar puncture and banked according to best practice guidelines outlined by the National Institute on Aging for Alzheimer's Disease Centers (<https://alz.washington.edu/BiospecimenTaskForce.html>), and identical pre-analytic steps were followed in all groups. Measurements of Amyloid-beta<sub>1-42</sub> (A $\beta$ <sub>42</sub>), total Tau (tTau), and phosphorylated Tau<sub>181</sub> (pTau<sub>181</sub>) was performed on the Roche Diagnostics Elecsys platform (249-251) using recommended protocols. In total, the cohort was comprised of 105 healthy controls and 98 AD. The racial background of each case was based upon self-identification. Of the 203 cases, 100 identified as Caucasian or White while 103 identified as African American or Black. Case metadata can be found in **Appendix Table 6.1**.

## **2.2 Protein digestion of CSF**

In order to sample the CSF proteome in an unbiased manner and given that we have previously shown that immunodepletion resulted in only a marginal improvement in proteomic coverage, the CSF samples were not immunodepleted prior to digestion (252; 253). First, 70  $\mu$ L of CSF was transferred to 1 mL deep well plates for digestion with lysyl endopeptidase (LysC) and trypsin. The samples were then reduced and alkylated with 1.4  $\mu$ L of 0.5 M tris-2(-carboxyethyl)-phosphine (ThermoFisher) and 7  $\mu$ L of 0.4 M chloroacetamide in a 90°C water bath for 10 min. The water bath was then turned off and allowed to cool to room temperature along with samples for 5 minutes. Following this, water bath sonication was performed for 5 min. The samples were then allowed to cool again to room temperature for 5 mins prior to adding urea. Then 78  $\mu$ L of 8M urea buffer (8M urea, 10mM Tris, 100mM  $\text{NaH}_2\text{PO}_4$ , pH 8.5) and 3.5  $\mu$ g of LysC (Wako), was added to each sample, resulting in a final urea concentration of 4M. The samples were then mixed well, gently spun down, and incubated overnight at 25°C for digestion with LysC. The following day, samples were diluted to 1M urea with a blend of 468  $\mu$ L of 50 mM ammonium bicarbonate (254) and 7  $\mu$ g of trypsin (ThermoFisher). The samples were subsequently incubated overnight at 25°C for digestion with trypsin. The next day, the digested peptides were acidified to a final concentration of 1% formic acid and 0.1% trifluoroacetic acid. This was immediately followed by desalting on 30 mg HLB columns (Waters) and then eluted with 1 mL of 50% acetonitrile (ACN) as previously described (228). To normalize protein quantification across batches, 100  $\mu$ L was taken from all CSF samples and then combined to generate a pooled sample. This pooled sample was then divided into global internal standards (GIS) (255). All individual samples and the pooled standards were then dried using a speed vacuum (Labconco).

## **2.3 Tandem mass tag labeling of CSF peptides**

All CSF samples were balanced for diagnosis, race, age, and sex (in that order) across 16 batches using ARTS (automated randomization of multiple traits for study design) (256). Using

a 16-plex Tandem Mass Tag (TMT) pro kit (Thermo Fisher Scientific, A44520, Lot number: VH3111511), 13 channels of each batch were allocated to a CSF sample (127N, 127C, 128N, 128C, 129N, 129C, 130N, 130C, 131N, 131C, 132N, 132C, 133N). The remaining 3 channels were occupied with a GIS pool (126), a standard biomarker negative pool (133C), and a standard biomarker positive pool sample (134N). Information regarding the origination of these pooled samples were reported previously (257). **Appendix Table 6.2** provides the sample to batch arrangement. In preparation for labeling, each CSF peptide digest was resuspended in 75  $\mu$ l of 100 mM triethylammonium bicarbonate buffer meanwhile 5 mg of TMT reagent was dissolved into 200  $\mu$ l of ACN. Once both were in suspension, 15  $\mu$ l of TMT reagent solution was subsequently added to the resuspended CSF peptide digest. After 1 hour, the reaction was quenched with 4  $\mu$ l of 5% hydroxylamine (Thermo Fisher Scientific, 90115) for 15 min. Then, the peptide solutions were combined according to the batch arrangement. Finally, each TMT batch was desalted with 60 mg HLB columns (Waters) and dried via speed vacuum (Labconco).

## **2.4 High-pH peptide fractionation**

Dried samples were re-suspended in high pH loading buffer (0.07% vol/vol  $\text{NH}_4\text{OH}$ , 0.045% vol/vol FA, 2% vol/vol ACN) and loaded onto a Water's BEH column (2.1 mm x 150 mm with 1.7  $\mu$ m particles). A Vanquish UPLC system (ThermoFisher Scientific) was used to carry out the fractionation. Solvent A consisted of 0.0175% (vol/vol)  $\text{NH}_4\text{OH}$ , 0.01125% (vol/vol) FA, and 2% (vol/vol) ACN; solvent B consisted of 0.0175% (vol/vol)  $\text{NH}_4\text{OH}$ , 0.01125% (vol/vol) FA, and 90% (vol/vol) ACN. The sample elution was performed over a 25 min gradient with a flow rate of 0.6 mL/min with a gradient from 0 to 50% solvent B. A total of 96 individual equal volume fractions were collected across the gradient. Fractions were concatenated to 48 fractions and dried to completeness using vacuum centrifugation.

## **2.5 Mass spectrometry analysis and data acquisition**

All samples (~1µg for each fraction) were loaded and eluted by an Easy-nLC 1200 (ThermoFisher Scientific) with an in-house packed 15 cm, 150 µm i.d. capillary column with 1.7 µm CSH (Water's) over a 35 min gradient. Mass spectrometry (MS) was performed with a high-field asymmetric waveform ion mobility spectrometry (FAIMS) Pro front-end equipped Orbitrap Lumos (Thermo) in positive ion mode using data-dependent acquisition with 1 second top speed cycles for each FAIMS compensative voltage. Each cycle consisted of one full MS scan followed by as many MS/MS events that could fit within the given 1 second cycle time limit. MS scans were collected at a resolution of 120,000 (410-1600 m/z range,  $4 \times 10^5$  AGC, 50 ms maximum ion injection time, FAIMS compensative voltage of -45 and -65). Only precursors with charge states between 2+ and 5+ were selected for MS/MS. All higher energy collision-induced dissociation MS/MS spectra were acquired at a resolution of 50,000 (0.7 m/z isolation width, 35% collision energy,  $1 \times 10^5$  AGC target, 86 ms maximum ion time). Dynamic exclusion was set to exclude previously sequenced peaks for 30 seconds within a 10-ppm isolation window.

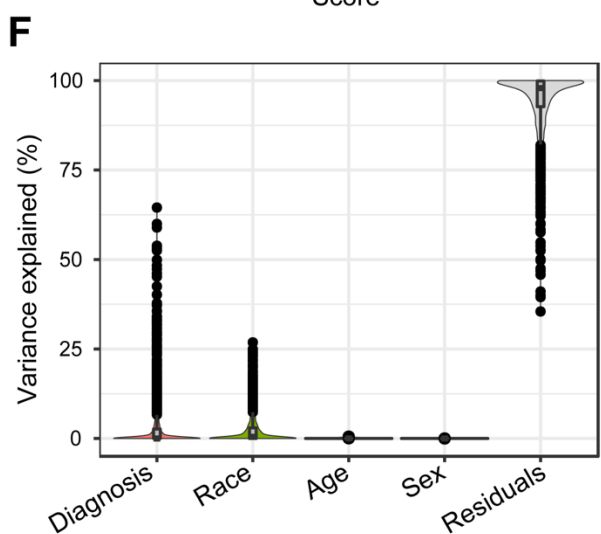
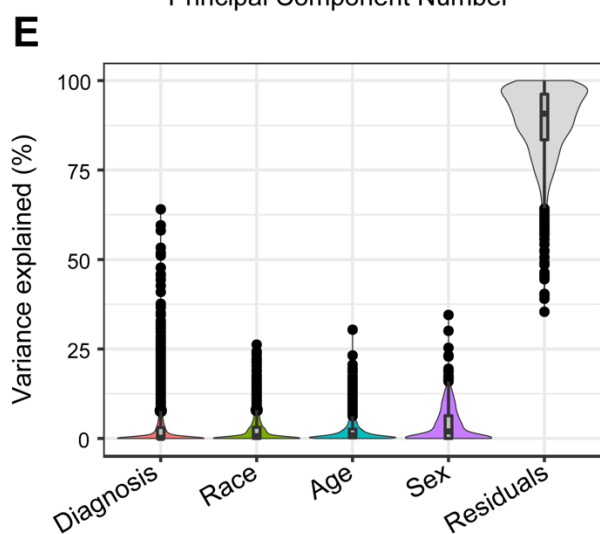
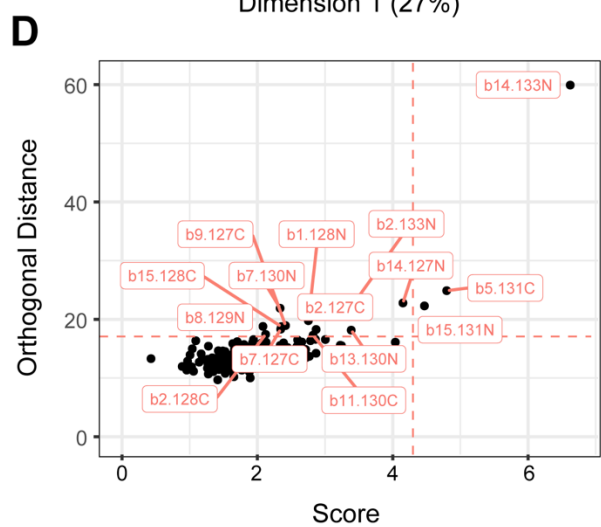
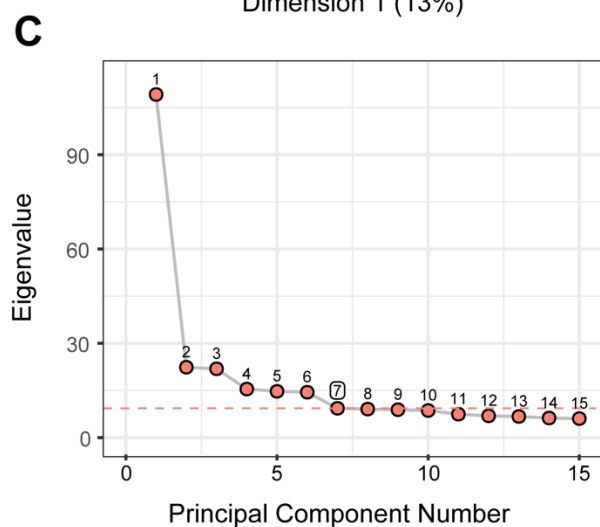
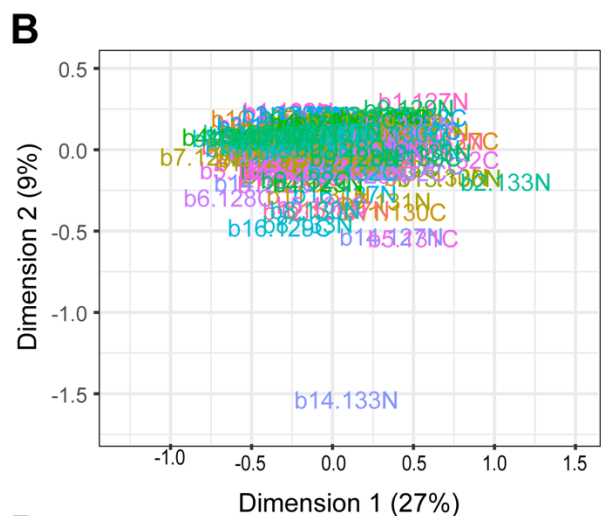
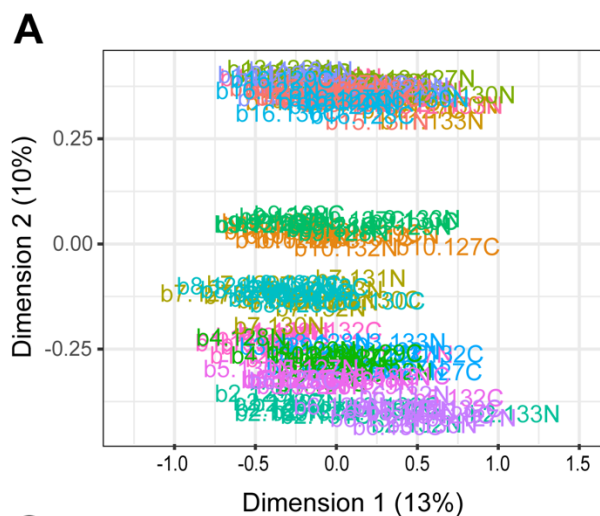
## **2.6 Database search and protein quantification**

All raw files were analyzed using the Proteome Discoverer Suite (v.2.4.1.15, Thermo Fisher Scientific). MS/MS spectra were searched against the UniProtKB human proteome database (downloaded in 2019 with 20338 total sequences). The Sequest HT search engine was used to search the RAW files, with search parameters specified as follows: fully tryptic specificity, maximum of two missed cleavages, minimum peptide length of six, fixed modifications for TMTPro tags on lysine residues and peptide N-termini (+304. 304.2071 Da) and carbamidomethylation of cysteine residues (+57.02146 Da), variable modifications for oxidation of methionine residues (+15.99492 Da), serine, threonine and tyrosine phosphorylation (+79.966 Da) and deamidation of asparagine and glutamine (+0.984 Da), precursor mass tolerance of 10 ppm and a fragment mass tolerance of 0.05 Da. Percolator was used to filter peptide spectral matches and peptides to a false discovery rate (FDR) <1%. Following spectral assignment, peptides were assembled into proteins and were further filtered based on the combined probabilities of their constituent peptides

to a final FDR of 1%. Peptides were grouped into proteins following strict parsimony principles. A complete TMT reporter ion abundance-based table output of assembled protein abundances without adjustments can be found at <https://www.synapse.org/EmoryDiversityCSF>.

## 2.7 Adjustment for batch and other sources of variance

Only proteins quantified in  $\geq 50\%$  of samples were included in subsequent analysis ( $n = 1,840$  proteins). Of the 1,840 proteins, 1,327 proteins were quantified across all samples. As previously reported (236; 237; 252; 258), batch correction was performed using a Tunable Approach for Median Polish of Ratio, (<https://github.com/edammer/TAMPOR>), an iterative median polish algorithm for removing technical variance across batch. Multidimensional scaling plots (MDS) were used to visualize batch contributions to variation before and after batch correction. Noticeably, prior to batch correction, cases within the same batch clustered together and batches ran consecutively tended to cluster more closely together (**Figure 2.1A**). Following batch correction using a median polish algorithm, the cases were no longer clustering by batch (**Figure 2.1B**). The data was then subjected to outlier removal using a robust principal component analysis method, *PcaGrid* (259). A scree plot graphing the eigenvalue against the principal component (PC) number was utilized to determine the number of PCs to include in the parameters (**Figure 2.1C**). Briefly, the parameters used for outlier detection were as follows: the desired number of principal components = 7, method = mean absolute deviation, and criterion for computing cutoff values = 0.99 (**Figure 2.1D**). This resulted in the detection and removal of 15 outliers, resulting in a final  $n=189$  samples. Bootstrap regression was then performed to remove for covariates such as age at collection and sex. Variance partition analysis was performed to confirm appropriate regression of these traits (**Figure 2.1E & F**). Since the *variancePartition* package does not allow missing values, proteins with missing quantifications were temporarily imputed using the *impute.knn* function of the *impute* R package. The final cleaned dataset after regression and log2 transformation can be found at <https://molecularneurodegeneration.biomedcentral.com/articles/10.1186/s13024-023-00638-z>.



**Figure 2.1: Batch correction, outlier removal and bootstrap regression.** Multidimensional scaling plots (MDS) were used to illustrate batch contributions to variance before and after batch correction. In MDS plots, the distance a case is from one another is reflective of how similar or dissimilar a case is from the other. **(A)** Prior to batch correction, the samples clustered by batch **(B)** After batch correction, the samples no longer cluster by batch. **(C)** After batch correction, a principal component (PC)-based outlier removal method was utilized to detect outliers. By graphing the eigenvalue of each component against the PC number, the elbow or bend in the graph, which in this case was 7, was indicative of the ideal number of components to include within the parameters. **(D)** With a criterion for computing cutoff values set to 0.99, the cutoffs for the detection of outliers for the orthogonal distance and score were 16.79257 and 4.654674 respectively. This resulted in the detection of 15 outliers (b1.128N, b11.130C, b13.130N, b14.127N, b14.133N, b15.128C, b15.131N, b2.127C, b2.128C, b2.133N, b5.131C, b7.127C, b7.130N, b8.129N, b9.127C). B14.133N was such an extreme outlier because it was an empty channel. **(E)** After outlier removal, the matrix underwent bootstrap regression to remove variations in the dataset that were due to age and sex. Variance partition plots were employed to illustrate the percent contribution of diagnosis, race, age, and sex to the variance of each protein. **(F)** Following bootstrap regression, variations explained by age and sex were removed.

## 2.8 Differential expression analysis

One-way ANOVA followed by Tukey's post hoc adjustment for multiple comparisons was performed on four groups (Control-Caucasian, Control-African American, AD-Caucasian, and AD-African American) to identify differentially expressed proteins across diagnosis and within each race. Differentially expressed proteins for comparisons of interest (i.e., Control-Caucasian vs AD-Caucasian and Control-African American vs AD-African American) were then presented as volcano plots using the *ggplot2* package in R v4.1.2. A list of all comparisons computed with corresponding adjusted p-values is provided in **Appendix Table 6.3**.

## 2.9 Weighted Gene Co-expression Network Analysis

As previously published (235-237; 252), the *blockwiseModules* function from the WGCNA package in R was utilized to derive the weighted protein co-expression network. Briefly, the following parameters were used: soft threshold power  $\beta = 3$ , *deepSplit* = 4, minimum module size = 5, merge cut height = 0.07, and a signed network with partitioning about medoids. Using the *pairwise.wilcox.test* R function with Bonferroni correction, a pairwise Wilcoxon test was performed to calculate pairwise comparisons between each group with corrections for multiple testing.

## 2.10 Gene ontology and cell type enrichment analysis

To characterize co-expressed protein module biology, gene ontology (GO) annotations were retrieved from the Bader Lab's monthly updated .GMT formatted ontology lists downloaded July 5, 2022 (260). A Fisher's exact test for enrichment was performed into each module's protein membership using an in-house script (<https://github.com/edammer/GOparallel>). For cell type enrichment analysis, an in-house marker list was used as previously described (236). A Fisher's exact test was performed for each module member list using the merged human cell type marker list to determine cell type enrichment. For brain-CSF module overlap a one-sided Fisher's exact test to compare significance of module membership.



## 2.11 Selected reaction monitoring

Selected reaction monitoring (SRM) assays were performed on 195 of the 203 cases to determine whether a separate targeted proteomic approach could replicate proteomic changes seen in TMT discovery proteomics. An attempt was made to include all 203 samples from discovery TMT for SRM analysis however, samples 52524, 51520, 52055, 48617, 48615, 48769, 49537, 45707 had low remaining sample volume and had to be removed. Sample 62762 was later removed due to irregularities in retention time shifts. Peptide selection, sample preparation, peptide quantification, and data acquisition for the SRM assay was performed as previously described (257). Briefly, peptides were selected based on their robust detection and significant differential expression in previous CSF discovery proteomic projects for synthesis as heavy standards (237; 252). More specifically, the peptide had to i) have one or more spectral matches, ii) be significantly differentially abundant when evaluating AD versus Control cases, iii) and map to proteins that appeared in brain-based biological panels outlined in Higginbotham et al 2020 (252) that differed in AD. Ultimately, this led to approximately 200 peptides being nominated for synthesis by Thermo Fisher Scientific (Thermo PEPotec SRM Peptide Libraries; Grade 2; crude as synthesized). In addition to the 195 clinical samples from before, two pools of CSF were utilized as AD biomarker positive and AD-biomarker negative quality controls (QC) standards (257). After the CSF samples were blinded and randomized, each sample (50  $\mu$ L) was reduced, alkylated, denatured and then subjected to digestion as described (257). After digestion, the heavy labeled standards, 15 $\mu$ L per 50  $\mu$ L of CSF, were added to each digested sample. Each digested sample then underwent acidified, desalted and dried under vacuum. Following this, the peptide targets were quantified using TSQ Altis Triple Quadrupole mass spectrometer as previously described (257). The resulting raw files were uploaded to Skyline-daily software (version 21.2.1.455) for peak integration and quantification by peptide ratios. Peptides were filtered by first assessing retention time reproducibility, then by matching light and heavy transitions, and finally by determining the peptide ratio precision using the coefficient of variation (CV) as described by

Watson et al 2023 (257). The technical CV of each peptide was calculated based on the peptide area ratio for the AD-positive and AD-negative QC pools (**Appendix Table 6.4**). CSF peptide targets with CVs  $\leq 20\%$  in at least one pooled standard were determined as peptides with high precision and were kept for subsequent analysis, leaving a total of 85 peptides that mapped to 58 proteins. The total area ratio for each targeted peptide in each sample made up the final data matrix. Due to the nature of SRM in that each peptide is explicitly targeted, a value for each peptide is always assigned in each sample (down to and including the limit of detection) as previously published by our group (257). As a result, the total area ratio for each targeted peptide in each sample made up the final data matrix, leaving a matrix with no blank cells or missing values. In preparation for analysis, this matrix of peptide ratios was  $\log_2$  transformed and true zero values were replaced after  $\log_2$ -transformation with the minimum value for that peptide minus 1. Bootstrap regression was then used to regress for age and sex (**Appendix Table 6.5**). Bicor was then utilized to calculate the correlation between SRM peptides and TMT-MS protein measurements (**Appendix Table 6.6**). In cases where multiple peptides mapped to one protein, the most correlated peptide was kept for further analysis (**Appendix Table 6.7**). One-way ANOVA analysis with Tukey adjustment was then utilized once again to examine pairwise interactions (**Appendix Table 6.8**) and receiver operating characteristic (ROC) curve analysis was performed as previously described (257) (**Appendix Table 6.9**).

## CHAPTER 3: RESULTS

These Results were originally published in *Molecular Neurodegeneration*:

Modeste, E.S., Ping, L., Watson, C.M. *et al.* Quantitative proteomics of cerebrospinal fluid from African Americans and Caucasians reveals shared and divergent changes in Alzheimer's disease. *Mol Neurodegeneration* **18**, 48 (2023). <https://doi.org/10.1186/s13024-023-00638-z>

A full list of tables can be accessed at the following link:

<https://molecularneurodegeneration.biomedcentral.com/articles/10.1186/s13024-023-00638-z>

### 3.1 CSF cohort characteristics

This study was comprised of two balanced groups of cerebrospinal fluid (CSF) samples from African American and Caucasian individuals, matched for age and sex with roughly equal numbers of control and Alzheimer disease (AD) cases (**Table 3.1**). This included 53 Caucasian controls, 52 African American controls, 47 AD Caucasians, and 51 AD African Americans. The majority were female and on average the controls (64.5 years) were slightly younger than AD (68 years). Notably, there were no statistical differences between the ages of the African Americans and the Caucasians within diagnosis (control:  $p=0.8848$ , AD:  $p=0.9998$ ). As expected, AD cases had lower Montreal Cognitive Assessment (MoCA) scores than controls, but there were no statistically significant differences between MoCA scores across race within controls and AD (control:  $p=0.7559$ , AD:  $p=0.2055$ ). The AD cases also had lower Amyloid-beta ( $A\beta_{42}$ ) levels and elevated total Tau (tTau) and phosphorylated Tau<sub>181</sub> (pTau<sub>181</sub>) levels. Notably,  $A\beta_{42}$  levels were significantly lower in African American Controls compared to Caucasian controls ( $p = 0.0021$ ) but not different between African American AD and Caucasian AD. This may indicate potentially early changes in brain amyloid deposition or processing of APP in African American controls versus Caucasian controls. Notably, the distribution of APOE4 carriers did not differ significantly by race in the control population and so does not account for the pattern observed (**Appendix Table 6.1**). Conversely, tTau and pTau<sub>181</sub> levels were significantly lower in African Americans with AD (tTau:  $p<0.0001$ , pTau<sub>181</sub>:  $p<0.0001$ ) but not different between African American and Caucasian controls. Data on comorbid conditions, including whether or not the person had hypertension, diabetes, dyslipidemia, or cerebrovascular disease, is presented for all cases in **Appendix Table 6.1**. Notably, none of the comorbid conditions was statistically overrepresented in either racial group.

Sample Size	CT Cau 53	CT AA 52	p – value <sup>a</sup>	AD Cau 47	AD AA 51	p – value <sup>a</sup>
<b>Characteristics</b>						
Sex	33 F, 20 M	33 F, 19 M	-	29 F, 18 M	32 F, 19 M	-
Age <sup>b</sup>	65 ± 8	64 ± 8	0.8848	68 ± 9	68 ± 9	0.9998
MoCA <sup>c</sup>	26 ± 2	25 ± 3	0.7559	16 ± 6	14 ± 6	0.2055
*Aβ <sub>42</sub> <sup>d</sup>	1195.2 ± 262.0	1021.4 ± 301.1	<b>0.0021</b>	558.2 ± 169.9	483.4 ± 151.8	0.4026
tTau <sup>d</sup>	186.2 ± 61.6	158.5 ± 56.5	0.6573	423.7 ± 189.2	301.5 ± 134.8	<b>&lt; 0.0001</b>
pTau <sub>181</sub> <sup>d</sup>	16.6 ± 5.6	14.1 ± 4.9	0.7787	43.3 ± 20.8	30.1 ± 14.1	<b>&lt; 0.0001</b>
tTau/Aβ <sub>42</sub> <sup>d</sup>	0.14 ± 0.03	0.14 ± 0.03	0.9994	0.78 ± 0.31	0.66 ± 0.30	0.0850

<sup>a</sup> p-values were calculated using one-way ANOVA with Tukey correction, bold indicates p < 0.05.

<sup>b</sup> Age in years. Values given as average ± standard deviation

<sup>c</sup> Most recent Montreal Cognitive Assessment (MoCA) score. Values given as average ± standard deviation

<sup>d</sup> Aβ<sub>42</sub>, tTau, pTau<sub>181</sub>, and tTau/Aβ<sub>42</sub> in pg/mL. Values given as average ± standard deviation

\*Aβ<sub>42</sub> levels that reached saturation (1700 pg / mL) were excluded from calculations and analysis

Abbreviations: CT, Control; AD, Alzheimer's disease; Cau, Caucasian / White; AA, African American / Black

**Table 3.1.** Cohort Characteristics

### **3.2: Discovery tandem mass spectrometry analysis of cerebrospinal fluid from African Americans and Caucasians reveals unique and shared changes in Alzheimer's disease**

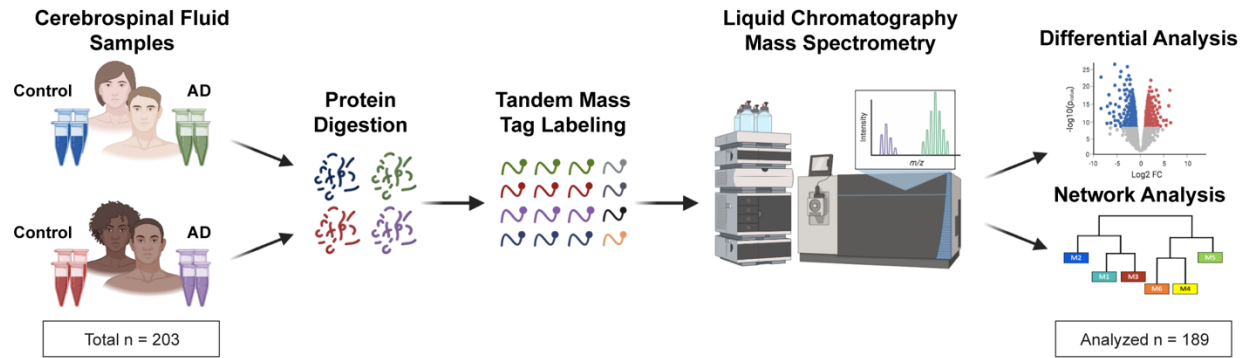
#### *3.2.1 Correlation analysis uncovers a strong relationship between mass spectrometry and immunoassay measurements of Tau*

Following enzymatic digestion, tandem mass tag (TMT) labeling, and off-line fractionation, all samples were subjected to liquid chromatography mass spectrometry (MS) (**Figure 3.1A**). In total, TMT-MS proteomic analysis identified 34,330 peptides mapping to 2,941 protein groups across the 203 samples (16 total batches). To account for missing protein measurements across batches, we included only those proteins quantified in at least 50% of samples following outlier removal as previously described (227; 235-237; 252), resulting in the final quantification of 1,840 proteins. Protein abundance was adjusted for batch and age and sex were regressed. As expected, Tau levels were significantly elevated in both African Americans and Caucasians with AD across both platforms compared to controls (**Figure 3.1B and C**). Consistent with the immunoassay measurements, TMT-MS Tau levels also showed significantly lower levels in African Americans with AD compared to Caucasians with AD (**Figure 3.1C**). Notably, protein levels of Tau (MAPT) by TMT-MS correlated strongly to independently measured tTau levels via immunoassay ( $r=0.83$ ,  $p = 4.7e-47$ ) (**Figure 3.1D**). Thus, in this study, both platform measures of CSF Tau support a reduction of total Tau levels in African Americans with AD, consistent with previous findings (261; 262).

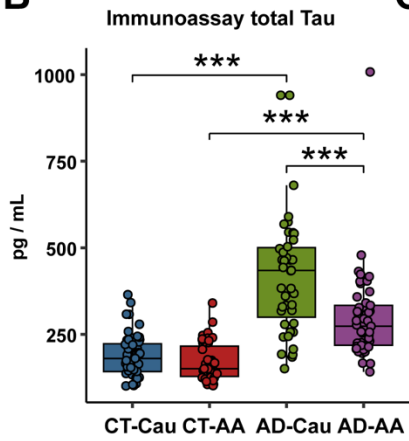
#### *3.2.2 Differential expression analysis of African American and Caucasian CSF proteome reveals unique and shared changes in AD*

Differential expression analysis was performed to identify changes in the CSF proteome by race in AD (**Appendix Table 6.3**). Consistent with previous proteomic analyses of AD CSF (237; 252; 263-265), there was a significant increase in Tau (MAPT), 14-3-3 proteins, (YWHAZ, YWHAG, and YWHAE), SMOC1, neurofilaments (NEFM and NEFL) and proteins involved in

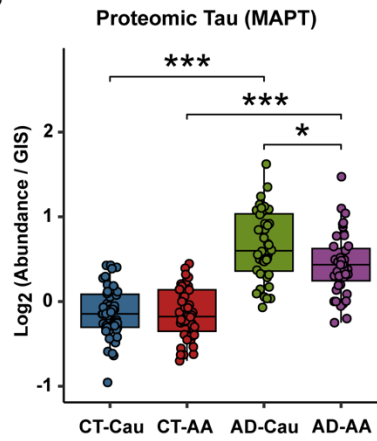
**A**



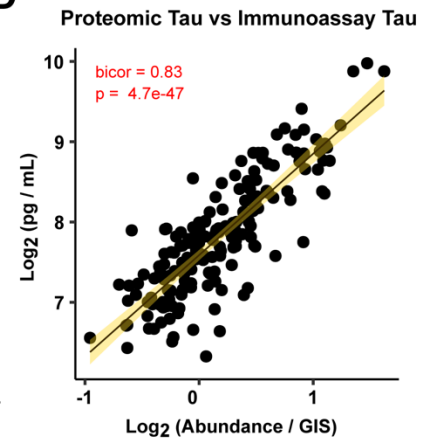
**B**



**C**



**D**



Part A of this figure was created with BioRender.com

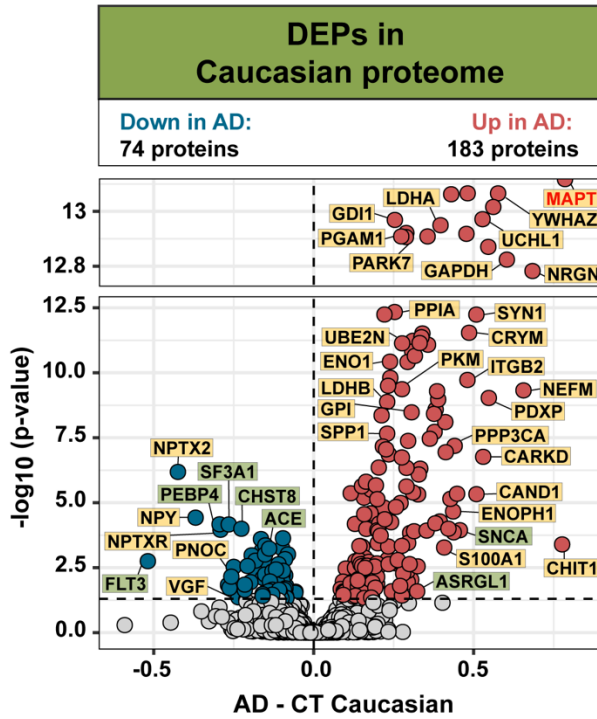
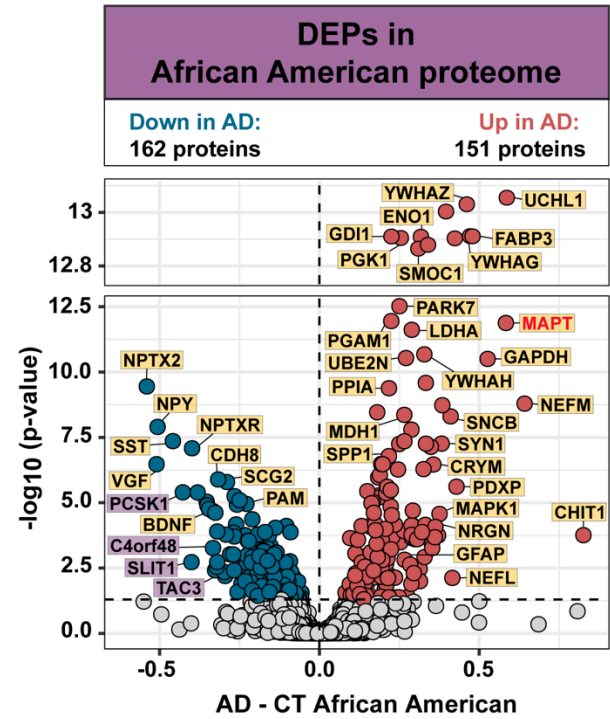
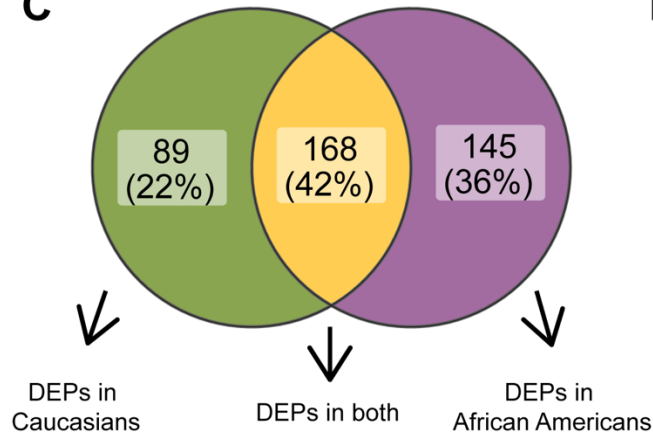
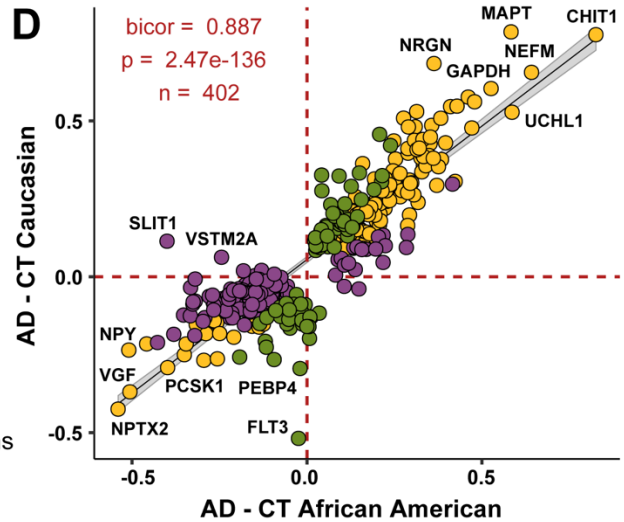
**Figure 3.1: Schematic of experimental workflow and correlation between proteomic Tau and total Tau immunoassay measurements.** (A) Schematic of experimental workflow for quantification of cerebrospinal fluid proteome. (B) Total Tau levels as measured by Roche Elecsys Platform between control (CT) and AD cases and stratified by self-identified race: Caucasian (Cau) or African American (AA) (C) Tau levels measured by mass spectrometry. One-way ANOVA with Tukey post-hoc correction determined pairwise relationships (D) Correlation of Tau levels by TMT-MS (x-axis) to paired immunoassay total Tau levels (y-axis). Biweight midcorrelation coefficient (bicor) with associated p-value is shown. Only 179 cases were included in the linear regression analysis because of sample outlier removal and missing values in the TMT-MS.



glucose metabolism in both African Americans and Caucasians with AD compared with race matched controls (**Figure 3.2A & B**). However, Caucasians with AD exhibited a bias towards proteins that were increased in AD, where the number of differentially expressed proteins (DEPs) was nearly double (n=183 proteins) the number of decreased DEPs in AD (n=74 proteins) (**Figure 3.2A**). In contrast, in African Americans, the number of increased and decreased DEPs was more balanced (151 increased proteins vs. 162 decreased proteins) (**Figure 3.2B**). A Venn diagram illustrates the overlap of DEPs from African Americans and Caucasians with AD (**Figure 3.2C**), with the majority of proteins (n=168 proteins) differentially expressed in both races. Furthermore, a correlation analysis of both shared and unique DEPs showed overall high agreement in direction of change (bicor=0.887,  $p=2.47e-136$ , **Figure 3.2D**). However, there were some exceptions including SLIT1 and VSTM2A, which were significantly increased in Caucasians, but decreased in African Americans with AD. Both proteins are predominantly enriched in neuronal-cell types (266; 267). Thus, despite the differences in the number of significant DEPs in African Americans compared to Caucasians with AD, the direction of change with disease remains largely similar across both races.

### *3.2.3 Network analysis of the CSF proteome reveals modules related to pathways and brain cell-types*

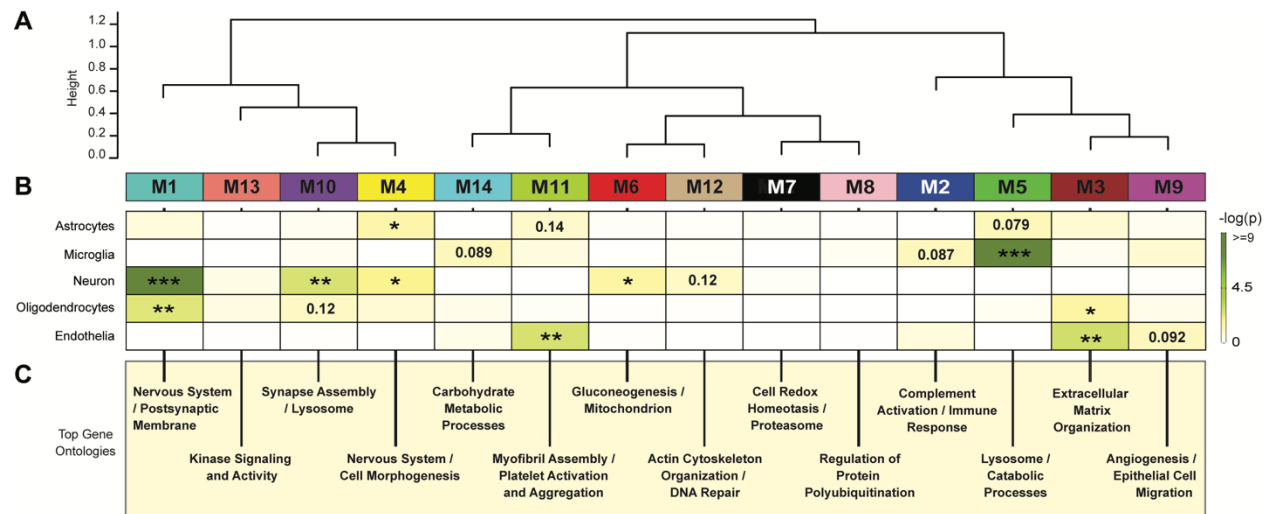
Co-expression network analysis of the AD brain proteome organizes proteins into modules related to molecular pathways, organelles, and cell types impacted by AD pathology (227; 235-237). Moreover, integration of the human AD brain and CSF proteome revealed that approximately 70% of the CSF proteome overlapped with the brain proteome (252). While proteomic networks in AD brain have been examined, network changes in the AD CSF proteome, including those associated with race and AD biomarkers are less well understood. Thus, we applied Weighted Gene Co-expression Network Analysis (WGCNA) to define trends in protein co-expression across 1840 CSF proteins in all individuals. These parameters identified 14 modules

**A****B****C****D**

**Figure 3.2. Differential expression of Caucasian and African American CSF proteomes in AD.** Volcano plot displaying the  $\log_2$  fold change (FC) (x-axis) against one-way ANOVA with Tukey correction derived  $-\log_{10}$  p-value (y-axis) for all proteins (n=1840) comparing AD versus Controls for Caucasians (**A**) and African Americans (**B**). Cutoffs were determined by significant differential expression ( $p < 0.05$ ) between control (CT) and AD cases. Proteins with significantly decreased levels in AD are shown in blue while proteins with significantly increased levels in disease were indicated in red. Select proteins were denoted and labeled by whether they were differentially expressed in both proteomes (yellow), in only the Caucasian proteome (green), or in only the African American proteome (purple). (**C**) Venn diagram illustrating the number of differentially expressed proteins (DEPs) that were uniquely changed in one proteome (green or purple) or changed in both proteomes (yellow) (**D**) The correlation between the fold change of all DEPs (n=402) across the African American proteome (x-axis) and the Caucasian proteome (y-axis) were strongly correlated (bicor=0.887,  $p=2.47 \times 10^{-136}$ ), regardless of whether the DEP was significant in one (green or purple) or both proteomes (yellow).

(M), ranked by size, ranging from the largest M1, with 370 proteins to the smallest, M14, with 16 proteins (**Figure 3.3A**). Many of these modules were significantly enriched for brain-specific cell types (**Figure 3.3B**) as well as established brain gene ontologies (GO), cellular functions and/or organelles (**Figure 3.3C**). The three largest modules were associated with categories of “Postsynaptic Membrane” (M1), “Complement Activation” (M2), and “Extracellular Matrix” (M3) whereas M5 represented “Lysosome / Catabolism” and M6 “Gluconeogenesis”. Other modules included those with GO terms linked to “Cell Morphogenesis” (M4), “Cell Redox / Proteasome” (M7), “Protein Polyubiquitination” (M8), “Angiogenesis / Cell Migration” (M9), “Synapse Assembly” (M10), Myofibril Assembly (M11), “Actin Cytoskeleton” (M12), “Kinase Signaling / Activity” (M13), and “Carbohydrate Metabolism” (M14).

Protein-based network analysis in AD brain tissue has shown that the cellular composition represents a major source of biological variance and that many of the network modules are enriched in proteins that are expressed by specific brain cell types (236; 237). To determine if a similar relationship exists with protein-based networks in CSF, we evaluated the overlap of proteins in each module with brain cell-type specific makers (**Figure 3.3B**), generated previously from cultured or acute isolated neurons, oligodendrocytes, astrocytes, endothelial, and microglia from brain (266; 267). The largest module, M1, was enriched with neuron/synaptic proteins (i.e., NPTX1, NPTXR, SCG2, VGF, NRN1, and L1CAM) and to a lesser degree oligodendrocyte proteins (i.e., IGSF8, VCAN, APLP1). Neuronal loss or the active secretion of neuronal proteins into the extracellular space could account for the presence of neuronal proteins in the CSF. The M4 module was also enriched for neuronal protein markers including RTN4R1, LINGO2, OLFM1, and PLXNA2, associated with “Nervous Systems and Cell Morphogenesis”. Modules most enriched with microglia markers were M2 (i.e., C2, C3, C1RL, C1QA, C1QB, C1QC, LCP1, etc.) and M5 (i.e., HEXB, CTSZ, HEXA, CTSA, CTSB) consistent with a role in complement activation and lysosome function, respectively. Finally, endothelial markers were mainly overrepresented in



**Figure 3.3: Network analysis classifies the CSF proteome into modules associated with specific brain cell-types and gene ontologies.** (A) Weighted Gene Co-expression Network Analysis cluster dendrogram groups proteins (n=1840) into 14 distinct protein modules (M1-M14). (B) Cell-type enrichment was assessed by cross referencing module proteins by matching gene symbols using a one-tailed Fisher's exact test against a list of proteins determined to be enriched in neurons, oligodendrocytes, astrocytes, microglia and endothelia. The degree of cell-type enrichment increases from yellow to dark green with asterisks denoting the following statistical significance (\* $p \leq 0.05$ ; \*\* $p \leq 0.01$ ; \*\*\* $p \leq 0.001$ ). Top gene ontology (GO) terms were selected from significant GO annotations.

modules M3 (i.e., NID2, ECM2, NID1, LTBP4, LAMA5, LAMC1), M9 (IGFBP7, F5, SDCBP, BGN) and M11 (FLNA, ANXA5, S100A11, MYL6) consistent with roles in extracellular matrix, angiogenesis and myofibril assembly, respectively. Thus, as seen in the network analysis of bulk proteome from human brain (236; 237), certain modules of co-expressed proteins in CSF were enriched with markers of specific brain cell-types. To further support this observation, we assessed the protein overlap between modules in CSF and modules from a recent large-scale consensus TMT-MS proteomic network of bulk human AD brain tissue (236). (**Figure 3.4**). Except for M9, M10 and M14, which had minimal overlap with the brain, all other modules (79% total) in the CSF network significantly overlapped with at least one of the 44 brain modules (B-M1 to B-M44). For example, there is overlap with CSF proteins in M1 “Postsynaptic Membrane” with several neuronal modules in the consensus brain network (B-M1, B-M4, B-M5, B-M10, and B-M15). In addition, M2 “Complement Activation” in CSF overlaps with modules in human brain associated with complement and immune response (B-M26 and B-M40), whereas M3 “Extracellular Matrix” strongly overlap with B-M27 in brain enriched with endothelial cell markers (**Figure 3.4**). Collectively, this supports that the co-expression in protein levels is, in part, shared between CSF and brain tissue, which could reflect changes in activation or phenotypes of specific brain cell types.

#### *3.2.4 CSF protein modules correlate to race and clinicopathological phenotypes of AD*

We assessed module correlation to race, cognitive scores (MoCA), and the hallmark AD biomarkers A $\beta$ <sub>42</sub>, tTau, and pTau<sub>181</sub>. The protein network resulted in three main groups/clusters based on module relatedness (**Figure 3.5A**). The first cluster (Group 1) was comprised of four modules (M2 “Complement Activation”, M5 “Lysosome / Catabolism”, M3 “Extracellular Matrix”, and M9 “Angiogenesis / Cell Migration”. Of these modules, M3 and M9 exhibited baseline racial differences in abundance levels (**Figure 3.5B**). Notably, the eigenprotein, which corresponds to

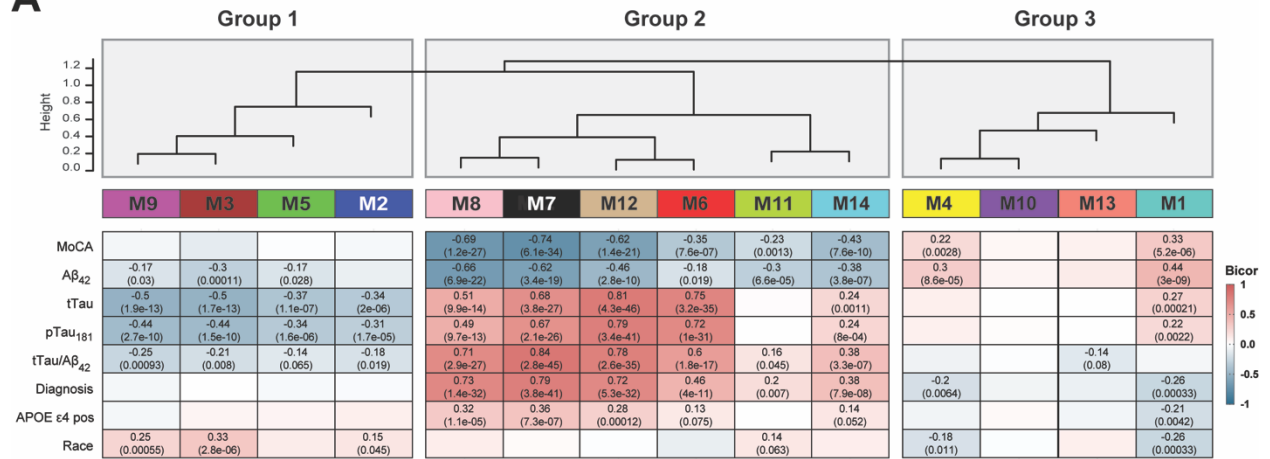
# B



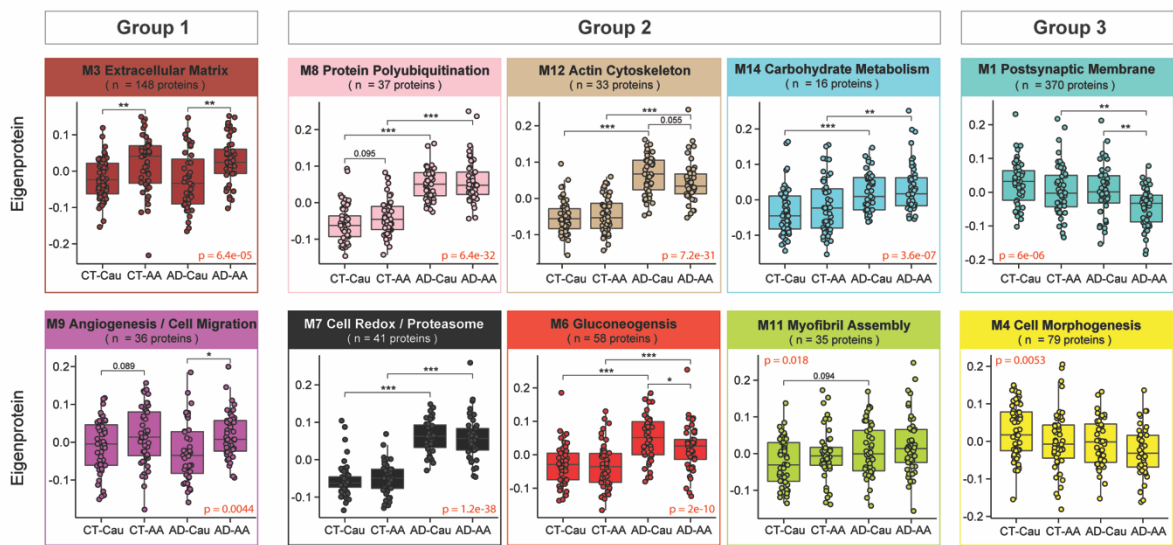


**Figure 3.4: Protein overlap between modules in CSF network and modules in a human AD brain network.** (A) Protein module enrichment across the CSF and brain was assessed by matching gene symbols of proteins in each module from the CSF network against gene symbols for protein in each module from a human AD consensus brain network using a one-tailed Fisher's exact test. The degree of enrichment increases from pink to light purple to dark purple with asterisks denoting the following statistical significance (\*\* $p \leq 0.01$  and \*\*\* $p \leq 0.001$ ). (B) Similar to CSF, cell-type enrichment was assessed by cross referencing brain module proteins against a list of proteins determined to be enriched in neurons, oligodendrocytes, astrocytes, and microglia using a one-tailed Fisher's exact test. The degree of cell-type enrichment increases from yellow to green-yellow to dark green with asterisks denoting the following statistical significance (\*\* $p \leq 0.01$  and \*\*\* $p \leq 0.001$ ).

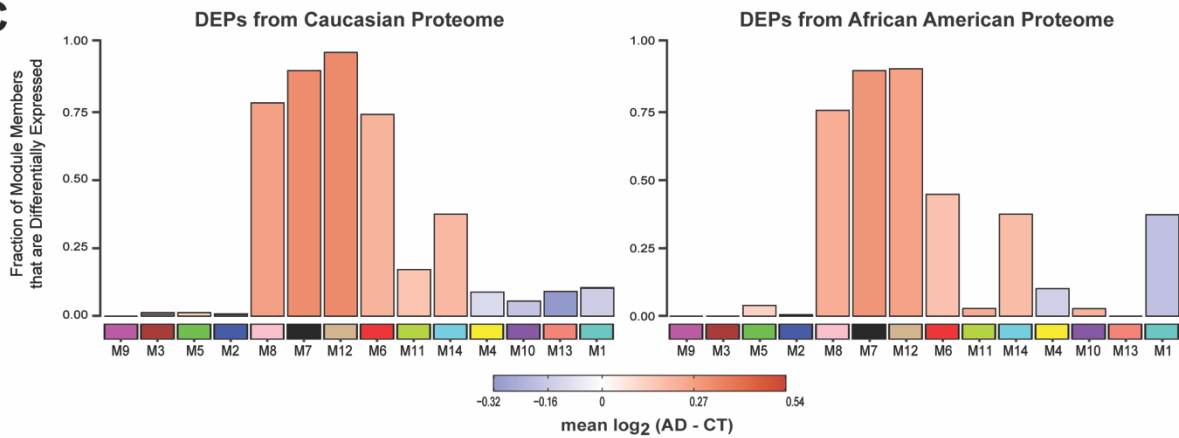
**A**



**B**



**C**

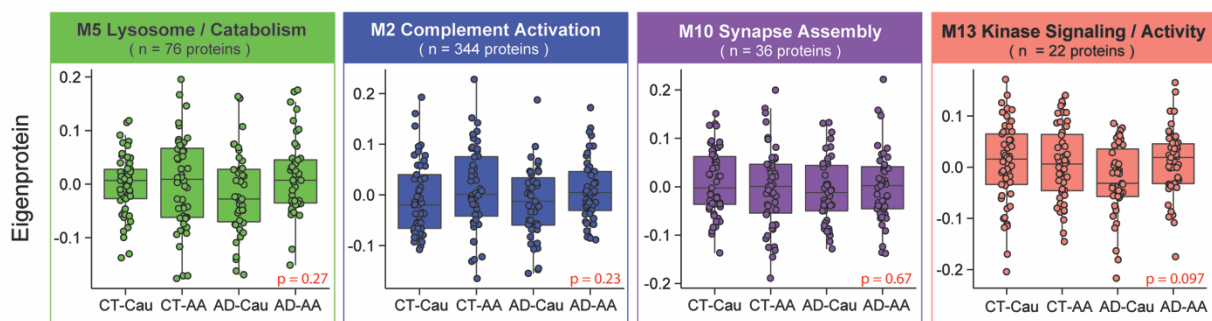


**Figure 3.5: CSF protein modules correlate to race and clinicopathological phenotypes of AD.** (A) Modules were clustered based on relatedness defined by correlation of protein co-expression eigenproteins (indicated by position in color bar). There were three main clusters in the network: Groups 1, 2 and 3. Biweight midcorrelation (bicor) analysis of module eigenprotein levels with diagnostic measures of AD, including MoCA score, immunoassay Amyloid-beta<sub>1-42</sub> (A $\beta$ <sub>42</sub>), total Tau (tTau), phosphorylated Tau<sub>181</sub> (pTau<sub>181</sub>), ratio measures of tTau/A $\beta$ <sub>42</sub>, diagnosis, whether the sample has *APOE*  $\epsilon$ 4 allele or not, and race. The strength of positive (red) and negative correlations are shown by a heatmap with annotated bicor correlations and associated p-values. (B) Eigenprotein values distributed by race and diagnosis of representative modules for each cluster. (C) Differential protein abundance AD samples compared to controls, by module with Caucasian proteome on the left and African Americans on the right. The height of the bars represents the fraction of module member proteins that DEPs compared to controls. The bars are color coded by heatmap for average log<sub>2</sub> difference in abundance, where red represents an increase in abundance in AD, and blue represents a decrease in abundance in AD.

the first principal component of a given module and serves as a summary expression profile for all proteins within a module, were increased for these two modules in African Americans compared to Caucasians. Of note, these modules were enriched with endothelial cell markers (**Figure 3.3B**) which suggests that genetic ancestry and/or environmental differences influence expression or secretion of these cell-type markers. Similarly, M2 and M5, both of demonstrated enrichment for microglial markers, trended towards higher levels in both African American controls and AD (**Figure 3.3B and 3.6**), suggesting an accompanying immune response to the vascular alterations seen in modules M3 and M9.

The second cluster of modules (Group 2) was comprised of six modules (M8, M7, M12, M6, M11, and M14) that were all increased in AD (**Figure 3.5A**). These AD modules also demonstrated significant negative correlations to MoCA scores and, conversely, significant positive correlations to tTau/A $\beta_{42}$  ratio. With the exception of M11, these modules also exhibited positive correlations to APOE  $\epsilon 4$  risk (**Figure 3.5A**). Interestingly, a hub protein of the M12 “Actin Cytoskeleton” module was Tau (MAPT). Consistent with CSF levels observed for Tau by immunoassay and TMT-MS (**Figure 3.1B and C**), the M12 eigenprotein had lower levels in African Americans, compared to Caucasians with AD, albeit not significant ( $p=0.055$ ) (**Figure 3.5B**). Notably, M6 “Gluconeogenesis” was significantly lower in African Americans compared to Caucasians with AD, highlighting another module of CSF proteins that differed by race in AD (**Figure 3.5A and B**). This also indicated that the increased glycolytic signature of AD previously reported in CSF (237; 252) is higher in Caucasians with AD. Consistently, a greater proportion of increased DEPs in Caucasians with AD mapped to M6 compared to African Americans with AD (**Figure 3.5C**). In contrast, M7 “Cell Redox / Proteasome” and M8 “Protein Polyubiquitination”, had the strongest correlations to tTau/A $\beta_{42}$  ratio and cognition (**Figure 3.5B**), and both demonstrated strong, equivalent elevations in African Americans and Caucasians with AD (**Figure 3.5B**). This is consistent with an equivalent fraction of increased DEPs mapping to these modules in African American and Caucasians with AD (**Figure 3.5C**). Therefore, proteins in these

**A**



**Figure 3.6: Additional CSF network protein modules.** (A) Eigenprotein levels were distributed by race and diagnosis for remaining modules not shown in main Figure 4. This includes M5, M2, M10, and M13.

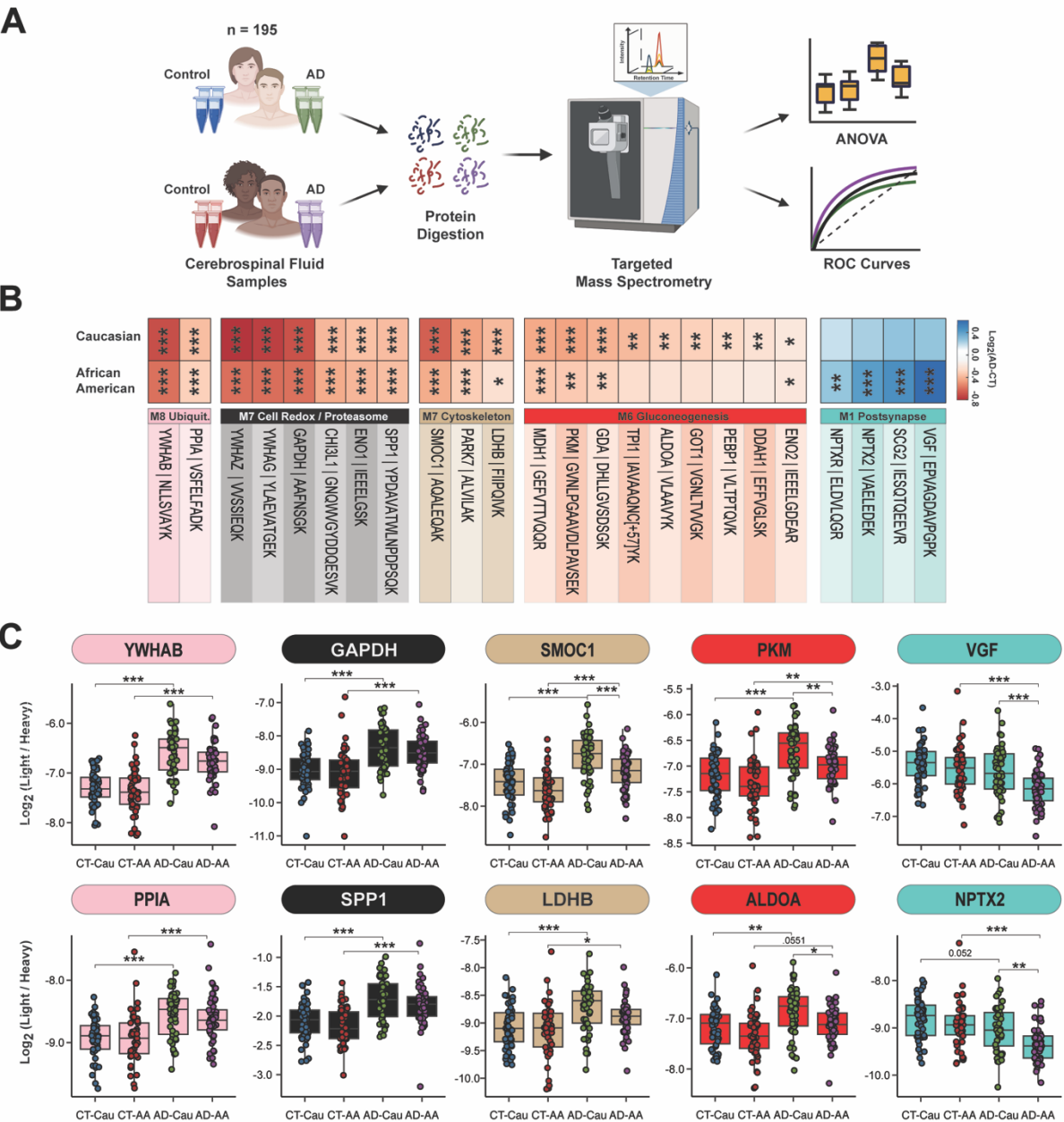
modules including 14-3-3 family members (YWHAZ, YWAHB, YWHAG, YWHAE) likely represent the best class of CSF AD biomarkers that are not influenced by race. M14 “Carbohydrate Metabolism” and M11 “Myofibril Assembly” were both elevated in both African Americans and Caucasians with AD (**Figure 3.5A and B**), yet to a lesser degree than M7 and M8.

The final group of modules (Group 3) contained two modules, M1 “Postsynaptic Membrane” and M4 “Cell Morphogenesis”, that showed strong correlations to both race and AD diagnosis (**Figure 3.5A**). Both modules were i) decreased in AD compared to controls and ii) and were lower in African Americans compared to Caucasians. In addition, both M1 and M4 were enriched with neuronal markers and positively associated with cognitive MoCA scores (**Figure 3.5A**). Markedly, pairwise statistical analysis of eigenprotein levels for M1 across diagnosis and race revealed significantly lower levels in African Americans with AD (**Figure 3.5B**). To this end, most of the decreased DEPs in African Americans with AD mapped to M1 and to a lesser degree M4, whereas decreased DEPs in Caucasians with AD were equally distributed to M1, M4, M13 and M10 (**Figure 3.5C**). Notably, M10 and M13 within Group 3 did not show any differences with AD or race and did not significantly correlate with traits explored in this study (**Figure 3.5 and Figure 3.6**). Overall, network analysis effectively organizes the CSF proteome into protein modules that are strongly linked to hallmark AD biomarkers ( $A\beta_{42}$ , tTau and pTau<sub>181</sub>) and cognition, which in some cases were also influenced by race.

### **3.3 Selected reaction monitoring validates protein alterations across Alzheimer's disease and race**

To further validate these network findings, we used a targeted mass spectrometry method, selected reaction monitoring (SRM), with heavy labeled internal standards to measure CSF proteins across 195 of the 203 cases included in the discovery TMT-MS assays (**Figure 3.7A**). The proteins and corresponding targeted peptides were previously selected based on their robust

detection and significant differential expression in previous CSF discovery proteomic datasets



Part A of this figure was created with BioRender.com



**Figure 3.7 Validation of shared and divergent CSF protein levels across AD and race. (A)**

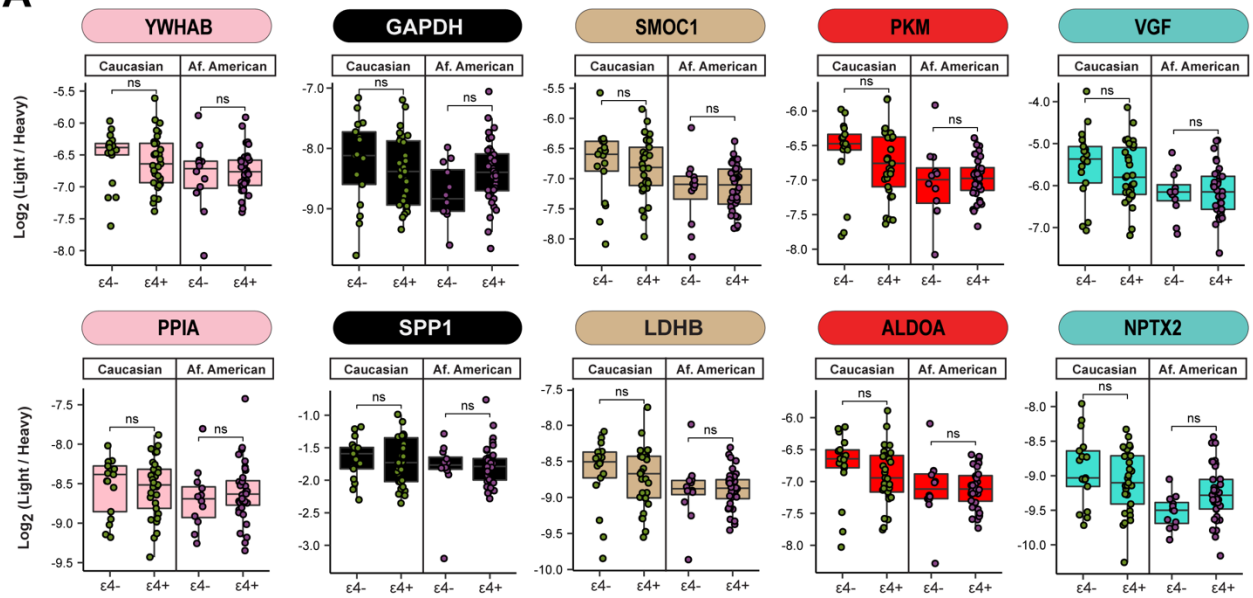
Schematic of experimental workflow for SRM analysis of cerebrospinal fluid proteome **(B)**

Heatmap of peptides that were significantly differentially expressed between Control and AD Caucasians or African Americans. Stars are indicative of the level of significant difference (\* $p \leq 0.05$ ; \*\* $p \leq 0.01$ ; \*\*\* $p \leq 0.001$ ) seen for each peptide between AD and Control within each race.

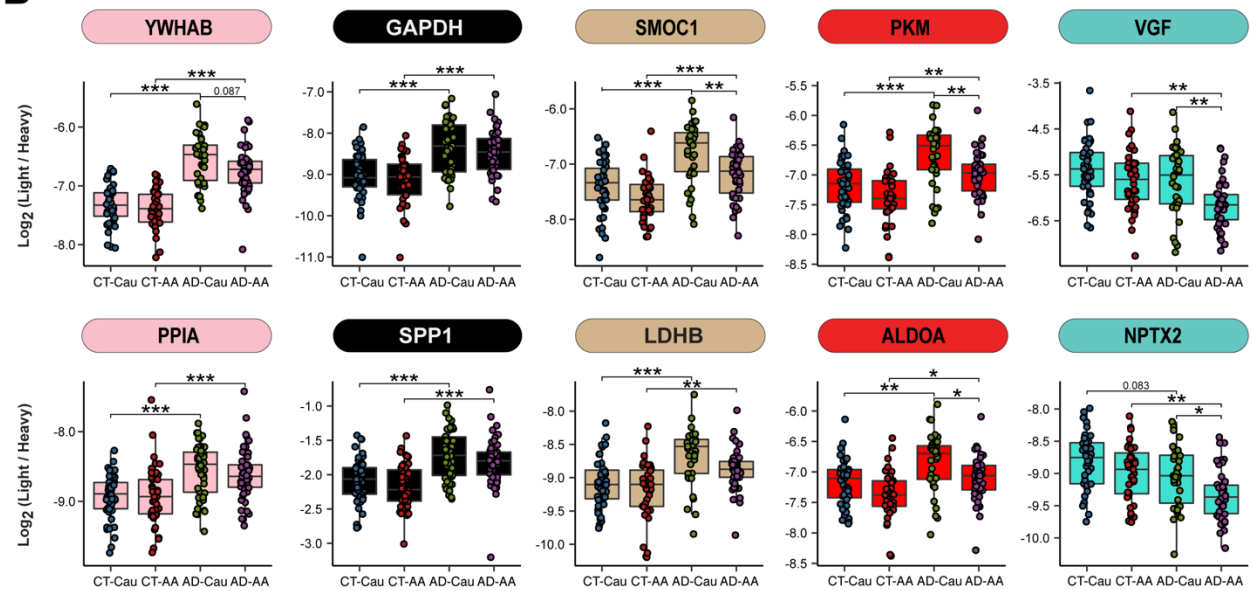
Meanwhile the colors are indicative of the  $\log_2$  fold change (FC) of each peptide from Control and AD for each race where blue is indicative of the degree of decrease and shade of red is indicative of the degree of increase. **(C)**  $\log_2$  abundance of peptides that mapped to modules of interest distributed by race and diagnosis. Pairwise significance was calculated using one-way ANOVA with Tukey adjustment.

(252; 268). We used pooled CSF samples of control, and AD cases as quality controls replicates (n=29 samples total) to assess technical reproducibility. Of the peptides targeted, 85 (mapping to 58 proteins) had a coefficient of variation of <20% in both the control and AD pools with no missing values (**Appendix Tables 6.4**). Following adjustments of co-variates (i.e., age and sex), peptide levels were highly correlated with protein levels measured by TMT-MS from the same samples (**Appendix Table 6.6**). If a protein was measured by more than one peptide the most correlated peptide to the TMT-MS protein level was selected for further analysis. The final peptide list can be found in **Appendix Table 6.7**. ANOVA analyses determined pairwise significance between the four groups (i.e., Control-Caucasians vs Control-African Americans vs AD-Caucasians vs AD-African Americans, **Appendix Table 6.8**). **Figure 3.7B** highlights peptides (n=24) that reached significance and that mapped to proteins in CSF modules associated with race and/or AD. Consistent with the TMT-MS protein measurements, proteins measured by SRM within M7 (GAPDH and YWHAG) and M8 (YWAHB and PPIA) had strong elevations ( $p < 0.001$ ) in abundance in AD in both races, whereas proteins in M12 (SMOC1, PARK7, and LDHB) had a greater magnitude of change in Caucasians than African Americans with AD (for a list of all M12 members, see Supplemental Table 6) . Similarly, a majority of the proteins measured by SRM in M6 (PKM, GDA, TPI1, GOT1, ALDOA and ENO2) were more increased in Caucasians than African Americans with AD (**Figure 3.7B and C**). Proteins in the synaptic M1 module (VGF, SCG2, NPTX2, and NPTXR) were significantly decreased in African Americans with AD compared to Caucasians (**Figure 3.7B and C**), again consistent with TMT-MS protein level abundance. Notably, African Americans with or without APOE  $\epsilon 4$  allele in the AD group had reduced levels of these CSF peptide biomarkers compared to Caucasians indicating that race and not APOE status was driving the difference in abundance (**Figure 3.8A**). Furthermore, these differences across race remained consistent even after removing patients with one or more comorbid condition (i.e., hypertension, diabetes, dyslipidemia, or cerebrovascular disease; **Figure 3.8B**).

**A**



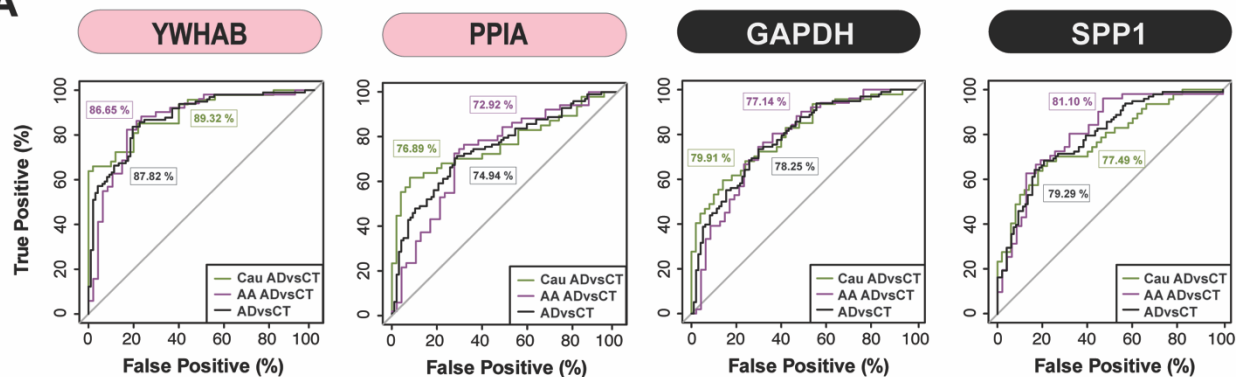
**B**



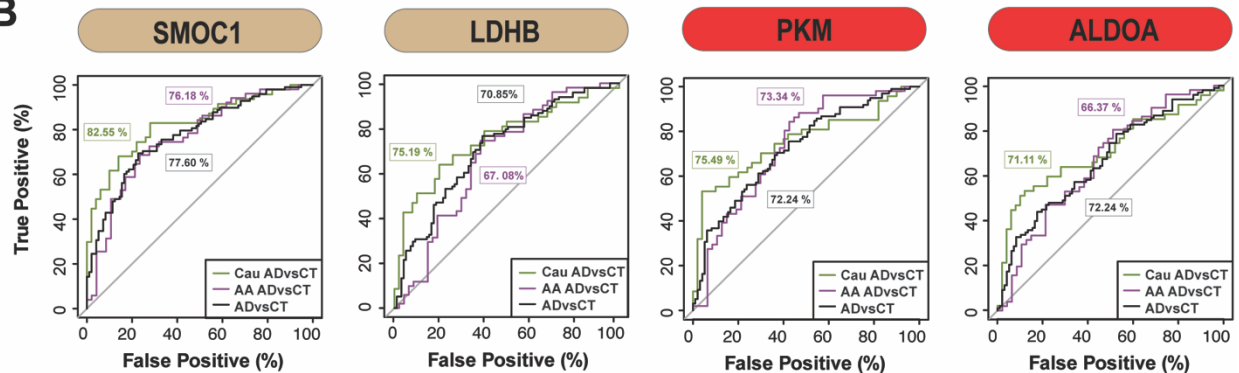
**Figure 3.8. Stratification of SRM CSF protein measurements by APOE genotype and comorbidity.** (A) Within each race, protein levels for were not affected by APOE  $\epsilon$ 4 genotype for YWHAB, GAPDH, SMOC1, PKM, VGF, PPIA, SPP1, LDHB, ALDOA, and NPTX2. (B) Within each race, protein levels were not affected by patient co-morbidities (hypertension, diabetes, dyslipidemia, or cerebrovascular disease) for YWHAB, GAPDH, SMOC1, PKM, VGF, PPIA, SPP1, LDHB, ALDOA, and NPTX2.

Finally, a receiver operating characteristic (ROC) curve analysis was performed to assess the performance of each peptide biomarker in differentiating controls and AD by race (**Figure 3.9 and Appendix Table 6.9**). We generated an area under the curve (AUC) for AD in African American and Caucasian individuals for each protein biomarker (considered separately in each race). As expected, proteins mapping to M8 and M7 including 14-3-3 proteins (YWHAB, YWHAG and YWHAZ) were equally able to discriminate AD from control irrespective of racial background. Notably, despite having lower levels in African Americans with AD compared to Caucasians with AD, only a modest improvement in the AUC for SMOC1 was observed for classifying AD in Caucasians AUC=0.8255 ( $p=1.71\text{e-}08$ , CI=0.7421-0.9090) compared to African Americans AUC=0.7618 ( $p=4.12\text{e-}06$ , CI=0.6660-0.8576). Similar findings were observed for another M12 protein, LDHB, as well as M6 proteins PKM and ALDOA. However, the M1 protein VGF was only nominally significant at classifying AD in Caucasian AUC=0.6030 ( $p=0.0406$ , CI=0.4887-0.7173), yet highly significant in African Americans AUC=0.7593 ( $p=5.03\text{e-}06$ , CI=0.6634-0.8552). Similar results were observed for other synaptic M1 proteins, NPTX2 and SCG2, whereas NPTXR showed only a modest improvement in the AUC between African Americans compared to Caucasians with AD (**Figure 4.9 and Appendix Table 7.15**). Collectively this supports a hypothesis that African Americans with AD have lower levels of a subset of neuronal biomarkers compared to Caucasians with AD.

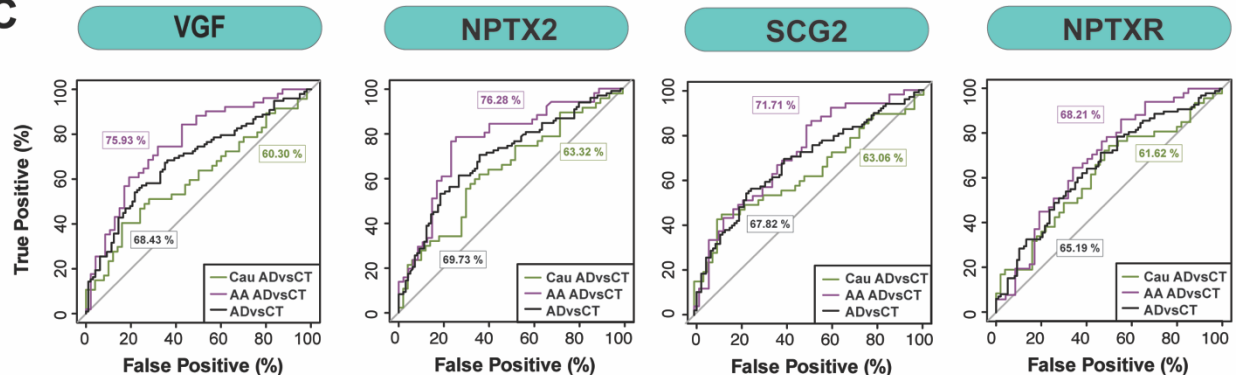
**A**



**B**



**C**



**Figure 3.9: ROC analysis evaluated CSF protein classification of AD by race.** (A) YWHAB, PPIA, GAPDH, and SPP1 had similar performance in classifying Caucasians and African Americans with AD (B) SMOC1, PKM, LDHB and ALDOA showed modest improvement in the AUC for Caucasians with AD compared to African Americans with AD (C) VGF, SCG2, and NPTX2 were better classifiers for AD in African Americans compared to Caucasians, whereas NPTXR showed modest improvement in classification of AD in African Americans. All protein AUCs with p-values and confidence intervals (CI) are provided in **Supplemental Table 15**.

## CHAPTER 4: DISCUSSION

Segments of this discussion were originally published in *Molecular Neurodegeneration*:

Modeste, E.S., Ping, L., Watson, C.M. *et al.* Quantitative proteomics of cerebrospinal fluid from African Americans and Caucasians reveals shared and divergent changes in Alzheimer's disease. *Mol Neurodegeneration* **18**, 48 (2023). <https://doi.org/10.1186/s13024-023-00638-z>



Here we performed an unbiased quantitative analysis of the CSF proteome to identify protein biomarkers reflective of underlying AD brain physiology that are shared or unique across race. Using network analysis, we organized the CSF proteome into 14 modules of proteins with highly correlated levels in CSF. Notably, these modules were associated with cell-types and biological pathways in brain and largely overlapped with modules from a consensus human AD brain proteomic network (236). Consistent with previous findings (261; 262), we also show that Tau levels were lower in African Americans with AD compared to Caucasians in CSF. Notably, Tau mapped to a CSF module enriched with other related neuronal/cytoskeletal proteins with a magnitude of increase greater in Caucasians than in African Americans with AD. This indicated that an entire network of proteins, rather than a single protein, is changing differently with disease between these two racial groups. In contrast, CSF modules which included 14-3-3 proteins, were elevated equivalently in both African Americans and Caucasians with AD, suggesting similar changes in pathophysiology. Lastly, a module enriched with neuronal/synaptic proteins including VGF, SCG2, and NPTX2 was significantly lower in African Americans than Caucasians with AD. These findings were consistent when VGF, SCG2, and NPTX2 levels in CSF were measured using SRM analysis, which also showed significantly better classification of African Americans with AD compared to Caucasians. Together, our findings suggest that there are likely distinct mechanisms underlying the abundance and/or secretion of neuronal markers including Tau and VGF that differ by race. Collectively, these data underscore the need for further investigations into how AD biomarkers and underlying physiology vary across different racial backgrounds.

#### **4.1 Protein co-expression between the brain and CSF reflects the intricate role of CSF in brain function and health.**

In a previous study we performed TMT-MS on a small discovery cohort of control and AD CSF samples (n=40) and mapped these proteins onto a human AD brain co-expression network, revealing that approximately 70% (n=1936) of the CSF proteome (N=2,875) overlapped

with the brain network (N=8817) (252). Additionally, it was found that 271 of the proteins that were significantly altered in the CSF were also differentially expressed in the brain (245). The increased sample size in this study afforded the opportunity to extend beyond this analysis by constructing an independent co-expression network on the CSF proteome and assessing its overlap with modules in a consensus brain network. This analysis revealed a strong overlap between CSF and brain modules, with 11 of the 14 CSF modules significantly overlapping with one or more brain modules, further supporting that protein co-expression in the brain is conserved in the CSF. These findings are not surprising considering the close relationship between CSF and brain. It is already known that substrates needed by the brain can be transported from the blood through the choroid plexus into the CSF, and then from the CSF into the extracellular space within the brain (269). Inversely, CSF aids in the removal of brain metabolism waste products, such as glycosylated proteins, excess neurotransmitters, and other unnecessary molecules, from the cerebral region (269). As a result of these exchanges, changes in brain chemistry can ultimately influence CSF composition, allowing the CSF to mirror neuropathological changes in the brain. Our studies suggests that the observed changes in CSF are mainly driven by cell-type alterations, as most CSF modules were enriched with either neuronal (M1, M4, M6, M10 and M12), glial (M2, M5, and M14), astrocyte (M4 and M5), oligodendrocyte (M1 and M3), and endothelial-specific markers (M3, M9, and M11). The remaining modules that did not exhibit enrichment with cell type markers represented processes related to cellular signaling (M13) and degradation pathways (M7 and M8), including kinase signaling and activity, protein polyubiquitination, and cell redox/proteasome processes. This reflects another crucial function of the CSF, which is aiding in the clearance of waste products from the brain (269). In conclusion, network analysis of the CSF underscores the intricate relationship between CSF and brain biology in AD, revealing shared protein alterations and cell-type enrichments across both compartments. These findings support our understanding of CSF as a conduit for biomarkers of neuropathological changes in AD and provide insights into the underlying mechanisms driving early disease progression.

#### **4.2 CSF network analysis indicated differences in endothelial markers across race, irrespective of disease, yet there is insufficient evidence to indicate that these differences stem from variations in endothelial damage.**

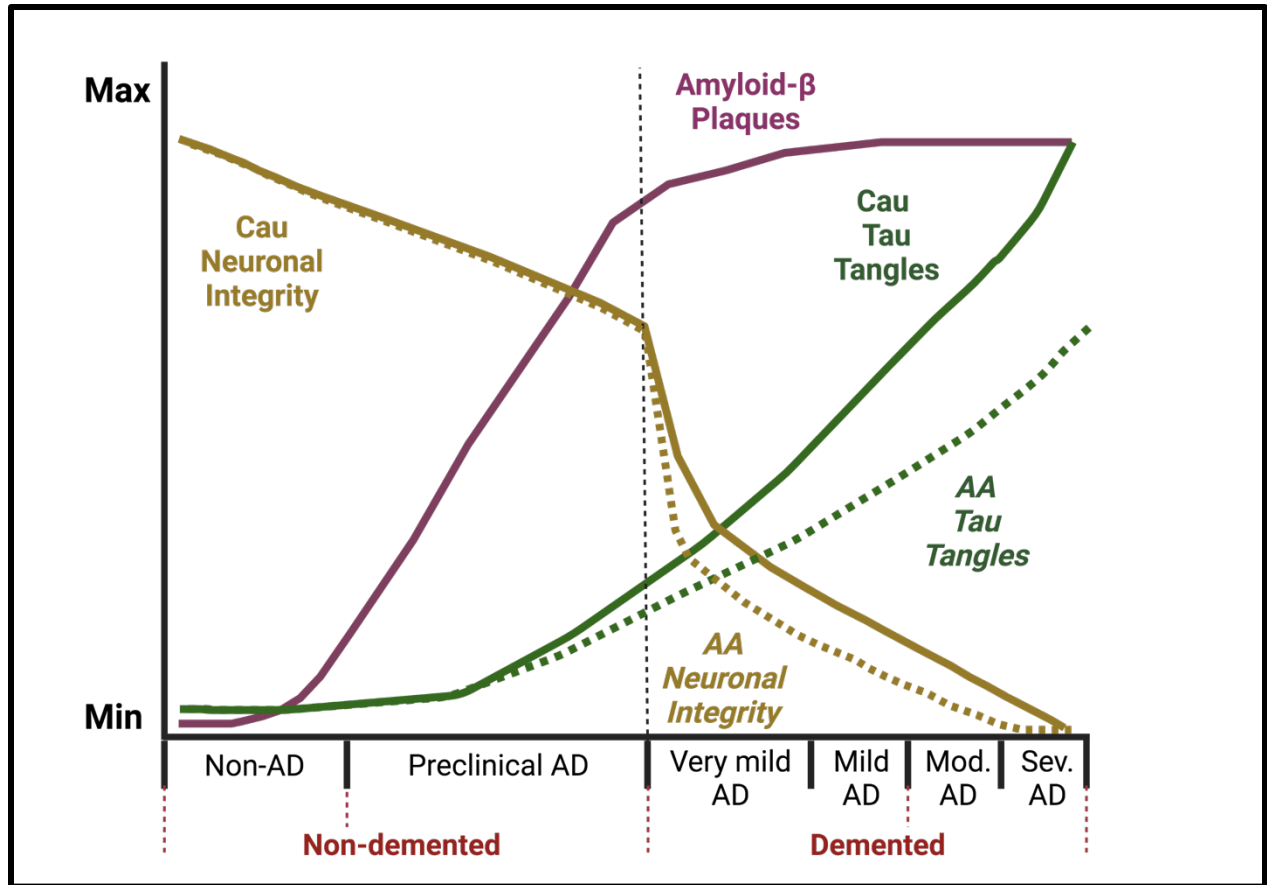
In regards to the CSF network biology that differed by race, it's noteworthy that modules significantly enriched in endothelial proteins (M3 and M9) were elevated in African Americans across both control and AD individuals. M3 is primarily comprised of extracellular matrix (ECM) proteins, and ECM proteins make up the dynamic network of macromolecules providing structural support for cells and tissues. In the brain, ECM proteins are vital for maintaining the integrity of the blood-brain barrier (BBB) and neurovascular units (262-265). ECM proteins in the BBB are crucial for preserving brain tissue homeostasis by preventing the entry of unwanted cells and molecules and by removing metabolic waste. Additionally, ECM proteins within the neurovascular unit play a crucial role in regulating cerebral blood flow (CBF), ensuring sufficient blood supply to meet the demands of neurons (266; 267). Consequently, malfunctioning ECM proteins in the brain can result in compromised function of both the BBB and neurovascular units. Notably, two critical vascular changes associated with AD are the breakdown of the BBB (270; 271) and compromised CBF (272). Moreover, these dysfunctions can subsequently trigger increases in proteins associated with angiogenesis, the process of forming new blood vessels. Pathological angiogenesis has been significantly implicated in perpetuating AD by fostering further A $\beta$  generation, which, in turn, can exacerbate BBB dysfunction and impaired CBF (273). It is noteworthy that the M9 module is enriched with proteins involved in angiogenesis and is also elevated in African Americans compared to Caucasians, irrespective of disease status. In conclusion, the increased presence of endothelial proteins among African Americans implies that vascular differences may play a role in the heightened susceptibility to AD within this demographic. This highlights the necessity for additional investigation into how differences in vascular health between racial groups may impact the susceptibility and advancement of AD.

Currently, growing evidence suggests that endothelial dysfunction plays a significant role in the cognitive decline associated with AD (268), raising the question of whether the elevated levels observed in African Americans could indicate such injury. Furthermore, endothelial impairment is common among individuals with atherosclerosis, hypertension, diabetes, and chronic kidney disease (266), conditions that are more prevalent in the African American population. Several studies have already highlighted plausible biomarkers for endothelial dysfunction (268). Osteopontin (OPN) (269; 270) and cell adhesion molecules like VCAM1 and ICAM1 (271-273) are indicators of vascular inflammation, while albumin (ALB) (274-277), soluble platelet-derived growth factor receptor-beta (sPDGFR $\beta$ ) (278), vasoactive molecules such as atrial natriuretic peptide (ANP), adrenomedullin (ADM), and B-type natriuretic (BNP) (279; 280), metalloproteinases (MMPs) (281-286), and blood coagulation proteins like fibrinogen (FGB) (287) and plasminogen activator inhibitor-1 (PAI1) (288) reflect vascular damage. Additionally, growth factors such as vascular endothelial cadherin (VEGF) (289-297), angiogenin (ANG) (292; 298), and angiopoietin-1 (ANG1) (299) have been shown to be altered during endothelial injury. When overlaying these indicators over proteins assigned to module memberships in the CSF proteome, it was found that only one of these markers, ANG, mapped to M9 or M3. Most of the other proteins identified within this CSF proteome (ICAM1, CDH5, ALB, MMP2, FGB) mapped to the blue module, which remained largely unchanged across both control and AD groups as well as between races. One exception was sPDGFR $\beta$ , which mapped to the M1 module. Increased CSF levels of sPDGFR $\beta$  have been linked to BBB breakdown in individuals with mild cognitive impairment (274). It has also been demonstrated that heightened levels of sPDGFR $\beta$  correlate with cognitive decline in the early stages of AD (275). Nevertheless, the module members of M1 decrease with disease progression, and even exhibit even greater declines in African Americans. Remarkably, alongside being identified as elevated in AD, sPDGFR $\beta$  levels have been noted to be lower in African Americans compared to Caucasians (276). Together, the data is insufficient to support that the elevated levels of endothelial markers observed in African Americans in this

study are indicative of endothelial impairment or injury. However, this study still indicates fundamental differences in the levels and/or activation states of cells residing in the vasculature between African Americans and Caucasians. Whether this biological difference is observed in brain tissues or relates to a higher incidence of vascular health disparities between African Americans and Caucasians (300) requires further investigation. Genomic analysis could prove invaluable in this endeavor, shedding light on whether these elevations are attributable to genetic variations. Furthermore, it is crucial to consider the influence of social determinants of health, such as education, socioeconomic status, and exposure to adversity and discrimination, on overall health, and thus AD risk and progression. Future studies should aim to integrate CSF protein levels with vascular risk factors, environmental metrics, and sociodemographic data to better elucidate the underlying racial differences in the CSF proteome. This holistic approach will help uncover the complex interplay between genetic, environmental, and social factors that contribute to AD pathogenesis and inform on the development of targeted interventions for diverse populations.

#### **4.3 Unveiling the interplay between neuronal alterations in AD and the role of the CSF in mirroring cognitive decline**

The current biological framework for the pre-symptomatic stages of AD is based on the presence of A $\beta$  deposition (A), tauopathy (T), and neurodegeneration (N) also termed the A/T/N framework (277). CSF remains the gold standard for A/T/N biomarkers of neurodegenerative disease as it maintains direct contact with the brain and reflects biochemical changes in amyloid (**Figure 4.1, purple line**), Tau (**green line**) and neurodegeneration (**yellow line**). A strength of our study was the balanced nature of African American samples, which offered the ability to examine racial differences in both cognitively normal controls with individuals diagnosed with AD. Our mass spectrometry measurements of Tau strongly correlated with immunoassay levels



Created with BioRender.com

**Figure 4.1: Hypothesized time course differences in neuropathological and clinical changes based on biomarker alterations between Caucasians and African Americans with Alzheimer's disease.** In Alzheimer's disease (AD), the conversion from a non-demented to demented state is associated with a buildup of amyloid-beta ( $A\beta$ ) plaques (purple line), the accumulation of neurofibrillary Tau tangles (green line), and neuronal and synaptic loss (yellow line). Based on biomarker studies, the trajectory of change for the accumulation of Tau and the subsequent neuronal loss differs in African Americans with AD (dashed lines).

measured on the Roche Elecsys platform reinforcing measurements made by TMT-MS. Increased Tau in CSF is considered to result from neurodegeneration, however, it has also been shown to be increased in early pre-symptomatic disease stages when neurodegeneration is limited (277; 278) (**Figure 4.1, preclinical AD**). Recently, Tau CSF levels have been linked to enhanced synaptic plasticity where high levels of CSF Tau levels can be reflective of increased neuronal plasticity (279). Network analysis revealed a cluster of proteins, M12, along with another module, M6, exhibiting similar fluctuations in levels as Tau across racial groups, suggesting the involvement of other proteins that may function similarly to Tau in early disease synaptic plasticity. Other proteins that have been associated with synaptic plasticity include Calcium/calmodulin-dependent protein kinase II (CaMKII), cAMP-response element binding protein (CREB), Protein Kinases A and B (PRKAC1A and PRKAC1B), and growth-associated protein (GAP43) (269-273). Interestingly, all these proteins, including CAMK2A, CAMK2B, PRKAC1A, PRKAC1B, and GAP43, were categorized within the M6 module, indicating the potential association of other proteins within this module in synaptic plasticity. Further exploration of these proteins and their implications in racial disparities could provide valuable insights into AD pathogenesis and aid in developing targeted interventions.

Significantly, a considerable portion of synaptic proteins identified in this study aligned with M1 and M4. These modules demonstrated an overall decrease in levels with cognitive decline. We, also, observed that African Americans in this study had on average lower levels of neuronal markers mapping to M1 and M4 in the network, which are reduced in AD. Paradoxically, African Americans also have lower levels of neuronal proteins in M6 and M12, which all increase in AD. Consistent with this observation, in a recent CSF proteomic study in an asymptomatic Caucasian European population stratified by Tau CSF levels, individuals deemed to have high Tau levels maintained levels of M1 post-synaptic proteins (CADM3, NEO1, NPTX1, CHGB, PCSK1, NEGR, L1CAM, PTPRN, CACNA2D, PAM, VEGFA, NBL1 etc.) compared to individuals with lower Tau levels (279). This observation is analogous to differences we see between African



Americans and Caucasians with AD. M1 members VGF and NPTX2, strongly correlate to antemortem cognitive measures (280-282) and VGF and NPTX2 have been nominated as biomarkers of neurodegeneration (N) as their CSF levels enhance prediction of MCI to AD (282-284). Collectively, this would suggest that a specific sub-group of individuals with AD, including African Americans, have a higher burden of neurodegeneration (N) despite low CSF Tau levels (**Figure 4.1, dashed lines**). Longitudinal studies examining changes in CSF levels of neuronal proteins and other module constituents over time, with a specific focus on diverse racial populations, will be essential. By tracking the temporal patterns of protein biomarkers, researchers can gain a better understanding of critical timeframes for potentially delaying cognitive decline associated with the disease and addressing racial disparities in disease progression. Moreover, longitudinal studies can offer insights into the efficacy of therapeutic interventions and assist in devising personalized treatment approaches.

Collectively, these data suggest that there are likely distinct mechanisms responsible for the dysregulation of neuronal proteins, resulting in two separate pools of neuronal proteins that either go up or down with disease in CSF. Further investigations should be conducted to explore the distinct mechanisms that contribute to the differences in abundance and/or secretion of neuronal markers such as Tau and other proteins increased in AD CSF like CAMK2A, SNCB, and SYN1. In conjunction, the interplay between the neuronal markers that increase and neuronal markers that decrease with disease like VGF, NPTX2, and SCG2, which have also been found to differ by race, should be further explored.

#### **4.4 Future directions**

Although a strength of our study was the large number of African Americans included, there are several limitations that should be noted. First, we acknowledge that many of the protein changes we observe in the CSF across race could be due to ancestral or genetic differences (285; 286). There were no genetics *a priori* performed on these study participants to confirm

enrichment of African *vis a vis* European ancestry (287) as we stratified race solely by self-identification. Future studies, which include the integration of genetics and protein abundance to define protein quantitative trait loci (pQTL) will be necessary to resolve which proteins are under genetic control across race (288-290). It is noteworthy that the expression level of most modules which differed between racial groups were decreased in African Americans relative to Caucasians. Upon integration with whole genome profiling of larger cohorts, these patterns may help in the future to identify pQTLs or other mechanisms influencing synthesis and turnover of proteins that differ by race. Additionally, only a few studies to date have investigated proteomic difference by race in AD (291; 292), which have predominately focused on brain tissues and not on the scale of this current study. However, a major initiative of the Accelerating Medicine Partnership (AMP)-AD partnership (293) is to increase the number of diverse tissues included in multi-omic analyses, which will complement data generated from these previous studies. To support this effort, 81 brain tissue samples, obtained from Emory's Alzheimer's Disease Research Center, were prepared for future analysis. These samples have since been integrated with brain tissues from other AMP-AD partners, broadening the scope of the large-scale brain analyses (294; 295). Furthermore, despite the well documented differences in the quality of education, higher rates of poverty, and greater exposure to adversity and discrimination that increase risk for dementia (214; 215), these metrics were not captured on the participants in this study. Integrating CSF protein levels with vascular risk factors, and other environmental metrics in larger cohorts may help better resolve some of the underlying racial differences in the CSF proteome. Finally, in this study we adjusted for co-factors such as age and sex to pinpoint changes that are most likely to be associated with race and AD. Sex and age have an impact on the abundance of CSF Tau and other protein levels (296). Therefore, future studies that assess the interactions between, age, sex and race will be informative. Nevertheless, this study reveals an impressive view of protein co-expression in AD CSF across race, which provides new insights into the pathways underlying cell-type changes and further evidence that race may mediate these in AD. Future

directions in AD research should aim to unravel the distinct mechanisms underlying racial differences in AD biomarkers and underlying physiology. Integrating genetic, proteomic, and sociodemographic data, along with longitudinal investigations, will contribute to a more comprehensive understanding of AD pathogenesis and facilitate the development of targeted interventions for diverse populations affected by AD.

## CHAPTER 5: REFERENCES

1. 2022. 2022 Alzheimer's disease facts and figures. *Alzheimers Dement* 18:700-89
2. 2023. 2023 Alzheimer's disease facts and figures. *Alzheimers Dement* 19:1598-695
3. Corder EH, Saunders AM, Risch NJ, Strittmatter WJ, Schmechel DE, et al. 1994. Protective effect of apolipoprotein E type 2 allele for late onset Alzheimer disease. *Nat Genet* 7:180-4
4. Corder EH, Saunders AM, Strittmatter WJ, Schmechel DE, Gaskell PC, et al. 1993. Gene dose of apolipoprotein E type 4 allele and the risk of Alzheimer's disease in late onset families. *Science* 261:921-3
5. Masters CL, Bateman R, Blennow K, Rowe CC, Sperling RA, Cummings JL. 2015. Alzheimer's disease. *Nat Rev Dis Primers* 1:15056
6. Stocco A, Coppede F. 2018. Role of epigenetics in Alzheimer's disease pathogenesis. *Neurodegener Dis Manag* 8:181-93
7. Hebert LE, Beckett LA, Scherr PA, Evans DA. 2001. Annual incidence of Alzheimer disease in the United States projected to the years 2000 through 2050. *Alzheimer Dis Assoc Disord* 15:169-73
8. Hebert LE, Weuve J, Scherr PA, Evans DA. 2013. Alzheimer disease in the United States (2010-2050) estimated using the 2010 census. *Neurology* 80:1778-83
9. Baker DJ, Petersen RC. 2018. Cellular senescence in brain aging and neurodegenerative diseases: evidence and perspectives. *J Clin Invest* 128:1208-16
10. Fasnacht JS, Wueest AS, Berres M, Thomann AE, Krumm S, et al. 2023. Conversion between the Montreal Cognitive Assessment and the Mini-Mental Status Examination. *J Am Geriatr Soc* 71:869-79
11. Nasreddine ZS, Phillips NA, Bedirian V, Charbonneau S, Whitehead V, et al. 2005. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* 53:695-9
12. Folstein MF, Folstein SE, McHugh PR. 1975. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 12:189-98
13. Hlavka JP, Kinoshita AT, Fang S, Hunt A. 2021. Clinical Outcome Measure Crosswalks in Alzheimer's Disease: A Systematic Review. *J Alzheimers Dis* 83:591-608
14. Ihl R, Frolich L, Dierks T, Martin EM, Maurer K. 1992. Differential validity of psychometric tests in dementia of the Alzheimer type. *Psychiatry Res* 44:93-106
15. Tombaugh TN, McIntyre NJ. 1992. The mini-mental state examination: a comprehensive review. *J Am Geriatr Soc* 40:922-35
16. Wind AW, Schellevis FG, Van Staveren G, Scholten RP, Jonker C, Van Eijk JT. 1997. Limitations of the Mini-Mental State Examination in diagnosing dementia in general practice. *Int J Geriatr Psychiatry* 12:101-8
17. Salis F, Costaggu D, Mandas A. 2023. Mini-Mental State Examination: Optimal Cut-Off Levels for Mild and Severe Cognitive Impairment. *Geriatrics (Basel)* 8
18. Carson N, Leach L, Murphy KJ. 2018. A re-examination of Montreal Cognitive Assessment (MoCA) cutoff scores. *Int J Geriatr Psychiatry* 33:379-88
19. Damian AM, Jacobson SA, Hentz JG, Belden CM, Shill HA, et al. 2011. The Montreal Cognitive Assessment and the mini-mental state examination as screening instruments for cognitive impairment: item analyses and threshold scores. *Dement Geriatr Cogn Disord* 31:126-31
20. Dalrymple-Alford JC, MacAskill MR, Nakas CT, Livingston L, Graham C, et al. 2010. The MoCA: well-suited screen for cognitive impairment in Parkinson disease. *Neurology* 75:1717-25

21. Freitas S, Simoes MR, Alves L, Santana I. 2013. Montreal cognitive assessment: validation study for mild cognitive impairment and Alzheimer disease. *Alzheimer Dis Assoc Disord* 27:37-43
22. Dong Y, Lee WY, Basri NA, Collinson SL, Merchant RA, et al. 2012. The Montreal Cognitive Assessment is superior to the Mini-Mental State Examination in detecting patients at higher risk of dementia. *Int Psychogeriatr* 24:1749-55
23. Freitas S, Simoes MR, Alves L, Santana I. 2012. Montreal Cognitive Assessment: influence of sociodemographic and health variables. *Arch Clin Neuropsychol* 27:165-75
24. Malek-Ahmadi M, Powell JJ, Belden CM, O'Connor K, Evans L, et al. 2015. Age- and education-adjusted normative data for the Montreal Cognitive Assessment (MoCA) in older adults age 70-99. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn* 22:755-61
25. Gagnon G, Hansen KT, Woolmore-Goodwin S, Gutmanis I, Wells J, et al. 2013. Correcting the MoCA for education: effect on sensitivity. *Can J Neurol Sci* 40:678-83
26. Rossetti HC, Lacritz LH, Cullum CM, Weiner MF. 2011. Normative data for the Montreal Cognitive Assessment (MoCA) in a population-based sample. *Neurology* 77:1272-5
27. Larouche E, Tremblay MP, Potvin O, Laforest S, Bergeron D, et al. 2016. Normative Data for the Montreal Cognitive Assessment in Middle-Aged and Elderly Quebec-French People. *Arch Clin Neuropsychol* 31:819-26
28. Goldstein FC, Ashley AV, Miller E, Alexeeva O, Zanders L, King V. 2014. Validity of the montreal cognitive assessment as a screen for mild cognitive impairment and dementia in African Americans. *J Geriatr Psychiatry Neurol* 27:199-203
29. Sink KM, Craft S, Smith SC, Maldjian JA, Bowden DW, et al. 2015. Montreal Cognitive Assessment and Modified Mini Mental State Examination in African Americans. *J Aging Res* 2015:872018
30. Milani SA, Marsiske M, Cottler LB, Chen X, Striley CW. 2018. Optimal cutoffs for the Montreal Cognitive Assessment vary by race and ethnicity. *Alzheimers Dement (Amst)* 10:773-81
31. Stelzma RA, Schnitzlein HN, Murlagh FR. 1995. An English l'ranslation of Alzheimer's 1907 Paper, "ijber eine eigenartige Erlranliung der Hirnrinde. *Clinical anatomy* 8:429-31
32. Karran E, Mercken M, De Strooper B. 2011. The amyloid cascade hypothesis for Alzheimer's disease: an appraisal for the development of therapeutics. *Nat Rev Drug Discov* 10:698-712
33. McGeer PL, McGeer EG. 2013. The amyloid cascade-inflammatory hypothesis of Alzheimer disease: implications for therapy. *Acta Neuropathol* 126:479-97
34. Ballatore C, Lee VM, Trojanowski JQ. 2007. Tau-mediated neurodegeneration in Alzheimer's disease and related disorders. *Nat Rev Neurosci* 8:663-72
35. Selkoe DJ. 1989. Amyloid beta protein precursor and the pathogenesis of Alzheimer's disease. *Cell* 58:611-2
36. Selkoe DJ. 1998. The cell biology of beta-amyloid precursor protein and presenilin in Alzheimer's disease. *Trends Cell Biol* 8:447-53
37. Zhang YW, Thompson R, Zhang H, Xu H. 2011. APP processing in Alzheimer's disease. *Mol Brain* 4:3
38. Kasim JK, Kavianinia I, Harris PWR, Brimble MA. 2019. Three Decades of Amyloid Beta Synthesis: Challenges and Advances. *Front Chem* 7:472
39. Chen GF, Xu TH, Yan Y, Zhou YR, Jiang Y, et al. 2017. Amyloid beta: structure, biology and structure-based therapeutic development. *Acta Pharmacol Sin* 38:1205-35
40. Roche J, Shen Y, Lee JH, Ying J, Bax A. 2016. Monomeric Abeta(1-40) and Abeta(1-42) Peptides in Solution Adopt Very Similar Ramachandran Map Distributions That Closely Resemble Random Coil. *Biochemistry* 55:762-75
41. Alvarez G, Munoz-Montano JR, Satrustegui J, Avila J, Bogonez E, Diaz-Nido J. 2002. Regulation of tau phosphorylation and protection against beta-amyloid-induced

- neurodegeneration by lithium. Possible implications for Alzheimer's disease. *Bipolar Disord* 4:153-65
42. Selkoe DJ. 1999. Translating cell biology into therapeutic advances in Alzheimer's disease. *Nature* 399:A23-31
  43. Selkoe DJ. 2000. Toward a comprehensive theory for Alzheimer's disease. Hypothesis: Alzheimer's disease is caused by the cerebral accumulation and cytotoxicity of amyloid beta-protein. *Ann N Y Acad Sci* 924:17-25
  44. Gakhar-Koppole N, Hundeshagen P, Mandl C, Weyer SW, Allinquant B, et al. 2008. Activity requires soluble amyloid precursor protein alpha to promote neurite outgrowth in neural stem cell-derived neurons via activation of the MAPK pathway. *Eur J Neurosci* 28:871-82
  45. Mattson MP. 1997. Cellular actions of beta-amyloid precursor protein and its soluble and fibrillogenic derivatives. *Physiol Rev* 77:1081-132
  46. Caille I, Allinquant B, Dupont E, Bouillot C, Langer A, et al. 2004. Soluble form of amyloid precursor protein regulates proliferation of progenitors in the adult subventricular zone. *Development* 131:2173-81
  47. Ohsawa I, Takamura C, Morimoto T, Ishiguro M, Kohsaka S. 1999. Amino-terminal region of secreted form of amyloid precursor protein stimulates proliferation of neural stem cells. *Eur J Neurosci* 11:1907-13
  48. Arakhamia T, Lee CE, Carlomagno Y, Duong DM, Kunder SR, et al. 2020. Posttranslational Modifications Mediate the Structural Diversity of Tauopathy Strains. *Cell* 180:633-44 e12
  49. Jack CR, Jr., Knopman DS, Jagust WJ, Shaw LM, Aisen PS, et al. 2010. Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade. *Lancet Neurol* 9:119-28
  50. Jack CR, Jr., Knopman DS, Jagust WJ, Petersen RC, Weiner MW, et al. 2013. Tracking pathophysiological processes in Alzheimer's disease: an updated hypothetical model of dynamic biomarkers. *Lancet Neurol* 12:207-16
  51. Jack CR, Jr., Holtzman DM. 2013. Biomarker modeling of Alzheimer's disease. *Neuron* 80:1347-58
  52. Jack CR, Jr., Bennett DA, Blennow K, Carrillo MC, Dunn B, et al. 2018. NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. *Alzheimers Dement* 14:535-62
  53. Bateman RJ, Xiong C, Benzinger TL, Fagan AM, Goate A, et al. 2012. Clinical and biomarker changes in dominantly inherited Alzheimer's disease. *N Engl J Med* 367:795-804
  54. Fleisher AS, Chen K, Quiroz YT, Jakimovich LJ, Gutierrez Gomez M, et al. 2015. Associations between biomarkers and age in the presenilin 1 E280A autosomal dominant Alzheimer disease kindred: a cross-sectional study. *JAMA Neurol* 72:316-24
  55. Donohue MC, Jacqmin-Gadda H, Le Goff M, Thomas RG, Raman R, et al. 2014. Estimating long-term multivariate progression from short-term data. *Alzheimers Dement* 10:S400-10
  56. Young AL, Oxtoby NP, Daga P, Cash DM, Fox NC, et al. 2014. A data-driven model of biomarker changes in sporadic Alzheimer's disease. *Brain* 137:2564-77
  57. Xiong C, Jasielec MS, Weng H, Fagan AM, Benzinger TL, et al. 2016. Longitudinal relationships among biomarkers for Alzheimer disease in the Adult Children Study. *Neurology* 86:1499-506
  58. Fagan AM, Roe CM, Xiong C, Mintun MA, Morris JC, Holtzman DM. 2007. Cerebrospinal fluid tau/beta-amyloid(42) ratio as a prediction of cognitive decline in nondemented older adults. *Arch Neurol* 64:343-9

59. Mattsson N, Zetterberg H, Hansson O, Andreasen N, Parnetti L, et al. 2009. CSF biomarkers and incipient Alzheimer disease in patients with mild cognitive impairment. *JAMA* 302:385-93
60. Visser PJ, Verhey F, Knol DL, Scheltens P, Wahlund LO, et al. 2009. Prevalence and prognostic value of CSF markers of Alzheimer's disease pathology in patients with subjective cognitive impairment or mild cognitive impairment in the DESCRIPA study: a prospective cohort study. *Lancet Neurol* 8:619-27
61. Klunk WE, Engler H, Nordberg A, Wang Y, Blomqvist G, et al. 2004. Imaging brain amyloid in Alzheimer's disease with Pittsburgh Compound-B. *Ann Neurol* 55:306-19
62. Villain N, Chetelat G, Grassiot B, Bourgeat P, Jones G, et al. 2012. Regional dynamics of amyloid-beta deposition in healthy elderly, mild cognitive impairment and Alzheimer's disease: a voxelwise PiB-PET longitudinal study. *Brain* 135:2126-39
63. Buerger K, Ewers M, Pirttila T, Zinkowski R, Alafuzoff I, et al. 2006. CSF phosphorylated tau protein correlates with neocortical neurofibrillary pathology in Alzheimer's disease. *Brain* 129:3035-41
64. Brier MR, Gordon B, Friedrichsen K, McCarthy J, Stern A, et al. 2016. Tau and Abeta imaging, CSF measures, and cognition in Alzheimer's disease. *Sci Transl Med* 8:338ra66
65. Chhatwal JP, Schultz AP, Marshall GA, Boot B, Gomez-Isla T, et al. 2016. Temporal T807 binding correlates with CSF tau and phospho-tau in normal elderly. *Neurology* 87:920-6
66. Blennow K, Hampel H, Weiner M, Zetterberg H. 2010. Cerebrospinal fluid and plasma biomarkers in Alzheimer disease. *Nat Rev Neurol* 6:131-44
67. Seab JP, Jagust WJ, Wong ST, Roos MS, Reed BR, Budinger TF. 1988. Quantitative NMR measurements of hippocampal atrophy in Alzheimer's disease. *Magn Reson Med* 8:200-8
68. Fox NC, Crum WR, Scahill RI, Stevens JM, Janssen JC, Rossor MN. 2001. Imaging of onset and progression of Alzheimer's disease with voxel-compression mapping of serial magnetic resonance images. *Lancet* 358:201-5
69. Minoshima S, Giordani B, Berent S, Frey KA, Foster NL, Kuhl DE. 1997. Metabolic reduction in the posterior cingulate cortex in very early Alzheimer's disease. *Ann Neurol* 42:85-94
70. Besson FL, La Joie R, Doeuvre L, Gaubert M, Mezenge F, et al. 2015. Cognitive and Brain Profiles Associated with Current Neuroimaging Biomarkers of Preclinical Alzheimer's Disease. *J Neurosci* 35:10402-11
71. Dickerson BC, Bakkour A, Salat DH, Feczko E, Pacheco J, et al. 2009. The cortical signature of Alzheimer's disease: regionally specific cortical thinning relates to symptom severity in very mild to mild AD dementia and is detectable in asymptomatic amyloid-positive individuals. *Cereb Cortex* 19:497-510
72. Knopman DS, Jack CR, Jr., Wiste HJ, Weigand SD, Vemuri P, et al. 2013. Selective worsening of brain injury biomarker abnormalities in cognitively normal elderly persons with beta-amyloidosis. *JAMA Neurol* 70:1030-8
73. Landau SM, Harvey D, Madison CM, Koeppe RA, Reiman EM, et al. 2011. Associations between cognitive, functional, and FDG-PET measures of decline in AD and MCI. *Neurobiol Aging* 32:1207-18
74. Hebert LE, Bienias JL, Aggarwal NT, Wilson RS, Bennett DA, et al. 2010. Change in risk of Alzheimer disease over time. *Neurology* 75:786-91
75. Saunders AM, Strittmatter WJ, Schmechel D, George-Hyslop PH, Pericak-Vance MA, et al. 1993. Association of apolipoprotein E allele epsilon 4 with late-onset familial and sporadic Alzheimer's disease. *Neurology* 43:1467-72

76. Farrer LA, Cupples LA, Haines JL, Hyman B, Kukull WA, et al. 1997. Effects of age, sex, and ethnicity on the association between apolipoprotein E genotype and Alzheimer disease. A meta-analysis. APOE and Alzheimer Disease Meta Analysis Consortium. *JAMA* 278:1349-56
77. Green RC, Cupples LA, Go R, Benke KS, Edeki T, et al. 2002. Risk of dementia among white and African American relatives of patients with Alzheimer disease. *JAMA* 287:329-36
78. Fratiglioni L, Ahlbom A, Viitanen M, Winblad B. 1993. Risk factors for late-onset Alzheimer's disease: a population-based, case-control study. *Ann Neurol* 33:258-66
79. Mayeux R, Sano M, Chen J, Tatemichi T, Stern Y. 1991. Risk of dementia in first-degree relatives of patients with Alzheimer's disease and related disorders. *Arch Neurol* 48:269-73
80. Lautenschlager NT, Cupples LA, Rao VS, Auerbach SA, Becker R, et al. 1996. Risk of dementia among relatives of Alzheimer's disease patients in the MIRAGE study: What is in store for the oldest old? *Neurology* 46:641-50
81. Duyckaerts C, Delatour B, Potier MC. 2009. Classification and basic pathology of Alzheimer disease. *Acta Neuropathol* 118:5-36
82. Hardy JA, Higgins GA. 1992. Alzheimer's disease: the amyloid cascade hypothesis. *Science* 256:184-5
83. Tcw J, Goate AM. 2017. Genetics of beta-Amyloid Precursor Protein in Alzheimer's Disease. *Cold Spring Harb Perspect Med* 7
84. Scheuner D, Eckman C, Jensen M, Song X, Citron M, et al. 1996. Secreted amyloid beta-protein similar to that in the senile plaques of Alzheimer's disease is increased in vivo by the presenilin 1 and 2 and APP mutations linked to familial Alzheimer's disease. *Nat Med* 2:864-70
85. Goate A, Chartier-Harlin MC, Mullan M, Brown J, Crawford F, et al. 1991. Segregation of a missense mutation in the amyloid precursor protein gene with familial Alzheimer's disease. *Nature* 349:704-6
86. Fortea J, Vilaplana E, Carmona-Iragui M, Benejam B, Videla L, et al. 2020. Clinical and biomarker changes of Alzheimer's disease in adults with Down syndrome: a cross-sectional study. *Lancet* 395:1988-97
87. Fortea J, Zaman SH, Hartley S, Rafii MS, Head E, Carmona-Iragui M. 2021. Alzheimer's disease associated with Down syndrome: a genetic form of dementia. *Lancet Neurol* 20:930-42
88. Penke B, Paragi G, Gera J, Berkecz R, Kovacs Z, et al. 2018. The Role of Lipids and Membranes in the Pathogenesis of Alzheimer's Disease: A Comprehensive View. *Curr Alzheimer Res* 15:1191-212
89. Makin S. 2018. The amyloid hypothesis on trial. *Nature* 559:S4-S7
90. Loy CT, Schofield PR, Turner AM, Kwok JB. 2014. Genetics of dementia. *Lancet* 383:828-40
91. Michaelson DM. 2014. APOE epsilon4: the most prevalent yet understudied risk factor for Alzheimer's disease. *Alzheimers Dement* 10:861-8
92. Holtzman DM, Herz J, Bu G. 2012. Apolipoprotein E and apolipoprotein E receptors: normal biology and roles in Alzheimer disease. *Cold Spring Harb Perspect Med* 2:a006312
93. Guerreiro R, Wojtas A, Bras J, Carrasquillo M, Rogaeva E, et al. 2013. TREM2 variants in Alzheimer's disease. *N Engl J Med* 368:117-27
94. Jonsson T, Stefansson H, Steinberg S, Jonsdottir I, Jonsson PV, et al. 2013. Variant of TREM2 associated with the risk of Alzheimer's disease. *N Engl J Med* 368:107-16



95. Rajan KB, Weuve J, Barnes LL, McAninch EA, Wilson RS, Evans DA. 2021. Population estimate of people with clinical Alzheimer's disease and mild cognitive impairment in the United States (2020-2060). *Alzheimers Dement* 17:1966-75
96. Nelson PT, Head E, Schmitt FA, Davis PR, Neltner JH, et al. 2011. Alzheimer's disease is not "brain aging": neuropathological, genetic, and epidemiological human studies. *Acta Neuropathol* 121:571-87
97. 2021. 2021 Alzheimer's disease facts and figures. *Alzheimers Dement* 17:327-406
98. Snyder HM, Asthana S, Bain L, Brinton R, Craft S, et al. 2016. Sex biology contributions to vulnerability to Alzheimer's disease: A think tank convened by the Women's Alzheimer's Research Initiative. *Alzheimers Dement* 12:1186-96
99. Xu H, Wang R, Zhang YW, Zhang X. 2006. Estrogen, beta-amyloid metabolism/trafficking, and Alzheimer's disease. *Ann N Y Acad Sci* 1089:324-42
100. Greenfield JP, Leung LW, Cai D, Kaasik K, Gross RS, et al. 2002. Estrogen lowers Alzheimer beta-amyloid generation by stimulating trans-Golgi network vesicle biogenesis. *J Biol Chem* 277:12128-36
101. Sisodia SS. 1992. Beta-amyloid precursor protein cleavage by a membrane-bound protease. *Proc Natl Acad Sci U S A* 89:6075-9
102. Nordstedt C, Caporaso GL, Thyberg J, Gandy SE, Greengard P. 1993. Identification of the Alzheimer beta/A4 amyloid precursor protein in clathrin-coated vesicles purified from PC12 cells. *J Biol Chem* 268:608-12
103. Caporaso GL, Takei K, Gandy SE, Matteoli M, Mundigl O, et al. 1994. Morphologic and biochemical analysis of the intracellular trafficking of the Alzheimer beta/A4 amyloid precursor protein. *J Neurosci* 14:3122-38
104. Xu H, Gouras GK, Greenfield JP, Vincent B, Naslund J, et al. 1998. Estrogen reduces neuronal generation of Alzheimer beta-amyloid peptides. *Nat Med* 4:447-51
105. Pinto-Almazan R, Calzada-Mendoza CC, Campos-Lara MG, Guerra-Araiza C. 2012. Effect of chronic administration of estradiol, progesterone, and tibolone on the expression and phosphorylation of glycogen synthase kinase-3beta and the microtubule-associated protein tau in the hippocampus and cerebellum of female rat. *J Neurosci Res* 90:878-86
106. Brinton RD, Yao J, Yin F, Mack WJ, Cadenas E. 2015. Perimenopause as a neurological transition state. *Nat Rev Endocrinol* 11:393-405
107. McCarthy M, Raval AP. 2020. The peri-menopause in a woman's life: a systemic inflammatory phase that enables later neurodegenerative disease. *J Neuroinflammation* 17:317
108. Zhao L, Mao Z, Brinton RD. 2009. A select combination of clinically relevant phytoestrogens enhances estrogen receptor beta-binding selectivity and neuroprotective activities in vitro and in vivo. *Endocrinology* 150:770-83
109. Burger HG, Dudley EC, Robertson DM, Dennerstein L. 2002. Hormonal changes in the menopause transition. *Recent Prog Horm Res* 57:257-75
110. Horstman AM, Dillon EL, Urban RJ, Sheffield-Moore M. 2012. The role of androgens and estrogens on healthy aging and longevity. *J Gerontol A Biol Sci Med Sci* 67:1140-52
111. Baumgart M, Snyder HM, Carrillo MC, Fazio S, Kim H, Johns H. 2015. Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective. *Alzheimers Dement* 11:718-26
112. Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, et al. 2020. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *Lancet* 396:413-46
113. Nianogo RA, Rosenwohl-Mack A, Yaffe K, Carrasco A, Hoffmann CM, Barnes DE. 2022. Risk Factors Associated With Alzheimer Disease and Related Dementias by Sex and Race and Ethnicity in the US. *JAMA Neurol* 79:584-91

114. Ronnemaa E, Zethelius B, Lannfelt L, Kilander L. 2011. Vascular risk factors and dementia: 40-year follow-up of a population-based cohort. *Dement Geriatr Cogn Disord* 31:460-6
115. Kivimaki M, Luukkonen R, Batty GD, Ferrie JE, Pentti J, et al. 2018. Body mass index and risk of dementia: Analysis of individual-level data from 1.3 million individuals. *Alzheimers Dement* 14:601-9
116. Gottesman RF, Albert MS, Alonso A, Coker LH, Coresh J, et al. 2017. Associations Between Midlife Vascular Risk Factors and 25-Year Incident Dementia in the Atherosclerosis Risk in Communities (ARIC) Cohort. *JAMA Neurol* 74:1246-54
117. Gottesman RF, Schneider AL, Zhou Y, Coresh J, Green E, et al. 2017. Association Between Midlife Vascular Risk Factors and Estimated Brain Amyloid Deposition. *JAMA* 317:1443-50
118. Abell JG, Kivimaki M, Dugravot A, Tabak AG, Fayosse A, et al. 2018. Association between systolic blood pressure and dementia in the Whitehall II cohort study: role of age, duration, and threshold used to define hypertension. *Eur Heart J* 39:3119-25
119. Debette S, Seshadri S, Beiser A, Au R, Himali JJ, et al. 2011. Midlife vascular risk factor exposure accelerates structural brain aging and cognitive decline. *Neurology* 77:461-8
120. Anstey KJ, Ashby-Mitchell K, Peters R. 2017. Updating the Evidence on the Association between Serum Cholesterol and Risk of Late-Life Dementia: Review and Meta-Analysis. *J Alzheimers Dis* 56:215-28
121. LaPlume AA, McKetton L, Levine B, Troyer AK, Anderson ND. 2022. The adverse effect of modifiable dementia risk factors on cognition amplifies across the adult lifespan. *Alzheimers Dement (Amst)* 14:e12337
122. Fitzpatrick AL, Kuller LH, Lopez OL, Diehr P, O'Meara ES, et al. 2009. Midlife and late-life obesity and the risk of dementia: cardiovascular health study. *Arch Neurol* 66:336-42
123. Corrada MM, Hayden KM, Paganini-Hill A, Bullain SS, DeMoss J, et al. 2017. Age of onset of hypertension and risk of dementia in the oldest-old: The 90+ Study. *Alzheimers Dement* 13:103-10
124. Tin A, Bressler J, Simino J, Sullivan KJ, Mei H, et al. 2022. Genetic Risk, Midlife Life's Simple 7, and Incident Dementia in the Atherosclerosis Risk in Communities Study. *Neurology* 99:e154-63
125. Samieri C, Perier MC, Gaye B, Proust-Lima C, Helmer C, et al. 2018. Association of Cardiovascular Health Level in Older Age With Cognitive Decline and Incident Dementia. *JAMA* 320:657-64
126. Zhong G, Wang Y, Zhang Y, Guo JJ, Zhao Y. 2015. Smoking is associated with an increased risk of dementia: a meta-analysis of prospective cohort studies with investigation of potential effect modifiers. *PLoS One* 10:e0118333
127. Ogino E, Manly JJ, Schupf N, Mayeux R, Gu Y. 2019. Current and past leisure time physical activity in relation to risk of Alzheimer's disease in older adults. *Alzheimers Dement* 15:1603-11
128. Najar J, Ostling S, Gudmundsson P, Sundh V, Johansson L, et al. 2019. Cognitive and physical activity and dementia: A 44-year longitudinal population study of women. *Neurology* 92:e1322-e30
129. Buchman AS, Yu L, Wilson RS, Lim A, Dawe RJ, et al. 2019. Physical activity, common brain pathologies, and cognition in community-dwelling older adults. *Neurology* 92:e811-e22
130. Tan ZS, Spartano NL, Beiser AS, DeCarli C, Auerbach SH, et al. 2017. Physical Activity, Brain Volume, and Dementia Risk: The Framingham Study. *J Gerontol A Biol Sci Med Sci* 72:789-95
131. Stephen R, Hongisto K, Solomon A, Lonnroos E. 2017. Physical Activity and Alzheimer's Disease: A Systematic Review. *J Gerontol A Biol Sci Med Sci* 72:733-9

132. Blondell SJ, Hammersley-Mather R, Veerman JL. 2014. Does physical activity prevent cognitive decline and dementia?: A systematic review and meta-analysis of longitudinal studies. *BMC Public Health* 14:510
133. Guure CB, Ibrahim NA, Adam MB, Said SM. 2017. Impact of Physical Activity on Cognitive Decline, Dementia, and Its Subtypes: Meta-Analysis of Prospective Studies. *Biomed Res Int* 2017:9016924
134. Jensen CS, Simonsen AH, Siersma V, Beyer N, Frederiksen KS, et al. 2019. Patients with Alzheimer's disease who carry the APOE epsilon4 allele benefit more from physical exercise. *Alzheimers Dement (N Y)* 5:99-106
135. Felisatti F, Gonneaud J, Palix C, Garnier-Crussard A, Mezenge F, et al. 2022. Role of Cardiovascular Risk Factors on the Association Between Physical Activity and Brain Integrity Markers in Older Adults. *Neurology* 98:e2023-e35
136. Casaletto K, Ramos-Miguel A, VandeBunte A, Memel M, Buchman A, et al. 2022. Late-life physical activity relates to brain tissue synaptic integrity markers in older adults. *Alzheimers Dement* 18:2023-35
137. Ballarini T, Melo van Lent D, Brunner J, Schroder A, Wolfsgruber S, et al. 2021. Mediterranean Diet, Alzheimer Disease Biomarkers and Brain Atrophy in Old Age. *Neurology* 96:e2920-32
138. van den Brink AC, Brouwer-Brolsma EM, Berendsen AAM, van de Rest O. 2019. The Mediterranean, Dietary Approaches to Stop Hypertension (DASH), and Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) Diets Are Associated with Less Cognitive Decline and a Lower Risk of Alzheimer's Disease-A Review. *Adv Nutr* 10:1040-65
139. Morris MC, Tangney CC, Wang Y, Sacks FM, Bennett DA, Aggarwal NT. 2015. MIND diet associated with reduced incidence of Alzheimer's disease. *Alzheimers Dement* 11:1007-14
140. Morris MC, Tangney CC, Wang Y, Sacks FM, Barnes LL, et al. 2015. MIND diet slows cognitive decline with aging. *Alzheimers Dement* 11:1015-22
141. Lourida I, Soni M, Thompson-Coon J, Purandare N, Lang IA, et al. 2013. Mediterranean diet, cognitive function, and dementia: a systematic review. *Epidemiology* 24:479-89
142. Hardman RJ, Kennedy G, Macpherson H, Scholey AB, Pipingas A. 2016. Adherence to a Mediterranean-Style Diet and Effects on Cognition in Adults: A Qualitative Evaluation and Systematic Review of Longitudinal and Prospective Trials. *Front Nutr* 3:22
143. Health WCoSDo, Organization WH. 2008. *Closing the gap in a generation: health equity through action on the social determinants of health: Commission on Social Determinants of Health final report*. World Health Organization
144. Braveman P, Egerter S, Williams DR. 2011. The social determinants of health: coming of age. *Annu Rev Public Health* 32:381-98
145. Barbeau EM, Krieger N, Soobader MJ. 2004. Working class matters: socioeconomic disadvantage, race/ethnicity, gender, and smoking in NHIS 2000. *Am J Public Health* 94:269-78
146. Cutler DM, Lleras-Muney A. 2006. Education and health: evaluating theories and evidence. National bureau of economic research Cambridge, Mass., USA
147. Dewalt DA, Berkman ND, Sheridan S, Lohr KN, Pignone MP. 2004. Literacy and health outcomes: a systematic review of the literature. *J Gen Intern Med* 19:1228-39
148. Sanders LM, Federico S, Klass P, Abrams MA, Dreyer B. 2009. Literacy and child health: a systematic review. *Arch Pediatr Adolesc Med* 163:131-40
149. Bartley M, Plewis I. 2002. Accumulated labour market disadvantage and limiting long-term illness: data from the 1971-1991 Office for National Statistics' Longitudinal Study. *Int J Epidemiol* 31:336-41

150. Gabel J, Levitt L, Holve E, Pickreign J, Whitmore H, et al. 2002. Job-based health benefits in 2002: some important trends. *Health Aff (Millwood)* 21:143-51
151. Crissey SR. 2009. Educational attainment in the United States: 2007. *US department of Commerce*
152. O'Neil BA, Forsythe ME, Stanish WD. 2001. Chronic occupational repetitive strain injury. *Can Fam Physician* 47:311-6
153. Warburton DE, Nicol CW, Bredin SS. 2006. Health benefits of physical activity: the evidence. *CMAJ* 174:801-9
154. de Jonge J, Bosma H, Peter R, Siegrist J. 2000. Job strain, effort-reward imbalance and employee well-being: a large-scale cross-sectional study. *Soc Sci Med* 50:1317-27
155. Karasek R. 1990. Stress, productivity, and the reconstruction of working life. *Health work*
156. Egerter S, Dekker M, An J, Grossman-Kahn R, Braveman P. 2008. Work matters for health. *Robert Wood Johnson Foundation Commission to Build a Healthier America*
157. Collins SR, Davis K, Doty MM, Ho A. 2004. Wages, health benefits, and workers' health. *Issue Brief (Commonw Fund)*:1-16
158. Heymann J, Boynton-Jarrett R, Carter P, Bond JT, Galinsky E. 2002. Work-family issues and low-income families. *Retrieved June 1:2003*
159. Booth KM, Pinkston MM, Poston WS. 2005. Obesity and the built environment. *J Am Diet Assoc* 105:S110-7
160. Chuang YC, Cubbin C, Ahn D, Winkleby MA. 2005. Effects of neighbourhood socioeconomic status and convenience store concentration on individual level smoking. *J Epidemiol Community Health* 59:568-73
161. Gordon-Larsen P, Nelson MC, Page P, Popkin BM. 2006. Inequality in the built environment underlies key health disparities in physical activity and obesity. *Pediatrics* 117:417-24
162. Giles-Corti B, Donovan RJ. 2002. The relative influence of individual, social and physical environment determinants of physical activity. *Soc Sci Med* 54:1793-812
163. Heinrich KM, Lee RE, Suminski RR, Regan GR, Reese-Smith JY, et al. 2007. Associations between the built environment and physical activity in public housing residents. *Int J Behav Nutr Phys Act* 4:56
164. Morland K, Diez Roux AV, Wing S. 2006. Supermarkets, other food stores, and obesity: the atherosclerosis risk in communities study. *Am J Prev Med* 30:333-9
165. Sallis JF, Glanz K. 2006. The role of built environments in physical activity, eating, and obesity in childhood. *Future Child* 16:89-108
166. Fernandez RM, Su C. 2004. Space in the study of labor markets. *Annu. Rev. Sociol.* 30:545-69
167. Pastor M. 2001. Geography and opportunity. *America becoming: Racial trends and their consequences* 1:435-68
168. Williams DR, Collins C. 2001. Racial residential segregation: a fundamental cause of racial disparities in health. *Public health reports*
169. Diez Roux AV, Mair C. 2010. Neighborhoods and health. *Annals of the New York academy of sciences* 1186:125-45
170. Pickett KE, Collins JW, Jr., Masi CM, Wilkinson RG. 2005. The effects of racial density and income incongruity on pregnancy outcomes. *Soc Sci Med* 60:2229-38
171. Robert SA. 1999. Socioeconomic position and health: the independent contribution of community socioeconomic context. *Annual review of sociology* 25:489-516
172. Winkleby M, Cubbin C, Ahn D. 2006. Effect of cross-level interaction between individual and neighborhood socioeconomic status on adult mortality rates. *Am J Public Health* 96:2145-53

173. Williams DR, Mohammed SA, Leavell J, Collins C. 2010. Race, socioeconomic status, and health: complexities, ongoing challenges, and research opportunities. *Ann N Y Acad Sci* 1186:69-101
174. McEwen BS, Gianaros PJ. 2010. Central role of the brain in stress and adaptation: links to socioeconomic status, health, and disease. *Ann N Y Acad Sci* 1186:190-222
175. Steptoe A, Marmot M. 2002. The role of psychobiological pathways in socio-economic inequalities in cardiovascular disease risk. *Eur Heart J* 23:13-25
176. Braveman P, Marchi K, Egerter S, Kim S, Metzler M, et al. 2010. Poverty, near-poverty, and hardship around the time of pregnancy. *Matern Child Health J* 14:20-35
177. Evans GW, Kim P. 2007. Childhood poverty and health: cumulative risk exposure and stress dysregulation. *Psychol Sci* 18:953-7
178. Williams DR, Mohammed SA. 2009. Discrimination and racial disparities in health: evidence and needed research. *J Behav Med* 32:20-47
179. Seeman T, Epel E, Gruenewald T, Karlamangla A, McEwen BS. 2010. Socio-economic differentials in peripheral biology: cumulative allostatic load. *Ann N Y Acad Sci* 1186:223-39
180. McEwen BS. 2006. Protective and damaging effects of stress mediators: central role of the brain. *Dialogues Clin Neurosci* 8:367-81
181. Seeman TE, McEwen BS, Rowe JW, Singer BH. 2001. Allostatic load as a marker of cumulative biological risk: MacArthur studies of successful aging. *Proc Natl Acad Sci U S A* 98:4770-5
182. Seeman TE, Singer BH, Rowe JW, Horwitz RI, McEwen BS. 1997. Price of adaptation--allostatic load and its health consequences. MacArthur studies of successful aging. *Arch Intern Med* 157:2259-68
183. Charles CZ. 2003. The dynamics of racial residential segregation. *Annual review of sociology* 29:167-207
184. Rouse CE, Barrow L. 2006. U.S. elementary and secondary schools: equalizing opportunity or replicating the status quo? *Future Child* 16:99-123
185. Nuru-Jeter A, Dominguez TP, Hammond WP, Leu J, Skaiff M, et al. 2009. "It's the skin you're in": African-American women talk about their experiences of racism. an exploratory study to develop measures of racism for birth outcome studies. *Matern Child Health J* 13:29-39
186. Holtzman DM, Morris JC, Goate AM. 2011. Alzheimer's disease: the challenge of the second century. *Sci Transl Med* 3:77sr1
187. Perrin RJ, Fagan AM, Holtzman DM. 2009. Multimodal techniques for diagnosis and prognosis of Alzheimer's disease. *Nature* 461:916-22
188. Craig-Schapiro R, Fagan AM, Holtzman DM. 2009. Biomarkers of Alzheimer's disease. *Neurobiol Dis* 35:128-40
189. Se Thoe E, Fauzi A, Tang YQ, Chamyuang S, Chia AYY. 2021. A review on advances of treatment modalities for Alzheimer's disease. *Life Sci* 276:119129
190. Teaktong T, Graham AJ, Court JA, Perry RH, Jaros E, et al. 2004. Nicotinic acetylcholine receptor immunohistochemistry in Alzheimer's disease and dementia with Lewy bodies: differential neuronal and astroglial pathology. *J Neurol Sci* 225:39-49
191. Mash DC, Flynn DD, Potter LT. 1985. Loss of M2 muscarine receptors in the cerebral cortex in Alzheimer's disease and experimental cholinergic denervation. *Science* 228:1115-7
192. Rinne JO, Brooks DJ, Rossor MN, Fox NC, Bullock R, et al. 2010. 11C-PiB PET assessment of change in fibrillar amyloid-beta load in patients with Alzheimer's disease treated with bapineuzumab: a phase 2, double-blind, placebo-controlled, ascending-dose study. *Lancet Neurol* 9:363-72

193. van Dyck CH, Swanson CJ, Aisen P, Bateman RJ, Chen C, et al. 2023. Lecanemab in Early Alzheimer's Disease. *N Engl J Med* 388:9-21
194. Sims JR, Zimmer JA, Evans CD, Lu M, Ardayfio P, et al. 2023. Donanemab in Early Symptomatic Alzheimer Disease: The TRAILBLAZER-ALZ 2 Randomized Clinical Trial. *JAMA*
195. Salloway S, Sperling R, Fox NC, Blennow K, Klunk W, et al. 2014. Two phase 3 trials of bapineuzumab in mild-to-moderate Alzheimer's disease. *N Engl J Med* 370:322-33
196. Liu E, Schmidt ME, Margolin R, Sperling R, Koeppe R, et al. 2015. Amyloid-beta 11C-PiB-PET imaging results from 2 randomized bapineuzumab phase 3 AD trials. *Neurology* 85:692-700
197. Morris JC, Selkoe DJ. 2011. Recommendations for the incorporation of biomarkers into Alzheimer clinical trials: an overview. *Neurobiol Aging* 32 Suppl 1:S1-3
198. Sperling RA, Jack CR, Jr., Aisen PS. 2011. Testing the right target and right drug at the right stage. *Sci Transl Med* 3:111cm33
199. Cushing H. 1914. Studies on the Cerebro-Spinal Fluid : I. Introduction. *J Med Res* 31:1-19
200. Henry MS, Passmore AP, Todd S, McGuinness B, Craig D, Johnston JA. 2013. The development of effective biomarkers for Alzheimer's disease: a review. *Int J Geriatr Psychiatry* 28:331-40
201. Hansson O, Zetterberg H, Buchhave P, Londos E, Blennow K, Minthon L. 2006. Association between CSF biomarkers and incipient Alzheimer's disease in patients with mild cognitive impairment: a follow-up study. *Lancet Neurol* 5:228-34
202. Mawuenyega KG, Sigurdson W, Ovod V, Munsell L, Kasten T, et al. 2010. Decreased clearance of CNS beta-amyloid in Alzheimer's disease. *Science* 330:1774
203. Brunello CA, Merezko M, Uronen RL, Huttunen HJ. 2020. Mechanisms of secretion and spreading of pathological tau protein. *Cell Mol Life Sci* 77:1721-44
204. Pooler AM, Phillips EC, Lau DH, Noble W, Hanger DP. 2013. Physiological release of endogenous tau is stimulated by neuronal activity. *EMBO Rep* 14:389-94
205. Yamada K, Holth JK, Liao F, Stewart FR, Mahan TE, et al. 2014. Neuronal activity regulates extracellular tau in vivo. *J Exp Med* 211:387-93
206. Wang Y, Balaji V, Kaniyappan S, Kruger L, Irsen S, et al. 2017. The release and trans-synaptic transmission of Tau via exosomes. *Mol Neurodegener* 12:5
207. Katsinelos T, Zeitler M, Dimou E, Karakatsani A, Muller HM, et al. 2018. Unconventional Secretion Mediates the Trans-cellular Spreading of Tau. *Cell Rep* 23:2039-55
208. Merezko M, Brunello CA, Yan X, Vihinen H, Jokitalo E, et al. 2018. Secretion of Tau via an Unconventional Non-vesicular Mechanism. *Cell Rep* 25:2027-35 e4
209. Arai H, Terajima M, Miura M, Higuchi S, Muramatsu T, et al. 1995. Tau in cerebrospinal fluid: a potential diagnostic marker in Alzheimer's disease. *Ann Neurol* 38:649-52
210. Ritchie C, Smailagic N, Noel-Storr AH, Ukoumunne O, Ladds EC, Martin S. 2017. CSF tau and the CSF tau/ABeta ratio for the diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI). *Cochrane Database Syst Rev* 3:CD010803
211. Rajan KB, Weuve J, Barnes LL, Wilson RS, Evans DA. 2019. Prevalence and incidence of clinically diagnosed Alzheimer's disease dementia from 1994 to 2012 in a population study. *Alzheimers Dement* 15:1-7
212. Potter GG, Plassman BL, Burke JR, Kabeto MU, Langa KM, et al. 2009. Cognitive performance and informant reports in the diagnosis of cognitive impairment and dementia in African Americans and whites. *Alzheimers Dement* 5:445-53
213. Gurland BJ, Wilder DE, Lantigua R, Stern Y, Chen J, et al. 1999. Rates of dementia in three ethnorracial groups. *Int J Geriatr Psychiatry* 14:481-93

214. Glymour MM, Manly JJ. 2008. Lifecourse social conditions and racial and ethnic patterns of cognitive aging. *Neuropsychol Rev* 18:223-54
215. Lines L, Sherif, N., & Wiener, J. . 2014. Racial and ethnic disparities among individuals with Alzheimer's disease in the United States: A literature review. *RTI Press*
216. Reitz C, Jun G, Naj A, Rajbhandary R, Vardarajan BN, et al. 2013. Variants in the ATP-binding cassette transporter (ABCA7), apolipoprotein E 4, and the risk of late-onset Alzheimer disease in African Americans. *JAMA* 309:1483-92
217. Logue MW, Schu M, Vardarajan BN, Buross J, Green RC, et al. 2011. A comprehensive genetic association study of Alzheimer disease in African Americans. *Arch Neurol* 68:1569-79
218. Rayaprolu S, Higginbotham L, Bagchi P, Watson CM, Zhang T, et al. 2021. Systems-based proteomics to resolve the biology of Alzheimer's disease beyond amyloid and tau. *Neuropsychopharmacology* 46:98-115
219. Yates JR, 3rd. 1998. Mass spectrometry and the age of the proteome. *J Mass Spectrom* 33:1-19
220. Wolters DA, Washburn MP, Yates JR, 3rd. 2001. An automated multidimensional protein identification technology for shotgun proteomics. *Anal Chem* 73:5683-90
221. Link AJ, Eng J, Schieltz DM, Carmack E, Mize GJ, et al. 1999. Direct analysis of protein complexes using mass spectrometry. *Nat Biotechnol* 17:676-82
222. Yates JR, 3rd. 2004. Mass spectral analysis in proteomics. *Annu Rev Biophys Biomol Struct* 33:297-316
223. Zhang Y, Fonslow BR, Shan B, Baek MC, Yates JR, 3rd. 2013. Protein analysis by shotgun/bottom-up proteomics. *Chem Rev* 113:2343-94
224. Aebersold R, Mann M. 2003. Mass spectrometry-based proteomics. *Nature* 422:198-207
225. Pappireddi N, Martin L, Wuhr M. 2019. A Review on Quantitative Multiplexed Proteomics. *Chembiochem* 20:1210-24
226. Gillet LC, Leitner A, Aebersold R. 2016. Mass Spectrometry Applied to Bottom-Up Proteomics: Entering the High-Throughput Era for Hypothesis Testing. *Annu Rev Anal Chem (Palo Alto Calif)* 9:449-72
227. Johnson ECB, Dammer EB, Duong DM, Yin L, Thambisetty M, et al. 2018. Deep proteomic network analysis of Alzheimer's disease brain reveals alterations in RNA binding proteins and RNA splicing associated with disease. *Mol Neurodegener* 13:52
228. Ping L, Duong DM, Yin L, Gearing M, Lah JJ, et al. 2018. Global quantitative analysis of the human brain proteome in Alzheimer's and Parkinson's Disease. *Sci Data* 5:180036
229. Rauniyar N, Yates JR, 3rd. 2014. Isobaric labeling-based relative quantification in shotgun proteomics. *J Proteome Res* 13:5293-309
230. Li J, Van Vranken JG, Pontano Vaitea L, Schweppe DK, Huttlin EL, et al. 2020. TMTpro reagents: a set of isobaric labeling mass tags enables simultaneous proteome-wide measurements across 16 samples. *Nat Methods* 17:399-404
231. Bai B, Wang X, Li Y, Chen PC, Yu K, et al. 2020. Deep Multilayer Brain Proteomics Identifies Molecular Networks in Alzheimer's Disease Progression. *Neuron* 105:975-91 e7
232. Ping L, Kunder SR, Duong DM, Yin L, Gearing M, et al. 2020. Global quantitative analysis of the human brain proteome and phosphoproteome in Alzheimer's disease. *Sci Data* 7:315
233. Brenes A, Hukelmann J, Bensaddek D, Lamond AI. 2019. Multibatch TMT Reveals False Positives, Batch Effects and Missing Values. *Mol Cell Proteomics* 18:1967-80
234. Meyer JG, Schilling B. 2017. Clinical applications of quantitative proteomics using targeted and untargeted data-independent acquisition techniques. *Expert Rev Proteomics* 14:419-29

235. Seyfried NT, Dammer EB, Swarup V, Nandakumar D, Duong DM, et al. 2017. A Multi-network Approach Identifies Protein-Specific Co-expression in Asymptomatic and Symptomatic Alzheimer's Disease. *Cell Syst* 4:60-72 e4
236. Johnson ECB, Carter EK, Dammer EB, Duong DM, Gerasimov ES, et al. 2022. Large-scale deep multi-layer analysis of Alzheimer's disease brain reveals strong proteomic disease-related changes not observed at the RNA level. *Nat Neurosci* 25:213-25
237. Johnson ECB, Dammer EB, Duong DM, Ping L, Zhou M, et al. 2020. Large-scale proteomic analysis of Alzheimer's disease brain and cerebrospinal fluid reveals early changes in energy metabolism associated with microglia and astrocyte activation. *Nat Med* 26:769-80
238. Parikshak NN, Gandal MJ, Geschwind DH. 2015. Systems biology and gene networks in neurodevelopmental and neurodegenerative disorders. *Nat Rev Genet* 16:441-58
239. Miller JA, Oldham MC, Geschwind DH. 2008. A systems level analysis of transcriptional changes in Alzheimer's disease and normal aging. *J Neurosci* 28:1410-20
240. Oldham MC, Konopka G, Iwamoto K, Langfelder P, Kato T, et al. 2008. Functional organization of the transcriptome in human brain. *Nat Neurosci* 11:1271-82
241. Prill RJ, Marbach D, Saez-Rodriguez J, Sorger PK, Alexopoulos LG, et al. 2010. Towards a rigorous assessment of systems biology models: the DREAM3 challenges. *PLoS One* 5:e9202
242. Zhang B, Horvath S. 2005. A general framework for weighted gene co-expression network analysis. *Stat Appl Genet Mol Biol* 4:Article17
243. Mostafavi S, Gaiteri C, Sullivan SE, White CC, Tasaki S, et al. 2018. A molecular network of the aging human brain provides insights into the pathology and cognitive decline of Alzheimer's disease. *Nat Neurosci* 21:811-9
244. Zambon AC, Gaj S, Ho I, Hanspers K, Vranizan K, et al. 2012. GO-Elite: a flexible solution for pathway and ontology over-representation. *Bioinformatics* 28:2209-10
245. Higginbotham L, Ping L, Dammer EB, Duong DM, Zhou M, et al. 2020. Integrated proteomics reveals brain-based cerebrospinal fluid biomarkers in asymptomatic and symptomatic Alzheimer's disease. *Sci Adv* 6
246. Swarup V, Chang TS, Duong DM, Dammer EB, Dai J, et al. 2020. Identification of Conserved Proteomic Networks in Neurodegenerative Dementia. *Cell Rep* 31:107807
247. McKhann GM, Knopman DS, Chertkow H, Hyman BT, Jack Jr CR, et al. 2011. The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's and Dementia* 7:263-9
248. Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, et al. 2011. The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's and Dementia* 7:270-9
249. Bittner T, Zetterberg H, Teunissen CE, Ostlund RE, Jr., Militello M, et al. 2016. Technical performance of a novel, fully automated electrochemiluminescence immunoassay for the quantitation of beta-amyloid (1-42) in human cerebrospinal fluid. *Alzheimers Dement* 12:517-26
250. Schindler SE, Gray JD, Gordon BA, Xiong C, Batrla-Utermann R, et al. 2018. Cerebrospinal fluid biomarkers measured by Elecsys assays compared to amyloid imaging. *Alzheimers Dement* 14:1460-9
251. Hansson O, Seibyl J, Stomrud E, Zetterberg H, Trojanowski JQ, et al. 2018. CSF biomarkers of Alzheimer's disease concord with amyloid-beta PET and predict clinical progression: A study of fully automated immunoassays in BioFINDER and ADNI cohorts. *Alzheimers Dement* 14:1470-81



252. Higginbotham L, Ping L, Dammer EB, Duong DM, Zhou M, et al. 2020. Integrated Proteomics Reveals Brain-Based Cerebrospinal Fluid Biomarkers in Asymptomatic and Symptomatic Alzheimer's Disease. *Science Advances* 6:eaaz9360
253. Dammer EB, Ping L, Duong DM, Modeste ES, Seyfried NT, et al. 2022. Multi-platform proteomic analysis of Alzheimer's disease cerebrospinal fluid and plasma reveals network biomarkers associated with proteostasis and the matrisome. *Alzheimers Res Ther* 14:174
254. Winiarska A, Zareba L, Krolczyk G, Czyzewicz G, Zabczyk M, Undas A. 2019. Decreased Levels of Histidine-Rich Glycoprotein in Advanced Lung Cancer: Association with Prothrombotic Alterations. *Dis Markers* 2019:8170759
255. Magistretti PJ, Allaman I. 2015. A cellular perspective on brain energy metabolism and functional imaging. *Neuron* 86:883-901
256. Maienschein-Cline M, Lei Z, Gardeux V, Abbasi T, Machado RF, et al. 2014. ARTS: automated randomization of multiple traits for study design. *Bioinformatics* 30:1637-9
257. Watson CM, Dammer EB, Ping L, Duong DM, Modeste E, et al. 2023. Quantitative Mass Spectrometry Analysis of Cerebrospinal Fluid Protein Biomarkers in Alzheimer's Disease. *Sci Data* 10:261
258. Dammer EB, Seyfried NT, Johnson ECB. 2023. Batch Correction and Harmonization of - Omics Datasets with a Tunable Median Polish of Ratio. *Front Syst Biol* 3
259. Chen X, Zhang B, Wang T, Bonni A, Zhao G. 2020. Robust principal component analysis for accurate outlier sample detection in RNA-Seq data. *BMC Bioinformatics* 21:269
260. Reimand J, Isserlin R, Voisin V, Kucera M, Tannus-Lopes C, et al. 2019. Pathway enrichment analysis and visualization of omics data using g:Profiler, GSEA, Cytoscape and EnrichmentMap. *Nature Protocols* 14:482-517
261. Morris JC, Schindler SE, McCue LM, Moulder KL, Benzinger TLS, et al. 2019. Assessment of Racial Disparities in Biomarkers for Alzheimer Disease. *JAMA Neurol*
262. Howell JC, Watts KD, Parker MW, Wu J, Kollhoff A, et al. 2017. Race modifies the relationship between cognition and Alzheimer's disease cerebrospinal fluid biomarkers. *Alzheimers Res Ther* 9:88
263. Bader JM, Geyer PE, Muller JB, Strauss MT, Koch M, et al. 2020. Proteome profiling in cerebrospinal fluid reveals novel biomarkers of Alzheimer's disease. *Mol Syst Biol* 16:e9356
264. Dayon L, Núñez Galindo A, Wojcik J, Cominetti O, Corthésy J, et al. 2018. Alzheimer disease pathology and the cerebrospinal fluid proteome. *Alzheimers Res Ther* 10:66
265. Tijms BM, Gobom J, Reus L, Jansen I, Hong S, et al. 2020. Pathophysiological subtypes of Alzheimer's disease based on cerebrospinal fluid proteomics. *Brain* 143:3776-92
266. Sharma K, Schmitt S, Bergner CG, Tyanova S, Kannaiyan N, et al. 2015. Cell type- and brain region-resolved mouse brain proteome. *Nat Neurosci* 18:1819-31
267. Zhang Y, Chen K, Sloan SA, Bennett ML, Scholze AR, et al. 2014. An RNA-sequencing transcriptome and splicing database of glia, neurons, and vascular cells of the cerebral cortex. *J Neurosci* 34:11929-47
268. Zhou M, Haque RU, Dammer EB, Duong DM, Ping L, et al. 2020. Targeted mass spectrometry to quantify brain-derived cerebrospinal fluid biomarkers in Alzheimer's disease. *Clin Proteomics* 17:19
269. Telano LN, Baker S. 2018. Physiology, cerebral spinal fluid.
270. Ujiie M, Dickstein DL, Carlow DA, Jefferies WA. 2003. Blood-brain barrier permeability precedes senile plaque formation in an Alzheimer disease model. *Microcirculation* 10:463-70

271. Dickstein DL, Biron KE, Ujiie M, Pfeifer CG, Jeffries AR, Jefferies WA. 2006. Abeta peptide immunization restores blood-brain barrier integrity in Alzheimer disease. *FASEB J* 20:426-33
272. Zlokovic BV. 2011. Neurovascular pathways to neurodegeneration in Alzheimer's disease and other disorders. *Nat Rev Neurosci* 12:723-38
273. Desai BS, Schneider JA, Li JL, Carvey PM, Hendey B. 2009. Evidence of angiogenic vessels in Alzheimer's disease. *J Neural Transm (Vienna)* 116:587-97
274. Montagne A, Barnes SR, Sweeney MD, Halliday MR, Sagare AP, et al. 2015. Blood-brain barrier breakdown in the aging human hippocampus. *Neuron* 85:296-302
275. Nation DA, Sweeney MD, Montagne A, Sagare AP, D'Orazio LM, et al. 2019. Blood-brain barrier breakdown is an early biomarker of human cognitive dysfunction. *Nat Med* 25:270-6
276. Butts B, Huang H, Hu WT, Kehoe PG, Miners JS, et al. 2024. sPDGFRbeta and neuroinflammation are associated with AD biomarkers and differ by race: The ASCEND Study. *Alzheimers Dement* 20:1175-89
277. Jack CR, Jr., Bennett DA, Blennow K, Carrillo MC, Dunn B, et al. 2018. NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. *Alzheimers Dement* 14:535-62
278. Hanseeuw BJ, Betensky RA, Jacobs HIL, Schultz AP, Sepulcre J, et al. 2019. Association of Amyloid and Tau With Cognition in Preclinical Alzheimer Disease: A Longitudinal Study. *JAMA Neurology* 76:915-24
279. Visser PJ, Reus LM, Gobom J, Jansen I, Dicks E, et al. 2022. Cerebrospinal fluid tau levels are associated with abnormal neuronal plasticity markers in Alzheimer's disease. *Molecular Neurodegeneration* 17:27
280. Quinn JP, Kandigian SE, Trombetta BA, Arnold SE, Carlyle BC. 2021. VGF as a biomarker and therapeutic target in neurodegenerative and psychiatric diseases. *Brain Communications* 3
281. Wingo AP, Dammer EB, Breen MS, Logsdon BA, Duong DM, et al. 2019. Large-scale proteomic analysis of human brain identifies proteins associated with cognitive trajectory in advanced age. *Nat Commun* 10:1619
282. Libiger O, Shaw LM, Watson MH, Nairn AC, Umaña KL, et al. 2021. Longitudinal CSF proteomics identifies NPTX2 as a prognostic biomarker of Alzheimer's disease. *Alzheimers Dement* 17:1976-87
283. Llano DA, Devanarayan P, Devanarayan V. 2023. CSF peptides from VGF and other markers enhance prediction of MCI to AD progression using the ATN framework. *Neurobiology of Aging* 121:15-27
284. Xiao M-F, Xu D, Craig MT, Pelkey KA, Chien C-C, et al. 2017. NPTX2 and cognitive dysfunction in Alzheimer's Disease. *eLife* 6:e23798
285. Sjaarda J, Gerstein HC, Kutalik Z, Mohammadi-Shemirani P, Pigeyre M, et al. 2020. Influence of Genetic Ancestry on Human Serum Proteome. *Am J Hum Genet* 106:303-14
286. Ghosh S, Nehme R, Barrett LE. 2022. Greater genetic diversity is needed in human pluripotent stem cell models. *Nature Communications* 13:7301
287. Peterson RE, Kuchenbaecker K, Walters RK, Chen CY, Popejoy AB, et al. 2019. Genome-wide Association Studies in Ancestrally Diverse Populations: Opportunities, Methods, Pitfalls, and Recommendations. *Cell* 179:589-603
288. Zhang J, Dutta D, Köttgen A, Tin A, Schlosser P, et al. 2022. Plasma proteome analyses in individuals of European and African ancestry identify cis-pQTLs and models for proteome-wide association studies. *Nature Genetics* 54:593-602

289. Kachuri L, Mak ACY, Hu D, Eng C, Huntsman S, et al. 2023. Gene expression in African Americans, Puerto Ricans and Mexican Americans reveals ancestry-specific patterns of genetic architecture. *Nat Genet*
290. Robins C, Liu Y, Fan W, Duong DM, Meigs J, et al. 2021. Genetic control of the human brain proteome. *Am J Hum Genet* 108:400-10
291. Stepler KE, Mahoney ER, Kofler J, Hohman TJ, Lopez OL, Robinson RAS. 2020. Inclusion of African American/Black adults in a pilot brain proteomics study of Alzheimer's disease. *Neurobiology of Disease* 146:105129
292. Desaire H, Stepler KE, Robinson RAS. 2022. Exposing the Brain Proteomic Signatures of Alzheimer's Disease in Diverse Racial Groups: Leveraging Multiple Data Sets and Machine Learning. *Journal of Proteome Research* 21:1095-104
293. Hodes RJ, Buckholtz N. 2016. Accelerating Medicines Partnership: Alzheimer's Disease (AMP-AD) Knowledge Portal Aids Alzheimer's Drug Discovery through Open Data Sharing. *Expert Opin Ther Targets* 20:389-91
294. Reddy JS, Heath L, Vander Linden A, Allen M, de Paiva Lopes K, et al. 2024. Bridging the Gap: Multi-Omics Profiling of Brain Tissue in Alzheimer's Disease and Older Controls in Multi-Ethnic Populations. *bioRxiv*
295. Seifar F, Fox EJ, Shantaraman A, Liu Y, Dammer EB, et al. 2024. Large-scale Deep Proteomic Analysis in Alzheimer's Disease Brain Regions Across Race and Ethnicity. *bioRxiv*
296. Wesenhagen KEJ, Gobom J, Bos I, Vos SJB, Martinez-Lage P, et al. 2022. Effects of age, amyloid, sex, and APOE  $\epsilon$ 4 on the CSF proteome in normal cognition. *Alzheimers Dement (Amst)* 14:e12286

## CHAPTER 6: Appendix

Table 6.1: Cohort characteristics

Number Cases	GUID	TMT ID	SRM ID	Study	Diagnosis	Age	Sex	Race	Educ	MOCA	APOE	Aβ42	tTau	pTau	tTau/Aβ42	pTau/Aβ42	Cerebrovascular	Diabetes	Dyslipidemia	Hypertension	Outlier
1	37512	b1.131N	S011_P1C02_37512	CRIN	AD	81.1	Female	Black or African American	18	19	e3/e4	498.5	277.1	31.12	0.5558676	0.0624273					
2	39138	b6.128C	S075_P1C10_39138	CRIN	AD	81	Female	Caucasian or White	16	23	e3/e4	644	680.5	76.64	1.056677	0.1190062					
3	42719	b12.130N	S147_P2D5_42719	CRIN	AD	73.9	Male	Black or African American	12	8	e4/e4	274.4	247.5	25.44	0.9019679	0.0927114					
4	44707	b15.129N	S192_P3D5_44707	CRIN	AD	68.9	Male	Caucasian or White	22	17	e3/e4	570.4	540.9	56.91	0.9482819	0.0997721					
5	44820	b15.132N	S187_P3G4_44820	CRIN	AD	50.9	Male	Black or African American	15	6	e3/e3	372.2	317.1	31.98	0.8519613	0.0859215					
6	45034	b1.129N	S005_P1E01_45034	CRIN	AD	76.6	Male	Caucasian or White	21	e3/e3	1066	464.8	44.54	0.4360225	0.0417824					YES	
7	45101	b11.131C	S137_P2C8_45101	CRIN	AD	74.9	Male	Caucasian or White	22	e3/e3	759.6	435.2	51.52	0.5729331	0.0678252	YES					
8	45128	b13.128C	S160_P3D1_45128	CRIN	AD	74.8	Male	Black or African American	18	19	e4/e4	414.6	308.6	31.34	0.7443319	0.0755909			YES	YES	
9	45130	b2.128C	S021_P1E03_45130	CRIN	AD	50	Female	Caucasian or White			e3/e4	487.9	972.8	109.5	1.9938512	0.2244312					YES
10	45573	b3.128C	S037_P1E05_45573	CRIN	AD	72.6	Female	Caucasian or White	12	12	e3/e4	520.8	434.3	42.33	0.8339094	0.0812788					
11	45739	b13.131C	S161_P3E1_45739	CRIN	AD	75.5	Male	Caucasian or White	16	21	e3/e4	485.9	184.4	17.96	0.379502	0.0369623	YES	YES	YES	YES	
12	45831	b12.132N	S149_P2G8_45831	CRIN	AD	75.8	Female	Caucasian or White	17			685.4	319.1	29.71	0.4655676	0.043347					
13	45918	b12.131C	S155_P2E10_45918	CRIN	AD	72.1	Female	Black or African American	18	18		475.2	195.3	18.51	0.4109848	0.038952					
14	46008	b11.132C	S140_P2F8_46008	CRIN	AD	68.7	Female	Caucasian or White	20		e3/e4	696.4	940.7	86.69	1.3508041	0.1244831					
15	46040	b3.131N	S038_P1F05_46040	CRIN	AD	84.1	Male	Caucasian or White	20	19	e3/e3	628.8	462.5	52.83	0.735528	0.0840172					
16	46076	b4.128C	S047_P1G06_46076	CRIN	AD	60.1	Female	Black or African American	12	20		677.4	199.5	22.21	0.2945084	0.0327871			YES	YES	
17	46246	b13.132C	S168_P3D2_46246	CRIN	AD	75.2	Female	Black or African American	18	22	e3/e3	674.3	230.3	24.35	0.3415394	0.0361115				YES	
18	46306	b14.130C	S173_P3A3_46306	CRIN	AD	61	Female	Caucasian or White	18	12	e3/e3	414	150.8	15.27	0.3642512	0.0368841				YES	
19	46640	b6.127C	S076_P1D10_46640	CRIN	AD	76.1	Male	Black or African American	14	9		368.2	273.3	27.83	0.7422596	0.0755839					
20	46642	b1.132C	S012_P1D02_46642	CRIN	AD	68.3	Female	Caucasian or White		14	e4/e4	433.6	433.5	40.91	0.9997694	0.0943496		YES			
21	47135	b14.128N	S177_P3E1_47135	CRIN	AD	74.5	Male	Caucasian or White	16	21	e3/e4	965.3	543.5	65.97	0.5630374	0.0683414					
22	47232	b6.133N	S077_P1E10_47232	CRIN	AD	49.8	Female	Black or African American	12	15	e3/e3	405.8	403.9	40.19	0.9953179	0.0990389					
23	47248	b10.129N	S128_P2B7_47248	CRIN	AD	59.4	Female	Caucasian or White	14	20	e4/e4	280.7	333.5	30.38	1.1881012	0.1082294			YES	YES	
24	47251	b16.130C	S204_P3H6_47251	CRIN	AD	65.5	Female	Caucasian or White	17	e2/e3	294.7	256.2	27.05	0.8693587	0.0917883						
25	43738	b14.127N	S174_P3B3_43738	EHBS	Control	69.9	Female	Black or African American	14	27	e3/e4	1039	147.1	13.06	0.1415784	0.0125698	YES	YES			YES
26	44869	b5.128N	S053_P1E07_44869	EHBS	Control	66.1	Male	Black or African American	18	23	e3/e3	1124	136.3	11.51	0.1212633	0.0102402					
27	45707	b16.128N		EHBS	Control	72.7	Female	Black or African American	18	24	e2/e3	1700	254.8	23.86	0.1498824	0.0140353	YES				
28	46085	b1.128N	S009_P1A02_46085	EHBS	Control	51.3	Male	Black or African American	16	25	e2/e4	768.5	83.66	8	0.1088614	0.0104099		YES			YES
29	48153	b8.127N	S093_P2G2_48153	EHBS	Control	72.4	Female	Caucasian or White	16	30	e2/e3	1387	174.4	15.06	0.125739	0.010858					
30	48358	b14.129N	S176_P3D3_48358	EHBS	Control	66.1	Female	Caucasian or White	16	24	e3/e3	1700	197.4	17.56	0.1161176	0.0103294					
31	48617	b12.127C		EHBS	Control	57.7	Female	Black or African American	13	28	e3/e3	1285	153.2	13.09	0.1192218	0.0101868					
32	48769	b15.133N		EHBS	Control	75	Female	Caucasian or White	14	26	e3/e3	1700	227.9	19.72	0.1340588	0.0116			YES	YES	
33	49324	b2.128C	S060_P1D08_49324	EHBS	Control	60.2	Female	Caucasian or White	20	27	e2/e3	1431	164.1	15	0.1146751	0.0104822					
34	49417	b2.128N	S016_P1H02_49417	EHBS	Control	71.6	Female	Caucasian or White	16	26	e3/e3	1411	177.8	15.41	0.1260099	0.0109213					
35	49537	b15.128N		EHBS	Control	51	Female	Black or African American	18	25	e2/e4	862.4	105.4	9.97	0.1222171	0.0115608					
36	49903	b10.131C	S126_P2H6_49903	EHBS	Control	64.9	Male	Caucasian or White	18	27	e3/e3	1084	180.2	15.51	0.1662362	0.0143081				YES	
37	49941	b6.132C	S074_P1B10_49941	EHBS	Control	69.7	Male	Caucasian or White	16	26	e3/e3	1165	156	13.65	0.1339056	0.0117167					
38	50259	b14.131N	S182_P3B4_50259	EHBS	Control	50.1	Female	Black or African American	20	28	e3/e4	447.4	80.22	8	0.1793026	0.0178811	YES				
39	50273	b8.133N	S094_P2H2_50273	EHBS	Control	69	Female	Caucasian or White	20	28	e3/e4	1700	220.9	19.62	0.1299412	0.0115412					
40	50409	b16.130N	S199_P3C6_50409	EHBS	Control	64.8	Female	Caucasian or White	18	23	e3/e4	823.1	166.1	14.15	0.2017981	0.0171911					
41	50452	b4.130N	S052_P1D07_50452	EHBS	Control	59.5	Female	Caucasian or White	18	29	e3/e4	920.5	123.8	10.98	0.1344921	0.0119283				YES	
42	50502	b13.130C	S165_P3A2_50502	EHBS	Control	55.5	Female	Black or African American	13	28	e3/e3	892	105.2	9.58	0.1179372	0.0107399					
43	50534	b4.128N	S041_P1A06_50534	EHBS	Control	71.5	Female	Caucasian or White	14	25	e3/e4	1595	364.5	35.32	0.2285266	0.0221442		YES			
44	50619	b5.127C	S056_P1H07_50619	EHBS	Control	64.7	Female	Caucasian or White	12	23	e3/e3	1700	191.3	17.42	0.1125294	0.0102471					
45	50650	b3.129C	S033_P1A05_50650	EHBS	Control	59.4	Female	Caucasian or White	18	28	e3/e3	1541	308.1	27.24	0.1999351	0.0176768					
46	51023	b9.129C	S107_P2E4_51023	EHBS	Control	68.4	Female	Black or African American	16	28	e3/e3	1239	236.4	21.54	0.190799	0.017385					
47	51123	b9.132C	S114_P2D5_51123	EHBS	Control	50	Female	Caucasian or White	14	26	e3/e3	1410	154	14.36	0.1092199	0.0101844					
48	51135	b6.129C	S067_P1C09_51135	EHBS	Control	61.9	Female	Caucasian or White	16	24	e3/e4	594.6	104.6	8.34	0.1759166	0.0140262				YES	
49	51175	b12.128C	S153_P2C10_51175	EHBS	Control	65.5	Female	Caucasian or White	20	24	e3/e3	1442	233.3	21.18	0.1617892	0.0146879					
50	51224	b16.127C	S200_P3D6_51224	EHBS	Control	66.2	Male	Caucasian or White	18	28	e3/e3	1235	142.2	14.92	0.1151417	0.012081					
51	51264	b8.128N	S095_P2A3_51264	EHBS	Control	61.2	Female	Caucasian or White	12	31	e3/e3	1700	241.6	21.36	0.1421176	0.0125647					YES
52	51319	b8.132C	S096_P2B3_51319	EHBS	Control	68.7	Female	Black or African American	18	20	e3/e3	762.1	116.5	10.26	0.1528671	0.0134628					
53	51370	b1.130C	S010_P1B02_51370	EHBS	Control	70.4	Female	Caucasian or White	16	26	e2/e3	1353	136.8	13.55	0.1011086	0.0100148					
54	51431	b7.128C	S082_P2D1_51431	EHBS	Control	69.8	Female	Caucasian or White	14	29	e3/e4	1700	208.2	18.12	0.1224706	0.0106588					
55	51499	b4.132N	S042_P1B06_51499	EHBS	Control	74.5	Male	Caucasian or White	20	28	e2/e3	832.6	125.4	10.12	0.1506125	0.0121547					
56	51520	b9.133N		EHBS	Control	53.5	Female	Black or African American	15	23	e3/e3	699.8	113.7	9.14	0.162475	0.0130609	YES				
57	51551	b2.130N	S023_P1G03_51551	EHBS	Control	66.4	Female	Caucasian or White	13	24	e2/e3	1423	147.8	13.02	0.1038651	0.0091497					
58	51559	b4.132C	S045_P1E06_51559	EHBS	Control	64.5	Female	Caucasian or White	18	25	e3/e3	1176	122.4	11.5	0.1040816	0.0097789					
59	51760	b13.131N	S159_P3C1_51760	EHBS	Control	57.1	Male	Black or African American	13	26	e3/e3	856.5	128.3	11.73	0.1497957	0.0136953					
60	52055	b10.127C		EHBS	Control	66.8	Female	Black or African American	16	28	e2/e3	997	149.1	15.38	0.1495486	0.0154263		YES	YES	YES	
61	52131	b3.130N	S034_P1B05_52131	EHBS	Control	75.7	Female	Caucasian or White	13	27	e2/e3	1242	170								

65	52538	b14.132N	S171_P362_52538	EHBS	Control	58.7	Female	Caucasian or White	18	25	e2/e4	1700	194.6	17.49	0.1144706	0.0102882			
66	52626	b9.131C	S108_P2F4_52626	EHBS	Control	66.6	Female	Caucasian or White	18	26	e3/e3	1700	219.5	23.23	0.1291176	0.0136647			
67	52791	b11.129C	S132_P2F7_52791	EHBS	Control	64	Female	Black or African American	13	28	e3/e3	501.8	86.27	8	0.1719211	0.0159426			
68	53030	b15.127N	S184_P3D4_53030	EHBS	Control	56.5	Female	Black or African American	13	29	e3/e3	1511	171.5	15.19	0.1129776	0.0106613			
69	53612	b1.132N	S002_P1D01_53612	EHBS	Control	52.7	Female	Black or African American	18	28	e3/e4	1240	174.9	16.67	0.1410484	0.0134435			
70	53618	b4.129N	S043_P1C06_53618	EHBS	Control	70.5	Female	Black or African American	18	26	e3/e3	1004	124	11.5	0.1235506	0.0114542			
71	53705	b12.129N	S146_P2D9_53705	EHBS	Control	54.5	Female	Caucasian or White	16	23	e2/e3	1459	162.6	13.71	0.1114462	0.0093968			
72	53729	b5.130C	S054_P1F10_53729	EHBS	Control	72.7	Female	Caucasian or White	18	28	e3/e3	986.2	144.7	14.81	0.1447448	0.0150172			
73	53731	b11.128N	S139_P2B3_53731	EHBS	Control	70.9	Female	Black or African American	18	27	e3/e3	1479	136.5	12.51	0.0922921	0.0084584			
74	53741	b6.129N	S068_P1D09_53741	EHBS	Control	53.6	Female	Caucasian or White	18	26	e3/e3	1532	213.8	18.31	0.1395561	0.0119517			
75	55244	b3.127N	S035_P1C05_55244	EHBS	Control	64.6	Female	Black or African American	14	24	e3/e4	1158	164.4	14.97	0.1393782	0.0129275			
76	55286	b7.128N	S084_P2F1_55286	EHBS	Control	56.6	Female	Black or African American	16	26	e3/e3	789.4	94.69	8.38	0.1199519	0.0106157			
77	55838	b13.132N	S166_P3B2_55838	EHBS	Control	66.7	Female	Caucasian or White	16	23	e3/e4	1177	258.1	24.54	0.2152863	0.0208496			
78	56007	b11.127N	S133_P2C7_56007	EHBS	Control	64.8	Male	Caucasian or White	16	25	e3/e4	890	208.8	19.3	0.1228235	0.0113529			
79	56326	b10.127N	S121_P2C5_56326	EHBS	Control	70.9	Female	Caucasian or White	16	25	e3/e3	1700	307.8	30.74	0.1810588	0.0180824			
80	56580	b12.127N	S154_P2D10_56580	EHBS	Control	57.3	Male	Caucasian or White	16	26	e3/e3	835	100.9	9.51	0.1208383	0.0113892			
81	57907	b4.127C	S044_P1D06_57907	EHBS	Control	64.4	Male	Caucasian or White	20	28	e3/e4	1005	133.1	10.98	0.1324378	0.0109254			YES
82	58595	b6.130N	S069_P1D09_58595	EHBS	Control	64.9	Male	Black or African American	18	22	e2/e3	600.4	91.22	8	0.1516932	0.0113345	YES	YES	YES
83	58815	b11.128C	S135_P2A8_58815	EHBS	Control	61.6	Male	Black or African American	14	25	e3/e3	943.3	145.6	13.16	0.1543517	0.0113951			
84	59913	b2.129C	S017_P1A03_59913	EHBS	Control	75.4	Male	Black or African American	12	22	e2/e3	1570	238.8	23.37	0.1521019	0.0148854			
85	62211	b2.131N	S088_P1B03_62211	EHBS	Control	57.1	Male	Caucasian or White	16	30	e2/e3	1583	189.3	16.31	0.1195831	0.0103032			
86	62762	b11.127C	EHBS	Control	57.2	Male	Caucasian or White	18	29	e3/e4	1473	196.5	17.48	0.1334012	0.0118669				
87	63141	b10.131N	S119_P3A6_63141	EHBS	Control	51.1	Male	Caucasian or White	16	25	e2/e3	1004	111	9.17	0.1165578	0.0091335			
88	63456	b1.127N	S003_P1D01_63456	EHBS	Control	69.5	Male	Black or African American	18	27	e2/e3	835	129.7	12.11	0.1552736	0.0144978			
89	66352	b5.133N	S061_P1E08_66352	EHBS	Control	77.8	Male	Black or African American	20	28	e3/e3	1498	176.6	15.66	0.1178905	0.0104539			
90	66827	b8.130C	S101_P2G3_66827	EHBS	Control	72.5	Male	Caucasian or White	16	24	e2/e4	1125	147.8	12.48	0.1313778	0.0110933			
91	66984	b2.133N	S019_P1C03_66984	EHBS	Control	51.7	Male	Black or African American	13	23	e3/e4	764.7	125.6	10.6	0.1642474	0.0138616			
92	68545	b9.130N	S110_P2H4_68545	EHBS	Control	57.3	Male	Black or African American	18	27	e3/e3	1368	167.5	17.34	0.1224545	0.0126754	YES	YES	YES
93	68620	b3.131C	S030_P1D04_68620	EHBS	Control	51.5	Male	Black or African American	13	20	e3/e3	935.7	120.5	10.99	0.1287806	0.0117452	YES	YES	YES
94	70714	b14.129C	S172_P3H4_70714	EHBS	Control	57.4	Male	Black or African American	12	21	e2/e4	1221	142	12.96	0.1162981	0.0106143			
95	72374	b6.131N	S070_P1F09_72374	EHBS	Control	52.1	Male	Black or African American	13	22	e2/e3	686.6	101.8	10.21	0.1482668	0.0148704			
96	73786	b8.129C	S097_P2C3_73786	EHBS	Control	61.6	Male	Caucasian or White	18	29	e2/e3	1700	244.2	20.31	0.1436471	0.0119471			YES
97	74682	b15.132C	S085_P3H4_74682	EHBS	Control	64.5	Male	Black or African American	18	26	e3/e3	1180	143.7	12.27	0.1217797	0.0103983			
98	75351	b1.129C	S004_P1D01_75351	EHBS	Control	72.1	Male	Caucasian or White	14	29	e2/e3	1700	185.6	17.01	0.1091765	0.0100059			
99	76023	b3.127C	S031_P1G04_76023	EHBS	Control	51.9	Male	Caucasian or White	18	26	e2/e3	869.6	107.5	9.97	0.1236201	0.011465			
100	76348	b6.127N	S071_P1G09_76348	EHBS	Control	52.1	Male	Caucasian or White	14	28	e3/e3	916.9	102	9.78	0.1112444	0.0106664			
101	76615	b15.130N	S186_P3H4_76615	EHBS	Control	64.6	Male	Black or African American	16	23	e3/e3	876.8	154	13	0.1756387	0.0148266			
102	76950	b8.127C	S086_P2D3_76950	EHBS	Control	69.4	Male	Caucasian or White	16	25	e2/e3	954.9	142.6	16	0.1489335	0.0115408			
103	78086	b10.132N	S120_P3B2_78086	EHBS	Control	72.6	Male	Black or African American	18	29	e3/e3	471.7	99.68	8.9	0.2113208	0.0188679			
104	86092	b13.129C	S167_P3C2_86092	EHBS	Control	51.5	Male	Caucasian or White	16	24	e3/e4	1176	131.1	11.57	0.1114796	0.0098384			
105	41483	b1.127C	S001_P1A01_41483	Memory	AD	66.8	Female	Black or African American	13	26	e4/e4	666.9	358.2	33.78	0.537112	0.0056523			
106	41484	b7.127N	S081_P2C1_41484	Memory	Control	77.3	Female	Black or African American	18	28	e3/e3	1700	234.1	18.9	0.1377059	0.0111176	YES		
107	42541	b2.132N	S016_P1F03_42541	Memory	Control	58.2	Female	Black or African American	22	19	e3/e4	207.6	207.6	18.2	0.531218	0.046085	YES		
108	42570	b8.130N	S103_P2A4_42570	Memory	Control	78.1	Female	Black or African American	18	22	e2/e3	1700	240.4	19.18	0.1414118	0.0112824			
109	42947	b15.129C	S183_P3C4_42947	Memory	Control	82	Female	Caucasian or White	18	24	e3/e3	1700	341.5	25.9	0.2008824	0.0152533			
110	43820	b16.128C	S197_P3A6_43820	Memory	Control	60.7	Female	Caucasian or White	18	29	e3/e3	878.4	94.12	8	0.1071494	0.0091075			
111	44067	b1.130N	S013_P1E02_44067	Memory	Control	61.1	Female	Black or African American	18	26	e2/e3	983.5	128.3	10.76	0.1304525	0.0109405	YES		
112	44291	b12.132C	S015_P1G04_44291	Memory	Control	71.5	Female	Black or African American	16	23	e3/e3	1196	163.8	14.46	0.1389565	0.0120903			
113	44511	b9.132N	S105_P2C4_44511	Memory	Control	77	Female	Black or African American	20	26	e3/e3	739	213.9	21.26	0.2894552	0.0287866			
114	44893	b16.131N	S198_P3B6_44893	Memory	Control	60.7	Female	Black or African American	14	26	e2/e3	691.8	121.5	10.25	0.1756288	0.0148164			
115	45238	b14.132C	S175_P3C3_45238	Memory	Control	62.2	Female	Black or African American	16	21	e3/e3	1700	246.8	25.07	0.1451765	0.0147471			
116	45487	b14.131C	S170_P3F2_45487	Memory	AD	75.6	Female	Black or African American	16	8	e4/e4	327.9	478.9	42.26	0.4605063	0.1288808			
117	45861	b4.127N	S045_P1D03_45861	Memory	Control	62.4	Female	Black or African American	16	23	e2/e3	898.3	125.8	12.7	0.1404923	0.0125486			
118	46043	b13.127N	S157_P3A1_46043	Memory	Control	70.3	Female	Caucasian or White	16	23	e3/e3	1700	238.1	18.9	0.1405088	0.0111776			
119	46103	b12.131N	S144_P2B9_46103	Memory	Control	70.3	Female	Black or African American	13	28	e3/e3	1045	141.9	12.36	0.1357895	0.0118278			
120	46233	b13.129N	S158_P3B1_46233	Memory	Control	61.3	Female	Black or African American	16	28	e2/e4	1608	340.3	29.25	0.2116294	0.0181903			
121	46390	b4.129C	S091_P1C07_46390	Memory	Control	55.3	Female	Black or African American	18	28	e2/e4	1075	150.3	13.18	0.139814	0.0122605			
122	46931	b1.133N	S019_P1E03_46931	Memory	Control	71.6	Female	Black or African American	18	25	e3/e3	1239	163.3	14.01	0.1269572	0.0113075			
123	47147	b10.130N	S118_P2H5_47147	Memory	Control	60.2	Female	Caucasian or White	16	25	e3/e4	1185	188.1	15.74	0.1587342	0.0132827			
124	47480	b11.132N	S131_P2E7_47480	Memory	Control	72.1	Male	Black or African American	16	29	e3/e3	1547	226	19.56	0.1460892	0.0126438			
125	48786	b9.130N	S113_P2C5_48786	Memory	Control	72.4	Female	Black or African American	18	27	e3/e4	1700	231.6	19.17	0.1362353	0.0112765	YES		
126	48937	b12.129C	S152_P2D10_48937	Memory	Control	65.5	Female	Black or African American	18	25	e3/e3	1700	225.2	19.33	0.1324706	0.0113706			YES
127	50313	b6.132N	S076_P1F08_50313	Memory	Control	66.4	Female	Caucasian or White	16	26	e3/e3	707	206.7	19.3	0.1618637	0.0148215			YES
128	56968	b5.131N	S055_P1G07_56968	Memory	Control	78.3	Male	Caucasian or White	18	27	e3/e3	1700	279	24.04	0.1641176	0.0141412			
129	57339	b2.129N	S020_P1D03_57339	Memory	Control	63.9	Female	Black or African American	20	27	e3/e3	816.1	125	10.81	0.1531675	0.0132459			
130	57450	b11.130C	S134_P2H7_57450	Memory	Control	69.4	Male	Black or African American	14	26	e2/e3	1034	146.2	12.62	0.1413927	0.012205			YES
131	57502	b2.131N	S045_P2G1_57502	Memory	Control	64.6	Female	Black or African American	14	29	e3/e3	897.7	150.6	12.35	0.1609597	0.0121312			
132	63982	b9.128C	S109_P2G4_63982	Memory	Control	75.2	Male	Caucasian or White	15	25	e3/e3	1566	234.8	19.28	0.1499361	0.0123116			
133	69030	b3.132N	S036_P1D05_69030	Memory	Control	69.7	Male	Black or African American	15	24	e3/e3	1700	285.2	21.76	0.167764				

195	84355	b5.129N	S065_P1A09_84355	NeuCog	AD	76	Male	Black or African American	20	20		564.5	315.6	30.98	0.5590788	0.0548804					
196	84561	b5.132N	S059_P1C08_84561	NeuCog	AD	50.1	Female	Black or African American	14	7	e3/e4	308	215.2	20.51	0.6987013	0.0665909					
197	85026	b9.128N	S112_P2B5_85026	NeuCog	AD	63.1	Female	Black or African American	12	16	e4/e4	200	209	20.3	1.045	0.1015					
198	85961	b15.127C	S195_P3G5_85961	NeuCog	AD	67	Female	Caucasian or White	14	17	e3/e4	540.8	382.5	39.76	0.7072855	0.0735207	YES	YES	YES		
199	86582	b10.130C	S125_P2G6_86582	NeuCog	AD	58.2	Male	Caucasian or White	18	9	e3/e3	598.3	471.6	51.68	0.7882333	0.0863781					
200	86780	b15.128C	S188_P3H4_86780	NeuCog	AD	63.6	Male	Black or African American	16	20		515.3	356.3	40.27	0.6914419	0.0781487					YES
201	86840	b7.133N	S088_P2B2_86840	NeuCog	AD	52.1	Male	Caucasian or White	14	12	e3/e3	436.5	522.8	66.65	1.197709	0.1526919					
202	87070	b7.130N	S089_P2C2_87070	NeuCog	AD	77	Female	Caucasian or White	22	13	e3/e3	273.5	155.9	14.33	0.5700183	0.0523949					YES
203	87124	b15.130C	S189_P3A5_87124	NeuCog	AD	64	Female	Black or African American	20	7	e3/e4	383.6	294.7	33.76	0.7682482	0.0880083					YES
Empty Channel		b14.133N																			

**Table 6.2: TMT Batch Arrangement.**

	Batch 1	Batch 2	Batch 3	Batch 4	Batch 5	Batch 6	Batch 7	Batch 8	Batch 9	Batch 10	Batch 11	Batch 12	Batch 13	Batch 14	Batch 15	Batch 16
Plex																
126	GIS	GIS	GIS	GIS	GIS	GIS	GIS	GIS	GIS	GIS	GIS	GIS	GIS	GIS	GIS	GIS
127N	63456	67976	55244	45861	73808	76348	41483	48153	47498	56326	56007	56580	46043	43738	53030	83314
127C	41324	64402	76023	57907	50619	46640	77792	76950	52945	52055	62762	48617	56582	83798	85961	51224
128N	46085	49417	47238	50534	44869	67579	55286	51264	85026	79243	53731	52475	49545	47135	49537	45707
128C	69732	45130	45573	46076	49324	39138	51431	66276	63982	73621	58815	51175	45128	47351	86780	43820
129N	45034	57339	54755	53618	84355	53741	70529	77355	53398	47248	82876	53705	46233	48358	44707	54601
129C	75351	59913	50650	46390	80265	51135	73518	73786	51023	74112	52791	48937	86092	70714	42947	49450
130N	44067	51551	52131	50452	59128	58595	87070	42570	48786	47147	47368	42719	73152	72191	76615	50409
130C	51370	52524	71200	68342	53729	66735	54179	66827	68545	86582	57450	84217	50502	46306	87124	47251
131N	37512	62211	46040	53819	56968	72374	57502	57056	57326	63141	57251	46103	51760	50259	77501	44893
131C	49419	74051	68620	83366	72848	83459	49087	46282	52626	49903	45101	45918	45739	45487	64149	GIS
132N	53612	42541	69030	51499	84561	50313	52154	48746	44511	78086	47480	45831	55838	52538	44820	GIS
132C	46642	44291	48024	51559	78317	49941	48615	51319	51123	51464	46008	46743	46246	45238	74682	GIS
133N	46442	66984	46931	58885	66352	47232	86840	50273	51520	80287	57498	48222	76896	48615	48769	GIS
133C	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
134N	High	High	High	High	High	High	High	High	High	High	High	High	High	High	High	High



Gene ID	Uniprot ID	ANOVA p-values with Adjusted										Difference (AD - CT)									
		F-Value	P(r=F)	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA
ALB	P02768	0.8887791	0.690420873	0.89373558	0.99594943	0.96432078	0.84908803	0.639042157	0.981868491	0.063232322	0.00918691	0.104026296	0.072445261	0.102489618	0.03184006	0.03184006	0.03184006	0.03184006	0.03184006	0.03184006	
CA	P01278	1.5942792	0.19227741	0.63456693	0.80701626	0.94060859	0.159239454	0.90772632	0.08373502	0.062748319	0.039047686	0.148577726	0.046682901	0.018948529	0.018948529	0.018948529	0.018948529	0.018948529	0.018948529	0.018948529	
FN1	P02761	0.8973104	0.436882271	0.84130859	0.99724617	0.80629626	0.917184738	0.31837771	0.75451727	0.030512959	0.009709267	0.026847470	0.023413692	0.057387667	0.033973975	0.033973975	0.033973975	0.033973975	0.033973975	0.033973975	
CAF	POC05	0.0367396	0.854843082	0.838330978	0.99680843	0.93216501	0.981018761	0.83597751	0.66775064	0.06842031	0.009706760	0.134247664	0.030652374	0.05827331	0.031740583	0.031740583	0.031740583	0.031740583	0.031740583	0.031740583	
CA	P02768	1.2704086	0.045841011	0.39891273	0.78438161	0.61474632	0.060030083	0.974151362	0.12038145	0.029618495	0.074819371	0.21879145	0.466032131	0.077693561	0.077693561	0.077693561	0.077693561	0.077693561	0.077693561	0.077693561	
CA	P01023	3.2996566	0.021594851	0.11383803	0.153819515	0.14803824	0.951761391	0.78627474	0.87978778	0.061388536	0.067493791	0.021594851	0.021594851	0.021594851	0.021594851	0.021594851	0.021594851	0.021594851	0.021594851	0.021594851	
SPARC1	Q14515	9.967679	4.00E-16	0.00138923	0.00426067	6.83E-06	0.29583705	0.96627351	0.04945222	0.22965524	0.173853957	0.23761425	0.00179857	0.00179857	0.00179857	0.00179857	0.00179857	0.00179857	0.00179857	0.00179857	
TP	P02787	2.3173075	0.07707361	0.99803766	0.38299583	0.185451461	0.34959277	0.16586297	0.79938326	0.003892701	0.07753477	0.095943693	0.081654458	0.098941434	0.081955886	0.081955886	0.081955886	0.081955886	0.081955886	0.081955886	
FCGBP	Q0Y67	21.2062133	7.49E-12	1.71E-09	0.43212066	1.54E-07	2.14E-06	0.63735382	0.00134496	0.74670703	0.177901721	0.042734031	0.06768991	0.123973202	0.013731689	0.013731689	0.013731689	0.013731689	0.013731689	0.013731689	
CP	PO4050	0.5907526	0.6217921	0.99164214	0.70654238	0.99545492	0.63800645	0.98275359	0.15866421	0.011092584	0.08729893	0.18630138	0.0893517	0.19237222	0.06688851	0.06688851	0.06688851	0.06688851	0.06688851	0.06688851	
CHGB	PO5080	8.6220351	2.19E-05	0.82653362	0.01188128	5.45E-05	0.12902085	0.00218793	0.42427249	0.03708315	0.130430914	0.18419324	0.09347759	0.1536168	0.059884099	0.059884099	0.059884099	0.059884099	0.059884099	0.059884099	
CHGB	PO5080	0.6407481	0.5679791	0.58793012	0.14803824	0.951761391	0.78627474	0.87978778	0.061388536	0.067493791	0.021594851	0.021594851	0.021594851	0.021594851							

130



Gene ID   Uniprot ID	F-Value	Pr[F]	ANOVA p-values with Tukey Adjustment								Difference (AD - CT)							
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau
VWF   P04275	1.3751776	0.25178434	0.916302355	0.702061436	0.749992542	0.316717948	0.3480429	0.99544119	-0.0254996	0.04138857	0.037404301	0.066888169	0.062903901	-0.003984269				
COL6A1   P12109	1.5093755	0.21059664	0.329685867	0.691410913	0.999948142	0.92026974	0.270927074	0.629886901	-0.068285094	0.043048513	0.020207924	0.025236581	0.070293101	0.045056437				
KLK6   Q92876	0.7735167	0.510163107	0.589296694	0.704674188	0.528980511	0.996385369	0.999911166	0.993927565	0.03947025	0.032782348	0.040345645	-0.006687902	0.000875395	0.007632327				
NFASC   Q94856	1.41983332	1.399E-05	0.02947684	0.041370857	1.05E-05	0.997161265	0.20085791	0.11486211	-0.104975817	0.09756908	0.176530425	-0.00740673	0.071554607	0.07861337				
MLL1   Q16610	5.59851432	0.00071829	0.438329846	0.000458421	0.11319566	0.069225096	0.910457037	0.226697965	0.058404966	0.103773117	0.083235902	0.094298151	0.024849636	0.069449215				
MANN2A   P49641	1.3176584	0.270023556	0.999909929	0.454490266	0.914564289	0.504745333	0.54370238	0.999674232	0.002765641	0.063008651	0.050393448	0.060203401	0.056273801	0.003969203				
COL1A1   P02452	1.39775873	0.244939355	0.861661329	0.97181506	0.628400656	0.609204787	0.192257191	0.870782392	-0.035553368	0.019327724	0.1567502	0.054880643	0.08723888	0.03247746				
PROS1   P07225	2.20543017	0.08884731	0.117210337	0.991896564	0.438053698	0.195456941	0.835207488	0.607544709	-0.088716307	-0.01100245	-0.06664945	0.077713858	0.032071362	-0.045642496				
LTBP4   Q8N251	18.2967197	1.94E-10	3.75E-05	0.999999367	4.37E-07	2.60E-05	0.8926395	2.53E-07	-0.152719483	0.000385659	-0.175205046	0.153105142	-0.024855631	-0.175590591				
NID1   P15453	6.6861259	0.000261357	0.002903891	0.086239016	0.002779503	0.037664508	0.998291052	0.040628343	-0.110250732	-0.027256019	-0.105186028	0.082994713	0.050064704	-0.077930008				
APLP1   Q06481	0.5430244	0.65283056	0.82534297	0.984115189	0.999988369	0.609712851	0.791429988	0.986258227	-0.049427572	0.02007083	0.001738963	0.069498402	0.051166535	-0.018331867				
LAMB2   P55268	4.11947765	0.007399478	0.865837823	0.077773049	0.992617597	0.009480349	0.95116237	0.02898218	-0.017893361	0.054277324	-0.00604538	0.07170885	0.001182884	-0.060341861				
IGHG3   P01860	10.3819681	2.39E-06	0.000308442	0.872720092	0.05644562	9.76E-06	0.283504001	0.068483878	-0.622247424	0.111054025	-0.36380471	0.73301447	0.25849812	-0.474861635				
AGRN   Q00468	1.0792407	0.359145513	0.572806272	0.773331479	0.30795381	0.98403412	0.984127718	0.86820926	0.036602033	0.026527332	0.06980122	-0.010074701	0.010378089	0.02045279				
PKM1   P14618	26.1545069	3.77E-14	0.103546667	2.82E-06	4.68E-05	1.67E-11	4.27E-10	0.871315639	0.094973813	-0.21052424	-0.181018146	-0.305480853	-0.27599196	0.029506093				
PLXNB1   Q15031	2.52157054	0.095276974	0.071508784	0.09955347	0.387419336	0.996908165	0.763235198	0.859534992	-0.081737308	-0.074977359	-0.050393829	0.06075995	0.03134348	0.02483853				
CTP2   P02748	0.27962137	0.840063947	0.9924705	0.956370495	0.91934826	0.862881599	0.999997421	0.852738721	-0.027673526	0.050401098	-0.025786651	0.078274624	0.001868875	-0.076387749				
FTSL4   Q8M272	2.69103299	0.047627048	0.819230175	0.249079083	0.040013284	0.777459599	0.30649742	0.859561048	0.052173786	0.108167664	0.152244004	0.059593878	0.100070217	-0.04407634				
IGFBP1   P24592	1.6744892	0.140271184	0.524077565	0.984816345	0.519676357	0.30922747	0.999927547	0.292759877	-0.075185787	0.018966932	-0.072075437	0.094152719	0.00311005	-0.091042369				
CFI   P05156	1.57135216	0.197825511	0.999990571	0.237109826	0.845015065	0.260411504	0.863934935	0.67077794	0.002517638	0.155737791	0.066398892	0.153220513	0.063581244	-0.089638059				
NCAN   Q14594	1.28485107	0.280696515	0.693626264	0.542146545	0.220052065	0.96821516	0.869166168	0.9405175	0.067859482	0.080543939	0.112684457	0.012684457	0.03579301	0.03810853				
NID2   Q14112	3.7751427	0.01160995	0.069367106	0.986661163	0.271126917	0.025996525	0.868283538	0.128402862	-0.105024023	0.014029135	-0.073451128	0.119053158	0.031572895	-0.087480263				
SERPINF1   P36955	9.27647657	9.56E-06	0.004329836	0.631985074	0.098072453	3.76E-05	0.682319599	0.001334997	-0.136992096	0.065861161	-0.039998979	0.183483777	0.024934017	-0.140593749				
B4GAT1   Q14305	5.7612962	0.000805095	0.2977124	0.131141434	0.003068538	0.98190806	0.110967216	0.217541009	0.054519793	0.00999274	0.122070629	0.011472947	0.067550413	0.05007466				
PTGS1   P14222	1.6411766	0.181395492	0.16446998	0.98201514	0.828295645	0.30350434	0.554869394	0.96238863	0.059238954	-0.01038632	0.023165059	0.049020213	0.036093895	0.012924728				
FLNA1   P08095	1.10048893	0.350277694	0.490466695	0.99505561	0.531840502	0.968269092	0.999071158	0.670865062	-0.056508384	-0.009602208	-0.051233008	0.07446176	0.005275376	-0.042170801				
ATRN   Q157882	4.80834079	0.00305536	0.066053799	0.684175222	0.654374064	0.002158085	0.478631478	0.054324641	-0.097344132	0.04233366	0.04314679	0.139679499	0.045196454	-0.085480349				
LAMB1   P07942	2.94880834	0.034098598	0.457852216	0.446452666	0.995263955	0.017925576	0.29511428	0.938742864	-0.038704188	0.088140615	0.005947906	0.076848003	0.044652904	0.032197209				
CNTNAP4   QCD0A0	2.38261077	0.070883023	0.862627465	0.973386286	0.270215337	0.982698686	0.372942772	0.172758192	0.043294802	0.02313173	0.12934348	-0.20153762	0.086048682	0.106206354				
ECM2   Q94769	1.3118074	0.271948126	0.781774032	0.96260589	0.039078374	0.963500141	0.815403828	0.849360681	-0.040963984	-0.02044291	-0.07774617	0.020521074	0.036782163	0.057032327				
FLNA1   Q14767	12.2150738	4.50E-07	0.03294378	0.72702589	0.458E-07	0.29105864	0.042361694	4.38E-05	-0.138899498	-0.05097717	-0.26780576	0.087923881	-0.128951298	-0.216877367				
AZGP1   P15311	0.75065888	0.5856467	0.470435173	0.97624707	0.938580777	0.13755337	0.754786176	0.99631319	-0.114402138	-0.026392025	0.07103167	0.082710101	0.073249891	-0.03047771				
TNPA1   P21333	0.8104256	0.40564607	0.900285948	0.672634767	0.445821584	0.976240763	0.96763776	0.986363249	-0.044894956	-0.071427714	-0.02913575	-0.026348329	0.047146279	-0.20707802				
KRT10   P13645	1.0028781	0.392810795	0.99993949	0.570330853	0.60673372	0.616681028	0.65360381	0.999744369	0.011450799	0.253019319	0.236211522	0.21456852	0.224760732	0.016807796				
WWP1   P08253	0.8231209	0.482591463	0.947177838	0.621846371	0.970303668	0.467700671	0.894865439	0.881868318	-0.010316374	0.047628232	0.01716653	0.057946607	0.027482905	-0.03601778				
KRT1   P35527	0.38876404	0.754053858	0.85005885	0.996882056	0.996435025	0.926629252	0.18519771	0.972450014	-0.205518928	-0.051056885	0.05219182	0.15445304	0.257710748	0.103257075				
SERPINF2   P08697	0.94665736	0.46980062	0.86111382	0.872145591	0.980972445	0.014604642	0.674455119	0.964905044	-0.069905602	0.065861417	0.06333821	0.13567019	0.096413223	0.093593796				
HBB   P04818	2.17938887	0.091955499	0.381331987	0.98199661	0.130247843	0.561312451	0.961041727	0.07307179	-0.30688111	-0.06998335	-0.712226873	0.441429708	-0.162392562	-0.60382327				
GALNS1   Q08380	3.67291297	0.012368063	0.279616273	0.89588077	0.13755337	0.060689161	0.995338869	0.93046419	-0.070661199	0.026836925	0.07103167	0.079598804	0.026468985	-0.01247771				
DAG1   Q11643	5.7578409	8.29E-05	0.011744643	0.716505089	0.000183371	0.514198477	0.755122102	0.00762311	0.048662493	0.016151177	0.063615101	-0.032542446	0.014945678	-0.047499924				
CTSD   P07339	1.37356883	0.021099662	0.039504559	0.726614252	0.053891477	0.328062121	0.994115343	0.424247425	-0.165997793	-0.062578921	-0.107969977	0.103419052	0.015200995	-0.088218057				
COL12A1   Q9N715	2.88952395	0.036826698	0.069596788	0.838914045	0.008491052	0.338999193	0.95676765	0.422006645	-0.097115002	-0.031969733	-0.058139693	0.065145269	0.008751097	-0.056394172				
PSAP   P07602	0.63184847	0.595567693	0.681184428	0.990899608	0.704751241	0.839575892	0.99968826	0.860694967	0.04008888	0.010382391	0.036786777	-0.029706489	-0.03002102	0.026404387				
CNTNAP2   Q9UHQ6	2.27186581	0.08170083	0.169920846	0.527907822	0.076748622	0.874881884	0.994580816	0.189090979	0.013938618	0.03376245	0.133284248	-0.043057168	0.01389643	0.05951799				
ITIH5   Q86U28	21.2820258	6.89E-12	0.7386437	0.574398073	1.40E-07	1.54E-06	0.74591623	0.91651623	-0.465173681	-0.046999513	-0.208733297	0.198174168	0.26440385	-0.16173784				
IGHA1   P01861	0.8484992	0.476271482	0.607847828	0.989399487	0.58647001	0.782424108	0.999901199	0.77151076	0.260647772	-0.054365055	0.5442372	0.196211267	0.006512405	-0.19087217				
TGFBI   Q15582	0.61356246	0.607006136	0.945972038	0.995266216	0.590286677	0.988041079	0.908285526	0.703170787	0.02097417	0.00878402	0.05483998	-0.012186769	0.025409828	0.036656597				

Gene ID   Uniprot ID	F-Value	Pr(>F)	ANOVA p-values with Tukey Adjustment										Difference (AD - CT)									
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA
HB2A   P69005	2.19820358	0.08977235	0.371124592	0.981522081	0.122549157	0.583576052	0.957059579	0.248493051					-0.617670194	-0.140490354	-0.804399653	0.47717984	-0.186729459	-0.66309299				
RBP4   P02753	1.28620825	0.28050696	0.715052017	0.807268849	0.999882548	0.647789222	0.824215085						-0.74381687	0.061208584	0.05497749	0.355900271	-0.79979436					
VCAN   P13611	9.48428222	7.38E-06	0.039149317	0.924475575	0.000871962	0.005481851	0.732097278	4.95E-05					0.084383291	-0.018854321	0.114254954	-0.102336711	0.030771663	0.133109279				
HPDI   P05090	1.21626838	0.30515423	0.614525716	0.935528212	0.392279025	0.897083368	0.276712225	0.296265658					0.037320207	-0.03466017	0.033051478	-0.102888024	-0.040668729	-0.057619495				
TMEM132C   QBN376	6.63637328	0.000278716	0.001509559	0.179942811	0.00672038	0.293512043	0.99994309	0.236698609					0.115797838	0.061596962	0.116549874	-0.054200876	0.000752036	0.054952912				
SEZ6   Q5319	2.25208151	0.08379635	0.965127301	0.996007314	0.274480123	0.993977853	0.108388925	0.167299502					-0.016375275	-0.007571079	0.059477744	0.008804196	0.075853019	0.067048823				
KEP1   Q8U1X7	7.95361106	5.13E-05	0.003687884	0.775208663	0.000291507	0.052583075	0.958217729	0.00792865					-0.142138943	-0.03817057	0.120401886	-0.19884179	-0.123886065					
POMGNT1   Q8WZ1A	13.2529454	7.10E-08	7.50E-05	0.836368296	5.32E-06	0.001458092	0.983656276	0.000016073					0.249610797	0.045378189	0.269027995	-0.204238912	0.019417198	0.22365611				
SERPINA6   P08185	0.92538066	0.42637079	0.97292474	0.805517807	0.778136822	0.547109649	0.5093982	0.099992032					-0.039641045	0.080258551	0.119899555	0.122475278	0.002575723					
ENO2   P09104	14.2160222	2.24E-08	0.302643471	1.08E-06	1.93E-06	0.002405202	0.004232567	0.994169033					-0.060916404	-0.184060549	-0.175753006	-0.12341445	-0.114836603	0.008073543				
SAPOH   P04006	4.27673764	4.83E-21	0.986554469	1.31E-11	2.44E-13	0.067298107	0.807298107	0.00792865					0.024774285	-0.526172023	-0.578982656	-0.355094687	0.006075676	-0.052817823				
CADMI   Q0807	3.79232745	0.1133665	0.409848678	0.274115083	0.005105091	0.967232249	0.319813416	0.13660276					0.08216461	0.065968667	0.120133829	0.007752207	0.061917369	0.05165162				
POCLCE   Q15113	2.36530212	0.07476248	0.320420592	0.998019324	0.265004512	0.225838407	0.9999532	0.176886155					-0.054045129	0.00541365	-0.054759096	0.059486494	-0.000713967	-0.06020461				
LGST   P43789	15.2925071	6.25E-09	0.001102805	0.908054304	1.41E-07	0.008708615	0.271167406	2.61E-06					0.152416121	0.026148455	0.222281174	-0.126267666	0.069865053	0.196132719				
ZNF   P07518	0.79225610	0.759205682	0.999478363	0.8464689	0.839117669	0.900320243	0.895329145	0.99999988					0.012089426	0.08473774	0.084411598	0.072648314	0.072329732	-0.000318583				
ZFP2   P02742	3.99126005	0.49963751	0.783781105	0.436116587	0.914243639	0.90641734	0.987500606	0.80307233					0.154538435	0.241072728	0.02119608	0.086534293	-0.05232445	-0.138876368				
LDH1B   P07195	25.1738043	1.05E-13	0.984166337	8.67E-07	6.48E-09	1.98E-07	1.31E-09	0.834343797					0.012738548	-0.189052477	-0.217000783	-0.201791025	-0.22973933	0.027948306				
SA55   Q14933	2.16752797	0.093786435	0.81507406	0.083032683	0.272326194	0.460575385	0.820265028	0.016173456					0.02138862	0.055444382	0.019735049	0.030554659	0.019148028	-0.014718823				
ENO1   P06733	52.1062461	1.85E-24	0.017798336	1.23E-13	1.18E-13	3.35E-09	3.73E-11	0.908293889					-0.00065444	-0.317050504	0.358618621	0.17459609	-0.238573177	-0.02113567				
HPAS1   P11021	3.56218625	0.01333353	0.973215246	0.163029577	0.026572514	0.369998237	0.091736785	0.893635848					0.007251864	0.03413282	0.045289797	0.026880956	0.038079592	0.01156977				
COL14A1   Q05707	2.85087584	0.03870255	0.224505693	0.850300024	0.988204134	0.93260876	0.01211983	0.956334648					-0.75846014	0.03133552	0.018979566	0.106956781	-0.093860751	-0.019386785				
HD1   P02042	2.47789505	0.06270781	0.3390059	0.997678439	0.11833191	0.428737075	0.966992571	0.164581885					-0.50824465	-0.055177053	-0.044055661	0.453647412	-0.135231195	-0.58887660				
NEGR1   Q7Z381	0.60562384	0.000590817	0.16205766	0.015440757	0.000319888	0.824559715	0.225339731	0.711587311					0.090131695	0.126819272	0.066857577	0.0796935	0.034059923					
LDLCO   P09972	9.00720054	1.34E-05	0.284943252	0.015960052	0.195020784	2.12E-05	0.001041983	0.089025313					0.073300935	-0.120145532	-0.07782537	-0.193446647	-0.151126305	0.042302162				
HPH1   Q04910	1.38463791	0.24745154	0.451369182	0.965402114	0.980250184	0.20385763	0.005713923	0.930121327					-0.088137899	0.106713771	0.084033913	0.086065076	0.014774441	-0.014718823				
PCP1   Q13146	11.5740799	5.48E-07	0.044596929	0.01401423	1.15E-07	0.987265116	0.032890178	0.02890031					0.02324567	0.1357275	0.35463421	0.117459609	0.05692477	0.06510777				
SANAB1   Q14697	5.43644825	0.00132822	0.264056278	0.301243816	0.43330797	0.002422206	0.004703204	0.991879582					-0.065636809	0.061163584	0.051585732	0.126080393	0.117225441	-0.009577851				
CP1   P43789	2.62992551	0.155788223	0.687071734	0.935890529	0.517617071	0.325488659	0.996781304	0.188528116					-0.060941722	0.031510151	-0.070215222	0.092451874	-0.011734949	-0.10525373				
CDH2   P19022	4.23729249	0.00632455	0.127655384	0.023908735	0.00612908	0.932424963	0.75783275	0.980660669					0.062892207	0.079754092	0.090036514	0.016882065	0.072314488	0.010282423				
DPPE   P47138	0.9251699	0.402778132	0.862360838	0.921358316	0.284275981	0.488523517	0.41554134	0.999734692					0.031557446	-0.024823003	0.026359447	-0.056389448	-0.059794917	-0.001405468				
MFGE8   Q08431	4.02930411	0.00832587	0.998092992	0.848979939	0.022736079	0.761268005	0.014825009	0.161390929					0.00872981	-0.039959793	-0.137699422	-0.04848878	-0.146492332	-0.099003443				
SPPL1   Q09486	1.38463791	0.24745154	0.451369182	0.965402114	0.980250184	0.20385763	0.005713923	0.930121327					-0.088137899	0.106713771	0.084033913	0.086065076	0.014774441	-0.014718823				
GFPT1   Q16270	1.98230996	0.118516104	0.193269929	0.987130465	0.775212008	0.131880074	0.681119348	0.0567676121					-0.121705122	0.057780352	0.132004947	-0.06592477	0.06510777	-0.014718823				
PAPLN   Q95428	0.58776711	0.623748131	0.911861274	0.725948083	0.600831654	0.984280158	0.948489151	0.997910274					-0.037094321	-0.056883627	-0.066535055	-0.01789346	-0.02925847	-0.00948388				
LGST1   P02750	2.0624237	0.11034242	0.17168696	0.559826061	0.120314651	0.88590644	0.999927081	0.84846619					0.02725944	0.12812426	0.129577074	0.005697458	0.08774472	-0.084817472				
PCDH7   Q14917	0.84725652	4.55E-05	0.038561365	0.105320291	1.30E-05	0.964374938	0.179856466	0.049708223					0.102663608	0.084000065	0.177280172	0.017865344	0.074617463	0.09248017				
THSD2   P35442	3.8993492	0.00954501	0.070127171	0.988059155	0.044625476	0.134189264	0.99995108	0.092154732					-0.097125021	-0.001251344	0.009024609	0.084611581	-0.001899588	-0.085811169				
SERPINA4   P29622	1.11813606	0.34303217	0.348621035	0.922717151	0.519183229	0.713198571	0.98277489	0.881514824					-0.154773133	-0.057226937	-0.122593692	0.097546197	0.033179441	-0.064366756				
HYD1   Q19411	8.6563709	2.18E-05	0.213199132	0.965402114	0.980250184	0.20385763	0.005713923	0.930121327					0.108475609	-0.019228959	-0.040514592	0.084033913	0.086065076	0.014774441				
SALNT   Q09672	1.98230996	0.118516104	0.193269929	0.987130465	0.775212008	0.131880074	0.681119348	0.0567676121					0.032476737	0.1357275	0.35463421	0.117459609	0.05692477	0.06510777				
PAPLN   Q95428	0.58776711	0.623748131	0.911861274	0.725948083	0.600831654	0.984280158	0.948489151	0.997910274					-0.037094321	-0.056883627	-0.066535055	-0.01789346	-0.02925847	-0.00948388				
GFPT1   Q16270	1.98230996	0.118516104	0.193269929	0.987130465	0.775212008	0.131880074	0.681119348	0.0567676121					-0.121705122	0.057780352	0.132004947	-0.06592477	0.06510777	-0.014718823				
CDH2   P19022	4.23729249	0.00632455	0.127655384	0.023908735	0.00612908	0.932424963	0.75783275	0.980660669					0.062892207	0.079754092	0.090036514	0.016882065	0.072314488	0.010282423				
DPPE   P47138	0.9251699	0.402778132	0.862360838	0.921358316	0.284275981	0.488523517	0.41554134	0.999734692					0.031557446	-0.024823003	0.026359447	-0.056389448	-0.059794917	-0.001405468				
MFGE8   Q08431	4.02930411	0.00832587	0.998092992	0.848979939	0.022736079	0.761268005	0.014825009	0.161390929					0.00872981	-0.039959793	-0.137699422	-0.04848878	-0.146492332					



Gene ID   Uniprot ID	F-Value	Pr(>F)	ANOVA p-values with Tukey Adjustment										Difference (AD - CT)									
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA
F10   P00742	1.6812552	0.17258465	0.33328509	0.99156031	0.31038279	0.48351283	0.99971042	0.46357015	-0.097224804	-0.016207216	-0.09483178	0.080187588	0.002393024	-0.07862564								
LMA2   Q12907	3.9652161	0.00953683	0.016108063	0.621822563	0.031472162	0.98053708	0.40705458	0.069956265	0.027435819	0.061314715	-0.042520446	-0.0864155	0.033878896									
CLE3C   P05452	1.15128467	0.329752487	0.886011218	0.942539866	0.689539815	0.566426214	0.987421979	0.322782116	-0.01941274	0.014649707	-0.027921531	0.034062447	-0.00850879	-0.042571238								
GDA   Q07273	21.6828795	4.44E-12	0.006042692	0.000231459	0.0077283496	2.18E-11	1.87E-08	0.462885249	0.208901137	-0.2530562	-0.168864266	-0.462000198	-0.77814404	0.084185794								
F12   P00748	5.87709942	0.00045926	0.298041125	0.986778693	0.006458268	0.151681807	0.483232208	0.001597684	0.027737468	0.082042192	-0.27199356	-0.04737348	0.179162304	0.45076166								
CAD3M3   Q08126	3.41216211	0.018650839	0.171198959	0.998438615	0.012672497	0.997250732	0.802761327	0.887959763	0.077920886	0.085297333	0.110871856	0.007376447	0.03295097	0.025574524								
TMEI132D   Q14C87	1.2416653	1.95E-07	0.000186797	0.00013892	1.50E-07	0.999967376	0.550246649	0.495428344	0.271394949	0.2685806	0.352373623	-0.002814349	0.080978674	0.088793023								
PRNP   P04156	6.31597272	0.000421969	0.002157468	0.036487812	0.000839553	0.753108643	0.999307926	0.634006514	0.129329511	0.094324483	0.133614071	-0.034987028	0.00284506	0.039271534								
CACNA2D3   Q8Z858	4.61106625	0.00389893	0.010198316	0.04321941	0.00878953	0.937411376	0.999857858	0.949717438	0.180523026	0.147684339	0.176476209	-0.032838687	-0.004046817	0.02978187								
COMP   P49747	0.18967443	0.90336606	0.886371667	0.949440447	0.969207457	0.996953035	0.989768857	0.999616681	-0.064983387	-0.046951297	-0.038411506	0.01803209	0.026571881	0.008539791								
PLOD1   Q0289	11.4585482	6.31E-07	3.20E-05	0.181760453	5.18E-06	0.032533953	0.998499851	0.013104089	-0.19612065	-0.002593692	-0.020644793	0.113548373	-0.005052728	-0.120511031								
ENED1   Q8TER0	0.3757026	0.76928205	0.961606432	0.979960948	0.968601514	0.815039521	0.774091604	0.999930619	0.015480178	0.109176355	0.035456713	-0.0076693	0.002702717									
GLD1   P80108	1.7718254	0.15407727	0.993881273	0.816414965	0.273579011	0.671144222	0.172510366	0.792185367	-0.020670226	0.068115004	0.136953697	0.08878523	0.157623923	0.068836693								
PRG4   Q29954	6.98654058	0.000177353	0.196395802	0.917203259	0.00330266	0.02368132	0.598673536	0.003838811	-0.234196634	0.073941933	-0.07355077	0.308138567	-0.141258443	-0.44939701								
PCDH9   Q9CH56	4.0663459	0.0079327	0.051715201	0.31593792	0.009588024	0.794492838	0.932505076	0.389630152	0.108277422	0.070275235	0.13244835	-0.038020027	0.024166688	0.062168615								
RTNAR   Q9BRZ6	3.77412916	0.011624028	0.902174001	0.34114557	0.00893828	0.774683648	0.979007971	0.45578852	0.033171435	0.078643838	0.145182619	0.045472403	0.112011814	0.066538781								
SUSD5   Q60279	1.222177	0.30300297	0.63548837	0.219831764	0.80094576	0.914536936	0.985361735	0.712889076	0.054459941	0.08392627	0.039056382	0.029466586	-0.015403559	-0.04847015								
LUMI   P51884	1.12259578	0.340013098	0.814192494	0.786508086	0.994604397	0.267729181	0.654007351	0.887446637	-0.05843674	0.057544998	0.014712121	0.113388572	0.070564795	-0.04282777								
CTP1   P03086	13.7222946	0.04-08	0.541805166	0.001033386	0.002701519	2.15E-06	6.38E-06	0.98240855	0.047839392	-0.120201341	-0.09156315	-0.16804704	-0.156959708	0.011504026								
CFD   P00746	3.21818316	0.02401881	0.999976947	0.958233363	0.114767838	0.96826036	0.11129185	0.079257078	0.002429994	0.029749415	-0.129739121	0.027319421	-0.132169106	-0.159488527								
LDHA   P03038	59.6974558	4.86E-27	0.159858062	2.42E-12	1.31E-13	1.24E-13	1.12E-13	0.857451166	0.79368356	-0.288917152	-0.371049208	-0.368285508	-0.396417564	-0.02832055								
LCAP   Q13449	6.31558216	0.00042182	0.027189347	0.014923619	0.000219329	0.999267312	0.60068265	0.66149215	0.102965224	0.105792767	0.146644437	0.00546543	0.043679213	0.03931467								
DNM1   P07585	6.8213654	0.00019487	0.002558186	0.999646255	0.05872905	0.001480548	0.616568041	0.00428152	-0.192070743	0.005945946	-0.147234467	0.225152989	0.071972525	0.113180413								
MDH1   P40295	34.7396746	1.04E-17	0.279548183	4.34E-09	1.14E-07	3.06E-13	5.86E-12	0.859037816	0.075330271	-0.26587587	-0.23460099	-0.340917846	-0.309931215	0.039986631								
RYT1   Q04985	0.39706778	0.752264946	0.794598837	0.99993838	0.99706540	0.96821504	0.867522504	0.99636656	-0.313067394	0.00853805	-0.060723465	0.231606149	-0.233644331	-0.05632776								
CACNA2D3   Q08126	3.41216211	0.018650839	0.171198959	0.998438615	0.012672497	0.997250732	0.802761327	0.887959763	0.077920886	0.085297333	0.110871856	0.007376447	0.03295097	0.025574524								
CTP1   P03086	13.7222946	0.04-08	0.541805166	0.001033386	0.002701519	2.15E-06	6.38E-06	0.98240855	0.047839392	-0.120201341	-0.09156315	-0.16804704	-0.156959708	0.011504026								
CFD   P00746	3.21818316	0.02401881	0.999976947	0.958233363	0.114767838	0.96826036	0.11129185	0.079257078	0.002429994	0.029749415	-0.129739121	0.027319421	-0.132169106	-0.159488527								
LDHA   P03038	59.6974558	4.86E-27	0.159858062	2.42E-12	1.31E-13	1.24E-13	1.12E-13	0.857451166	0.79368356	-0.288917152	-0.371049208	-0.368285508	-0.396417564	-0.02832055								
LCAP   Q13449	6.31558216	0.00042182	0.027189347	0.014923619	0.000219329	0.999267312	0.60068265	0.66149215	0.102965224	0.105792767	0.146644437	0.00546543	0.043679213	0.03931467								
DNM1   P07585	6.8213654	0.00019487	0.002558186	0.999646255	0.05872905	0.001480548	0.616568041	0.00428152	-0.192070743	0.005945946	-0.147234467	0.225152989	0.071972525	0.113180413								
MDH1   P40295	34.7396746	1.04E-17	0.279548183	4.34E-09	1.14E-07	3.06E-13	5.86E-12	0.859037816	0.075330271	-0.26587587	-0.23460099	-0.340917846	-0.309931215	0.039986631								
RYT1   Q04985	0.39706778	0.752264946	0.794598837	0.99993838	0.99706540	0.96821504	0.867522504	0.99636656	-0.313067394	0.00853805	-0.060723465	0.231606149	-0.233644331	-0.05632776								
CACNA2D3   Q08126	3.41216211	0.018650839	0.171198959	0.998438615	0.012672497	0.997250732	0.802761327	0.887959763	0.077920886	0.085297333	0.110871856	0.007376447	0.03295097	0.025574524								
CTP1   P03086	13.7222946	0.04-08	0.541805166	0.001033386	0.002701519	2.15E-06	6.38E-06	0.98240855	0.047839392	-0.120201341	-0.09156315	-0.16804704	-0.156959708	0.011504026								
CFD   P00746	3.21818316	0.02401881	0.999976947	0.958233363	0.114767838	0.96826036	0.11129185	0.079257078	0.002429994	0.029749415	-0.129739121	0.027319421	-0.132169106	-0.159488527								
LDHA   P03038	59.6974558	4.86E-27	0.159858062	2.42E-12	1.31E-13	1.24E-13	1.12E-13	0.857451166	0.79368356	-0.288917152	-0.371049208	-0.368285508	-0.396417564	-0.02832055								
LCAP   Q13449	6.31558216	0.00042182	0.027189347	0.014923619	0.000219329	0.999267312	0.60068265	0.66149215	0.102965224	0.105792767	0.146644437	0.00546543	0.043679213	0.03931467								
DNM1   P07585	6.8213654	0.00019487	0.002558186	0.999646255	0.05872905	0.001480548	0.616568041	0.00428152	-0.192070743	0.005945946	-0.147234467	0.225152989	0.071972525	0.113180413								
MDH1   P40295	34.7396746	1.04E-17	0.279548183	4.34E-09	1.14E-07	3.06E-13	5.86E-12	0.859037816	0.075330271	-0.26587587	-0.23460099	-0.340917846	-0.309931215	0.039986631								
RYT1   Q04985	0.39706778	0.752264946	0.794598837	0.99993838	0.99706540	0.96821504	0.867522504	0.99636656	-0.313067394	0.00853805	-0.060723465	0.231606149	-0.233644331	-0.05632776								
CACNA2D3   Q08126	3.41216211	0.018650839	0.171198959	0.998438615	0.012672497	0.997250732	0.802761327	0.887959763	0.077920886	0.085297333	0.110871856	0.007376447	0.03295097	0.025574524								
CTP1   P03086	13.7222946	0.04-08	0.541805166	0.001033386	0.002701519	2.15E-06	6.38E-06	0.98240855	0.047839392	-0.120201341	-0.09156315	-0.16804704	-0.156959708	0.011504026								
CFD   P00746	3.21818316	0.02401881	0.999976947	0.958233363	0.114767838	0.96826036	0.11129185	0.079257078	0.002429994	0.029749415	-0.129739121	0.027319421	-0.132169106	-0.159488527								
LDHA   P03038	59.6974558	4.86E-27	0.159858062	2.42E-12	1.31E-13	1.24E-13	1.12E-13															

Gene ID   Uniprot ID	F-Value	Pr(>F)	ANOVA p-values with Tukey Adjustment										Difference (AD - CT)									
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA
PCDHGC   QY5F6	13.3685254	6.18E-08	0.022181954	5.59E-06	1.65E-07	0.163849207	0.034756896	0.932515432	0.155294962	0.26526881	0.296445761	0.109971849	0.141150799	0.03117895	0.155294962	0.26526881	0.296445761	0.109971849	0.141150799	0.03117895	0.155294962	0.26526881
CDTG1   P00505	14.4124342	1.77E-08	0.213353376	5.34E-06	2.00E-07	0.013855661	0.001756574	0.904919109	-0.071791603	-0.182686602	-0.202402512	-0.110869998	-0.130610998	-0.019739191	-0.071791603	-0.182686602	-0.202402512	-0.110869998	-0.130610998	-0.019739191	-0.071791603	-0.182686602
RGMB   Q6N4W0	8.27957115	3.38E-05	0.078908904	0.014577098	9.94E-06	0.94620165	0.083677675	0.242234185	0.1059581	0.12985103	0.206941776	0.023866003	0.100956676	0.077096762	0.1059581	0.12985103	0.206941776	0.023866003	0.100956676	0.077096762	0.1059581	0.12985103
PNKSA1   P14314	1.40869038	0.24168795	0.93914634	0.89199418	0.200741577	0.999391428	0.530317716	0.984287385	0.017424293	0.028678596	0.036515664	0.003135664	0.039211953	0.036515664	0.017424293	0.028678596	0.036515664	0.003135664	0.039211953	0.036515664	0.017424293	0.028678596
EA1   P00915	2.53674356	0.05812766	0.16266793	0.982047109	0.146367653	0.303578042	0.999935108	0.285937501	-0.652165712	-0.114101767	-0.635142245	-0.538063944	-0.017023467	-0.521040478	-0.652165712	-0.114101767	-0.635142245	-0.538063944	-0.017023467	-0.521040478	-0.652165712	-0.114101767
CAT   P04180	0.32472136	0.807487889	0.872701922	0.989909102	0.999101346	0.966122061	0.792657366	0.967951693	-0.041245177	-0.016244977	-0.00701928	0.0250002	0.048264557	0.023264257	-0.041245177	-0.016244977	-0.00701928	0.0250002	0.048264557	0.023264257	-0.041245177	-0.016244977
DRM2   P19652	1.160822	0.32608271	0.808529666	0.811596897	0.967371862	0.284552256	0.511452868	0.968652683	-0.095722669	0.092523303	0.046985081	0.188245972	0.142707751	-0.045538221	-0.095722669	0.092523303	0.046985081	0.188245972	0.142707751	-0.045538221	-0.095722669	0.092523303
CDM11   P55287	11.278447	7.88E-07	0.375056657	0.010387867	5.02E-07	0.457138699	0.000695931	0.079912905	0.035225489	0.066897869	0.116009582	0.03167236	0.080784039	0.049111733	0.035225489	0.066897869	0.116009582	0.03167236	0.080784039	0.049111733	0.035225489	0.066897869
126orf99   GUXK73	6.93221489	0.000192442	0.008406922	0.808849122	0.000810182	0.084572586	0.958559594	0.014957189	0.115263846	0.031163164	0.132598205	-0.084100683	0.017334593	0.017334593	0.115263846	0.031163164	0.132598205	-0.084100683	0.017334593	0.017334593	0.115263846	0.031163164
F13B1   P05160	1.12518146	0.340180157	0.857394273	0.764213107	0.965989915	0.291758816	0.572701005	0.949460962	-0.075900611	0.090699888	0.042549059	0.1666005	0.118449671	-0.048150829	-0.075900611	0.090699888	0.042549059	0.1666005	0.118449671	-0.048150829	-0.075900611	0.090699888
COL18A1   P39060	0.83572865	0.47526637	0.699232381	0.968958707	0.995699905	0.410194414	0.80480785	0.949465428	-0.037037984	0.01505152	-0.00746166	0.052089505	0.029517818	-0.022515686	-0.037037984	0.01505152	-0.00746166	0.052089505	0.029517818	-0.022515686	-0.037037984	0.01505152
EMA3B   Q13214	1.96839653	0.120256943	0.186140345	0.990351906	0.356491243	0.302252885	0.965587005	0.527534816	-0.100637599	-0.014702873	-0.07804895	0.085934726	0.022582703	-0.06352022	-0.100637599	-0.014702873	-0.07804895	0.085934726	0.022582703	-0.06352022	-0.100637599	-0.014702873
HGAC   Q04756	0.20192273	0.894963621	0.992792623	0.87056184	0.973343613	0.964151482	0.999026908	0.984166207	0.029661826	0.080475213	0.040240104	0.050813387	0.014542278	-0.036271109	0.029661826	0.080475213	0.040240104	0.050813387	0.014542278	-0.036271109	0.029661826	0.080475213
DJLML3   Q0N4N5	3.14152367	0.026540046	0.807251818	0.879629747	0.821184936	0.99807833	0.219038264	0.134661184	-0.030233857	-0.024044112	-0.09259829	0.05029745	-0.062724432	-0.068554177	-0.030233857	-0.024044112	-0.09259829	0.05029745	-0.062724432	-0.068554177	-0.030233857	-0.024044112
EMA6A   Q2H926	3.30379939	0.021482403	0.992807528	0.769531424	0.026651542	0.906270798	0.062224007	0.244680403	0.01095709	0.037575308	0.1074932	0.026618218	0.09653623	0.06991801	0.01095709	0.037575308	0.1074932	0.026618218	0.09653623	0.06991801	0.01095709	0.037575308
F11   P03951	1.1751859	0.93120701	0.995495087	0.965435897	0.99833619	0.896067138	0.977026014	0.988634137	-0.02555525	0.05008094	0.07378699	0.075636465	0.024934224	0.03702241	-0.02555525	0.05008094	0.07378699	0.075636465	0.024934224	0.03702241	-0.02555525	0.05008094
DPF7   P0H414	0.5477494	0.650261344	0.999982308	0.686613826	0.99564017	0.717093798	0.998168274	0.784643591	0.003413282	0.10060242	0.01900492	0.097426942	0.015571638	-0.081855304	0.003413282	0.10060242	0.01900492	0.097426942	0.015571638	-0.081855304	0.003413282	0.10060242
FM2   P20562	6.69369163	0.000258813	0.043424077	0.711880199	0.089535052	0.021393995	0.974384764	0.003136055	-0.146155835	0.057167477	0.123641707	0.203313312	0.022514128	-0.188090184	-0.146155835	0.057167477	0.123641707	0.203313312	0.022514128	-0.188090184	-0.146155835	0.057167477
PRP1   P8147	1.80362909	0.02404367	0.991351368	0.915613036	0.925398018	0.780114716	0.298896508	0.945860096	-0.015091098	-0.04429203	-0.071933859	0.033838105	-0.057027657	-0.07504656	-0.015091098	-0.04429203	-0.071933859	0.033838105	-0.057027657	-0.07504656	-0.015091098	-0.04429203
DOR1   Q08345	4.04948484	0.008157235	0.147937114	0.630607147	0.005561219	0.760709524	0.698039297	0.140562281	0.123978548	0.067742544	0.184903386	-0.056236003	0.060924839	-0.017160842	0.123978548	0.067742544	0.184903386	-0.056236003	0.060924839	-0.017160842	0.123978548	0.067742544
PARK7   Q99497	56.0326555	8.35E-26	0.777101688	3.01E-13	1.14E-11	9.48E-11	1.24E-13	0.008803842	-0.029669333	-0.250360922	-0.37755047	-0.220691589	-0.067394125	-0.067394125	-0.250360922	-0.250360922	-0.37755047	-0.220691589	-0.067394125	-0.067394125	-0.250360922	-0.250360922
BCAM   P05895	4.36760806	0.005418833	0.096932943	0.938427623	0.162716665	0.019839341	0.984592986	0.035614425	-0.058666465	0.014226621	-0.050002629	0.072893086	0.008406167	-0.064252918	-0.058666465	0.014226621	-0.050002629	0.072893086	0.008406167	-0.064252918	-0.058666465	0.014226621
CTSH   P06969	1.98786969	0.117326478	0.294117178	0.951157092	0.998709905	0.097809221	0.294771395	0.923482173	-0.135380622	0.039732828	-0.005186295	0.117513435	0.01394426	0.031940223	-0.135380622	0.039732828	-0.005186295	0.117513435	0.01394426	0.031940223	-0.135380622	0.039732828
CHIT1   Q13231	11.7233506	4.56E-07	0.985746622	0.000173904	7.51E-05	0.000832197	0.000401949	0.999592585	-0.068557788	-0.825804551	-0.845121777	-0.757246763	-0.776593989	-0.019312026	-0.068557788	-0.825804551	-0.845121777	-0.757246763	-0.776593989	-0.019312026	-0.068557788	-0.825804551
F3   P00740	1.41382918	0.240173447	0.999922464	0.990218083	0.997407164	0.921641376	0.996161015	0.975723809	-0.00061468	-0.01278917	-0.0117537	0.003856695	0.015613731	-0.00061468	-0.01278917	-0.0117537	0.003856695	0.015613731	-0.00061468	-0.01278917	-0.0117537	0.003856695
PHR1   Q03591	0.44129796	0.723740462	0.998037122	0.915473165	0.99056166	0.924058244	0.992902988	0.0229722	0.129067508	0.027469331	0.106095408	-0.070597687	-0.112206275	-0.070597687	0.129067508	0.027469331	0.106095408	-0.070597687	-0.112206275	-0.070597687	-0.112206275	-0.070597687
C10C   P02747	0.55749568	0.643745031	0.986026343	0.595590541	0.947000011	0.811668223	0.997770821	0.878791573	-0.013791091	-0.048854072	-0.020913649	-0.035062981	-0.007122558	-0.027940423	-0.013791091	-0.048854072	-0.020913649	-0.035062981	-0.007122558	-0.027940423	-0.013791091	-0.048854072
HP90A1   P07900	27.7560262	8.69E-15	0.929183768	3.29E-07	3.36E-09	1.95E-08	1.56E-10	0.087471546	0.021329534	0.01737456	-0.218045336	-0.214506999	-0.023937481	-0.023937481	0.021329534	0.01737456	-0.218045336	-0.214506999	-0.023937481	-0.023937481	-0.023937481	-0.023937481
NUG2   Q9UN36	0.40391234	0.008219626	0.93572786	0.353063645	0.343360471	0.119552398	0.727785578	0.043038703	0.017840097	-0.048758161	0.048148888	-0.066598259	0.030308791	0.096907049	0.017840097	-0.048758161	0.048148888	-0.066598259	0.030308791	0.096907049	0.017840097	-0.048758161
CDR21   P80303	0.89390886	0.445822422	0.46767631	0.6160643	0.52589091	0.929006908	0.75501867	0.883691422	-0.080612426	-0.065730698	-0.014881728	0.058262198	0.037890047	-0.080612426	-0.065730698	-0.014881728	0.058262198	0.037890047	-0.080612426	-0.065730698	-0.014881728	0.058262198
PNASE1   P07998	15.0484004	3.90E-09	5.18E-07	0.062251749	8.11E-08	0.009128853	0.999826248	0.00041004	0.23932398	0.104882524	0.242565517	-0.134641456	0.00324157	0.137893033	0.009128853	0.999826248	0.00041004	0.23932398	0.104882524	0.242565517	-0.134641456	0.00324157
PNAB1   P30101	0.29020035	0.823731047	0.999922464	0.990218083	0.997407164	0.921641376	0.996161015	0.975723809	-0.00061468	-0.01278917	-0.0117537	0.003856695	0.015613731	-0.00061468	-0.01278917	-0.0117537	0.003856695	0.015613731	-0.00061468	-0.01278917	-0.0117537	0.003856695
PVL   Q09055	0.66559053	0.64146958	0.951020848	0.833175768	0.902737958	0.305323448	0.982910612	0.921345921	-0.234632499	-0.013856698	-0.026166514	0.133246802	-0.07531915	-0.160778717								



Gene ID   Uniprot ID	F-Value	Pr(>F)	ANOVA p-values with Tukey Adjustment								Difference (AD - CT)							
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-Cau vs CT-AA
SFLRA2   Q00451	7.29312494	0.00011952	0.009217759	0.000941225	0.000210973	0.941154518	0.818079634	0.990494552	0.237674777	0.279523778	0.300531195	0.041849001	0.062856419	0.021007417	0.000000000	0.000000000	0.000000000	0.000000000
CALB1   P05937	2.068388	0.11166703	0.165667927	0.131091934	0.53839028	0.999943478	0.839926235	0.9981852	-0.102131625	-0.104744742	-0.062761945	-0.002615818	0.03936698	0.041985497	0.000000000	0.000000000	0.000000000	0.000000000
PAPPA2   Q98088	6.12658287	0.000539455	0.968644233	0.037380858	0.02193279	0.01075368	0.005784488	0.999288619	-0.021551223	0.124651513	0.130216556	0.146202736	0.151767779	0.005650544	0.000000000	0.000000000	0.000000000	0.000000000
MAN1   P04957	3.54319153	0.01578496	0.57925988	0.99997198	0.03469657	0.54002149	0.524499206	0.02711949	0.034654345	-0.01137818	0.073934659	-0.037603163	0.037468715	0.070714877	0.000000000	0.000000000	0.000000000	0.000000000
PROCT   P04070	0.65837322	0.578668352	0.531140258	0.957580077	0.982543735	0.818779788	0.727052461	0.9988012	0.071201753	0.025928469	0.018563731	-0.045273283	-0.052638021	-0.072647378	0.000000000	0.000000000	0.000000000	0.000000000
PIGR   P01833	0.64494466	0.000601118	0.923504111	0.126448133	0.000825542	0.415741388	0.009194004	0.350328197	-0.062333122	-0.213246651	-0.367190744	-0.150913459	-0.304857621	-0.153941622	0.000000000	0.000000000	0.000000000	0.000000000
CAN1T1   Q8WVQ1	10.895756	1.26E-06	0.07439808	0.001901496	4.60E-07	0.616743555	0.016040897	0.25318921	0.072787612	0.106324558	0.159195245	0.033536946	0.086407633	0.052870687	0.000000000	0.000000000	0.000000000	0.000000000
STB5A1   Q43173	1.80027375	0.148667756	0.965847085	0.310267626	0.949552368	0.130617445	0.738791036	0.592295063	-0.02033434	0.073114123	0.02220438	0.093447563	0.04253782	0.05009743	0.000000000	0.000000000	0.000000000	0.000000000
CDH6   P55285	0.189431	7.97E-11	0.01586409	9.05E-05	1.26E-11	0.923527257	0.002330005	0.01315531	0.117696373	0.137291962	0.227595948	0.019595589	0.109963788	0.090367788	0.000000000	0.000000000	0.000000000	0.000000000
COL4A2   P08572	0.1381497	0.59170545	0.943014197	0.994304237	0.95245306	0.988494811	0.999906318	0.99287797	-0.02028974	-0.088877471	-0.018073532	0.011412269	0.002216028	0.001996061	0.000000000	0.000000000	0.000000000	0.000000000
FN2   D22792	2.26366279	0.082561285	0.21889818	0.967328419	0.787343627	0.075275603	0.599557274	0.462632081	-0.2248867	0.051830756	-0.102389222	0.274719516	0.12049538	-0.154219978	0.000000000	0.000000000	0.000000000	0.000000000
MGAT5   Q90328	0.34357384	0.793840649	0.92653406	0.933351997	0.9983414	0.995979749	0.851442791	0.985887813	-0.01500865	-0.014084101	0.00250865	0.009916763	0.01886288	-0.017946117	0.000000000	0.000000000	0.000000000	0.000000000
HSPA13   P48723	3.09738384	0.028092753	0.01863068	0.70548823	0.252328651	0.217096909	0.60465497	0.869788867	-0.099449075	-0.035232813	-0.093530529	0.064210863	0.040098537	-0.024112326	0.000000000	0.000000000	0.000000000	0.000000000
HSPA2   P54652	0.40577143	0.427337411	0.846846216	0.91183528	0.71278586	0.998168507	0.997730757	0.982172615	-0.044406919	-0.035069717	-0.054107958	0.009372701	-0.090701039	-0.019038241	0.000000000	0.000000000	0.000000000	0.000000000
NDST1   P52848	0.36727453	0.0039496	0.460609351	0.614107458	0.037476868	0.038188841	0.000249771	0.453497514	-0.05987207	0.048561959	0.10495338	0.108430429	0.1648255	0.056391421	0.000000000	0.000000000	0.000000000	0.000000000
TAGLN   Q01995	0.84695867	0.469821421	0.962042598	0.961890124	0.73772136	0.76364965	0.431216569	0.951286015	-0.040942349	-0.039893599	-0.081703123	-0.080835947	-0.122645472	-0.041809525	0.000000000	0.000000000	0.000000000	0.000000000
EMEA60   Q8N1Y4	6.161894169	0.000285069	0.074306562	0.162966936	9.21E-05	0.975855832	0.252547001	0.091734577	0.089313963	0.074504082	0.155102412	-0.015029881	0.065548849	0.080598383	0.000000000	0.000000000	0.000000000	0.000000000
SGH1   Q92820	1.44118016	0.232259767	0.452670555	0.983245579	0.793860179	0.247796398	0.923951187	0.551888717	-0.07622433	0.01834722	-0.045211321	0.094567052	0.031013009	0.063554043	0.000000000	0.000000000	0.000000000	0.000000000
CTP1   Q96105	3.85215005	0.01049674	0.9479933	0.027877977	0.063472441	0.120601586	0.230757179	0.980625086	0.19627487	0.098593504	0.085639741	0.047586077	0.066012254	-0.012953763	0.000000000	0.000000000	0.000000000	0.000000000
GPX3   P22352	9.32948158	0.005900406	0.138543127	0.188909225	0.004587489	0.996742829	0.682880909	0.522499845	-0.08474757	-0.076656118	-0.126728223	0.08091452	-0.041980654	-0.050072106	0.000000000	0.000000000	0.000000000	0.000000000
FAT1   Q14517	0.5427187	0.00065696	0.003039808	0.999618131	0.004274323	0.00355645	0.503974531	0.1208886	-0.154900839	-0.00431466	-0.095793739	0.150529373	0.0591071	-0.019038241	0.000000000	0.000000000	0.000000000	0.000000000
EPHMA1   Q6886	11.5404088	5.71E-07	2.54E-05	0.03446012	1.68E-06	0.153536176	0.986003916	0.95188962	0.223977947	0.12575242	0.239613423	-0.008252526	0.015635477	0.113888003	0.000000000	0.000000000	0.000000000	0.000000000
RHGA   E015197	4.9784996	0.002417729	0.002514519	0.069825586	0.012809285	0.96394252	0.941468692	0.232429	0.232429	0.1562011	0.19088162	-0.074790941	-0.042410389	0.034637062	0.000000000	0.000000000	0.000000000	0.000000000
TFP   Q02788	11.493788	6.05E-07	0.001747097	0.998585644	0.000148529	0.000798401	0.970261171	5.47E-05	0.356539129	-0.149277196	0.398193849	-0.371466325	0.046157472	0.413211044	0.000000000	0.000000000	0.000000000	0.000000000
CTF5   Q01459	1.11090151	0.34508194	0.5458496	0.97257354	0.99988237	0.311443256	0.524852816	0.97711849	-0.068577648	-0.001343028	0.001889626	0.077901956	0.059967307	-0.017934649	0.000000000	0.000000000	0.000000000	0.000000000
TSMT2A   Q8T4G5	0.50017904	0.023847268	0.03454331	0.01302718	0.024354229	0.958577139	0.856587743	0.950170222	0.284728996	0.244328314	0.222193979	-0.040040682	0.061504772	0.012323635	0.000000000	0.000000000	0.000000000	0.000000000
LAMC1   Q9Y6N6	0.90361169	0.440496867	0.998839142	0.533649901	0.68251858	0.639151258	0.780841333	0.909215757	0.006386089	0.056570267	-0.05594231	0.05018478	0.039204182	-0.010976036	0.000000000	0.000000000	0.000000000	0.000000000
APOL1   Q14791	0.90577063	0.427235314	0.90950766	0.916986384	0.849026763	0.554574998	0.999538897	0.90221687	-0.096420125	0.090849897	-0.115501474	0.187270022	-0.015130888	-0.024009111	0.000000000	0.000000000	0.000000000	0.000000000
INGO1   Q96F65	6.48146144	0.000340558	0.103595507	0.012893797	0.01159071	0.893154592	0.24570647	0.642961902	0.168507164	0.21988117	0.300638628	0.051374006	0.132131464	0.080757458	0.000000000	0.000000000	0.000000000	0.000000000
FMOD   Q60828	0.57729809	0.63020094	0.727515451	0.954958775	0.641218014	0.948291092	0.99774162	0.911702313	-0.065323273	-0.031660513	-0.070511237	0.0366276	-0.005187964	-0.038807024	0.000000000	0.000000000	0.000000000	0.000000000
B3GNT2   Q19Y97	10.5490773	1.94E-06	0.122509145	0.000113265	1.76E-06	0.175847126	0.029176946	0.887542825	0.047358993	0.090523931	0.104798825	0.042939397	0.057439832	0.014445895	0.000000000	0.000000000	0.000000000	0.000000000
HMG1   P04738	0.61354583	0.607028093	0.996540949	0.97964075	0.996887063	0.677774427	0.999961873	0.999961873	-0.008472482	-0.110081273	0.29808137	0.134543617	0.020636992	0.13981231	0.000000000	0.000000000	0.000000000	0.000000000
PMH1   P23515	4.54363115	0.004298757	0.069258489	0.051774584	0.008151344	0.669385354	0.801669265	0.148707589	0.13048517	0.07359368	0.176676223	-0.059122201	0.064273328	0.051847903	0.000000000	0.000000000	0.000000000	0.000000000
SGCE   Q43556	6.12947183	0.000537436	0.020053744	0.07308968	0.00407623	0.943944678	0.688932565	0.314144786	0.081525013	0.066182334	-0.011703721	-0.015342679	0.029548258	0.048490937	0.000000000	0.000000000	0.000000000	0.000000000
MDGA2   Q7Z553	6.90248841	0.000197209	0.016275957	0.032252777	7.90E-05	0.98876737	0.61555116	0.33779022	0.125884638	0.11270919	0.178608633	-0.031375449	0.005723994	0.068899443	0.000000000	0.000000000	0.000000000	0.000000000
PLXNB1   Q43157	1.04946813	0.37195421	0.99926517	0.937393226	0.890802161	0.789437587	0.868799485	0.291200155	-0.001616518	-0.02678166	0.018677746	-0.025211648	0.020294623	0.045409143	0.000000000	0.000000000	0.000000000	0.000000000
CPB2   Q96194	0.32939705	0.804167709	0.95958665	0.991951206	0.96459143	0.80605707	0.79011804	0.99267146	-0.047196004	0.026264535	0.037518174	0.074605399	0.084714178	0.011253639	0.000000000	0.000000000	0.000000000	0.000000000
NDRG4   Q9ULP0	1.7204661	0.16604885	0.523578406	0.401147416	0.123046519	0.998495848	0.867832076	0.934522885	0.054165738	0.060475531	0.083600546	0.006309397	0.029344827	0.023125033	0.000000000	0.000000000	0.000000000	0.000000000
FOH1   Q99523	0.24070832	0.108833586	0.968078794	0.976607754	0.996887063	0.677774427	0.999961873	0.999961873	-0.008472482	-0.110081273	0.29808137	0.134543617	0.020636992	0.13981231	0.000000000	0.000000000	0.000000000	0.000000000
PLXNB1   P63010	3.22655	0.023847268	0.796319765	0.153788017	0.00305205	0.15382789	0.504261314	0.30507										

Gene ID   Uniprot ID	F-Value	Pr[F]	ANOVA p-values with Tukey Adjustment										Difference (AD - CT)									
			AD-Cau vs AD-AA	CT-AA vs AD-AA	AD-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-AA	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-Cau vs CT-AA		
PCS1   P29120	12.4598532	1.85E-07	0.044991375	4.00E-06	1.39E-06	0.078304692	0.053179162	0.999598693	0.224606163	0.427195894	0.435466092	0.20289731	0.210859299	0.008270199	0.008270199	0.008270199	0.008270199	0.008270199	0.008270199	0.008270199	0.008270199	
ART3   Q13508	9.9838191	3.93E-06	0.00084074	0.976143533	0.002060265	0.02936307	0.999634104	0.001028497	0.26931428	0.02793775	0.276041271	0.241381505	0.006726991	0.248108496	0.006726991	0.248108496	0.006726991	0.248108496	0.006726991	0.248108496		
EGFR   P00533	4.3606258	0.005397483	0.176655481	0.728313124	0.311335062	0.011657562	0.975294005	0.025293743	0.064459399	0.032122998	-0.051790559	0.096862897	0.012668839	-0.089135588	0.096862897	0.012668839	-0.089135588	0.096862897	0.012668839	-0.089135588		
HMPL1   Q92118	13.0138744	5.47E-08	0.728159678	0.000260591	0.003489918	3.37E-06	6.55E-05	0.94942661	0.000714609	0.120514454	-0.098688543	-0.151220662	-0.128802312	0.02425911	-0.098688543	-0.151220662	-0.128802312	0.02425911	-0.098688543	-0.151220662		
SEKIPMB6   P35237	3.0193346	0.1311845	0.09736517	0.898286504	0.064306118	0.34408517	0.999948104	0.275223202	0.07756088	0.175223202	-0.02204005	0.053375482	-0.050160309	0.053375482	-0.02204005	0.053375482	-0.050160309	0.053375482	-0.02204005	0.053375482		
MATN2   Q00339	1.7360362	0.161139611	0.162182053	0.994236567	0.798471057	0.246540509	0.58664214	0.91966609	-0.081305853	-0.099646091	-0.038822615	0.071665162	0.047483238	-0.024181924	-0.099646091	-0.038822615	0.071665162	0.047483238	-0.024181924	0.071665162		
MARCKS   P29966	0.6293688	0.006403655	0.74157601	0.252199474	0.203268134	0.16556276	0.021459952	0.016165966	0.03785605	-0.060080831	-0.056939813	-0.093866634	-0.06734488	-0.002312031	-0.060080831	-0.056939813	-0.093866634	-0.06734488	-0.002312031	-0.060080831		
OPD10   Q8N08	2.1547745	0.094889814	0.703642464	0.525475414	0.90532738	0.07348945	0.281746812	0.885984891	0.055282229	-0.067934509	-0.03306304	-0.123216738	-0.088345269	0.03487147	-0.067934509	-0.03306304	-0.123216738	-0.088345269	0.03487147	-0.067934509		
CTSL   P07711	0.30173691	0.824115444	0.941208841	0.992248122	0.988788458	0.990567335	0.801842214	0.926725596	-0.022563574	-0.010838089	-0.012707759	0.011725485	0.034571333	-0.022563574	-0.010838089	-0.012707759	0.011725485	0.034571333	-0.022563574	-0.010838089		
TRND1   Q9UKU6	1.9072967	0.129917361	0.496513313	0.890568145	0.930918941	0.145361413	0.170961714	0.999174552	-0.063625991	0.031510372	0.02593019	0.095136362	0.08955618	-0.00580182	-0.063625991	0.031510372	0.02593019	0.095136362	0.08955618	-0.00580182		
PDCH10   Q9PZ27	13.8081833	5.46E-08	5.36E-06	0.080039615	0.99171696	1.79E-07	0.200860461	0.958613721	0.265676635	0.164060928	0.287547188	-0.101669707	0.021870512	0.12840259	0.164060928	0.287547188	-0.101669707	0.021870512	0.12840259	0.164060928		
GP1   Q06744	43.6257454	2.28E-21	0.8316542	1.25E-13	2.24E-07	1.22E-13	3.31E-09	0.00354276	0.040982836	-0.423647743	-0.364978359	-0.464630579	-0.395951195	0.158662833	-0.423647743	-0.364978359	-0.464630579	-0.395951195	0.158662833	-0.423647743		
SLTRKS   Q04991	7.7922553	6.30E-05	0.016807538	0.062371688	2.01E-05	0.944685328	0.36475382	0.110182127	0.144477761	0.11796326	0.220357264	-0.026514535	0.075879504	0.102394039	0.11796326	0.220357264	-0.026514535	0.075879504	0.102394039	0.11796326		
CLEC11A   Q9V240	4.6293688	0.003797996	0.006493323	0.997873996	0.454580417	0.059857987	0.205691028	0.565686903	-0.133673798	-0.007168513	-0.056939913	0.126052896	0.076734485	-0.049778081	-0.133673798	-0.007168513	-0.056939913	0.126052896	0.076734485	-0.049778081		
CSF1   P09603	0.11507907	0.95187649	0.937454661	0.995171191	0.988287471	0.984673426	0.991884239	0.999817073	0.012352589	0.004940961	0.006524205	-0.007411627	-0.005828383	0.001583244	0.012352589	0.004940961	0.006524205	-0.007411627	-0.005828383	0.001583244		
NEFM1   P07197	30.7172494	3.48E-16	0.997373022	1.61E-09	8.36E-10	4.75E-10	0.999932895	0.019228954	-0.63653267	-0.61800702	-0.661029656	-0.655761641	-0.002568015	-0.63653267	-0.61800702	-0.661029656	-0.655761641	-0.002568015	-0.63653267	-0.61800702		
H5S51   Q8B7P7	9.9721025	3.99E-06	0.00068829	0.00105044	3.11E-06	0.995797865	0.722983506	0.533064815	0.240469793	0.226746914	0.301917491	-0.013722879	0.064147699	0.075170577	0.226746914	0.301917491	-0.013722879	0.064147699	0.075170577	0.226746914		
OUFM1   Q9B784	10.7998622	1.42E-06	0.000261705	0.020979039	1.02E-06	0.520391454	0.734103359	0.063186814	0.136084907	0.09219322	0.168255618	-0.043891687	0.032170711	0.076062398	0.136084907	0.09219322	0.168255618	-0.043891687	0.032170711	0.076062398		
OJ   P01782	3.6927089	0.01292356	0.15730029	0.360235534	0.189206096	0.046525069	0.99277071	0.058435552	-0.238849454	0.253753948	-0.296304002	-0.021776259	-0.12787143	0.058435552	-0.238849454	0.253753948	-0.296304002	-0.021776259	-0.12787143	0.058435552		
PPH1   P23284	7.2621088	0.001631463	0.00142374	0.594044833	0.045431023	0.055218272	0.575737233	0.519125235	-0.141427165	-0.046179433	0.090473239	0.095247732	0.046723926	-0.046523806	-0.046179433	0.090473239	0.095247732	0.046723926	-0.046523806	-0.046179433		
PRH1   Q9UHI8	1.7668784	0.15186074	0.945013472	0.122221858	0.682276229	0.365643548	0.953747538	0.641667939	0.0280745	0.109105599	0.053466799	0.081026059	0.055239191	-0.045634068	0.109105599	0.053466799	0.081026059	0.055239191	-0.045634068	-0.045634068		
FGFR1   P13362	3.12291953	0.027190606	0.879525114	0.221779062	0.43454922	0.042426454	0.110864834	0.96588771	-0.023983111	0.060408115	0.046282691	0.084391226	0.070265801	0.014125425	-0.023983111	0.060408115	0.046282691	0.084391226	0.070265801	0.014125425		
CTSL1   Q00299	4.5361187	0.004290404	0.030971321	0.958922026	0.023931454	0.096976164	0.999504881	0.082017889	-0.149076253	-0.026176019	-0.022902764	0.002671147	-0.120290807	0.096976164	-0.149076253	-0.026176019	-0.022902764	0.002671147	-0.120290807	0.096976164		
PDCH7   Q60245	11.9511149	3.45E-07	0.000538469	4.30E-05	4.41E-07	0.957912518	0.500637203	0.799079862	0.186617211	0.209827906	0.245888918	0.023210694	0.062971787	0.039761037	0.209827906	0.245888918	0.023210694	0.062971787	0.039761037	0.209827906		
CPH1   P14384	0.45184835	0.716249629	0.935222085	0.942613369	0.99171696	0.65449923	0.953947552	0.936199492	-0.02902969	0.027107107	-0.004326672	0.056136797	0.024704397	0.034839798	-0.02902969	0.027107107	-0.004326672	0.056136797	0.024704397	0.034839798		
IGFBP3   P17936	0.5721066	2.47E-05	0.036924953	0.123285666	7.16E-06	0.943122076	0.14277915	0.028479369	-0.183841356	-0.146260968	-0.293580084	-0.037580388	-0.015987541	-0.177797515	-0.183841356	-0.146260968	-0.293580084	-0.037580388	-0.015987541	-0.177797515		
FETUB1   Q9UGM5	1.28927412	0.27968326	0.903585514	0.8770345	0.71374702	0.480161898	0.989784596	0.2633389	-0.072111911	0.076972119	-0.103475879	0.14908403	-0.031363698	-0.18047998	-0.072111911	0.076972119	-0.103475879	0.14908403	-0.031363698	-0.18047998		
LRPH1   Q14114	7.90091092	5.48E-05	0.30679049	0.022904009	2.48E-05	0.702448415	0.023002526	0.624101226	0.065542485	0.105611418	0.065542485	0.040068934	0.004639248	0.004639248	0.065542485	0.105611418	0.065542485	0.040068934	0.004639248	0.004639248		
HEG1   Q9ULI3	5.65875639	0.00090968	0.137669368	0.011166675	0.000702989	0.81135434	0.365001218	0.879749881	0.094543974	0.132747165	0.16307636	0.038203191	0.068532398	0.030329195	0.132747165	0.16307636	0.038203191	0.068532398	0.030329195	0.132747165		
PNH1   P07237	3.6066249	0.01218985	0.04647625	0.997603479	0.30419949	0.025027709	0.749039673	0.202919624	-0.057686773	0.004057672	-0.057686773	0.004057672	0.012171006	-0.057686773	0.004057672	-0.057686773	0.004057672	0.012171006	-0.057686773	0.004057672		
PSK9   Q8B8P7	2.9631227	0.03344917	0.881932769	0.244860918	0.003217525	0.69363789	0.203853088	0.818083132	0.039398001	0.09698293	0.140616309	0.057560292	0.01218308	0.043680161	0.039398001	0.09698293	0.140616309	0.057560292	0.01218308	0.043680161		
SPCK1   Q9R016	1.38435628	0.24809098	0.379528137	0.999861457	0.932528791	0.384671082	0.974102692	0.601278176	0.05981069	0.001068479	0.03796787	-0.04091239	0.038981618	0.038981618	0.05981069	0.001068479	0.03796787	-0.04091239	0.038981618	0.038981618		
SLR2   Q9UKM2	0.50321239	0.00227369	0.050428983	0.489375777	0.009357377	0.192801127	0.986548634	0.928340729	0.163754021	0.065737958	0.147789481	0.024856747	0.080251523	0.065737958	0.147789481	0.024856747	0.080251523	0.065737958	0.147789481	0.024856747		
DDAH1   Q9A760	24.3590051	2.45E-10	0.016307467	6.41E-06	0.021549533	7.95E-13	6.84E-08	0.101107606	0.112555979	-0.184424858	-0.103587787	-0.269808303	-0.21614477	0.080836086	-0.184424858	-0.103587787	-0.269808303	-0.21614477	0.080836086	-0.21614477		
F3A1   P00488	0.4524215	0.7180962	0.837637853	0.999717263	0.812495141	0.873546128	0.99999889	0.82236971	0.073457147	0.007899354	0.104070956	-0.06557793	0.000553809	-0.06557793	0.007899354	0.104070956	-0.06557793	0.000553809	-0.06557793	0.000553809		
CIRL1   Q9N278	1.1740547	0.320714166	0.991043854	0.688421929	0.333763083	0.858954839	0.52663089	0.946104688	0.020633472	0.075038497	0.112126582	0.054404755	0.09149284	0.037088085	0.0750							



Gene ID   Uniprot ID	F-Value	Pr(F)	ANOVA p-values with Tukey Adjustment										Difference (AD - CT)									
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA
CKB   P12277	15.7074497	4.51E-09	0.359301209	0.0002364	1.06E-08	0.059045227	5.62E-05	0.181918399	-0.09049197	-0.227865861	-0.332408991	-0.137373891	-0.241917021	-0.10454313								
COL5A1   P02908	3.0609207	0.029474836	0.274200957	0.639826043	0.99833912	0.016100511	0.210243477	0.658489131	-0.09405995	0.059859371	0.030827896	0.153918966	0.097887441	-0.056031525								
FOXR2   P14207	2.07883296	0.10452796	0.188950977	0.492723648	0.10072018	0.918113593	0.997555757	0.818974078	0.09844246	0.067429731	0.10741509	-0.031012729	0.00897263	0.039985395								
TM2B2   Q97287	0.70887921	0.547836204	0.60575015	0.99994371	0.978752377	0.56153419	0.809366077	0.968365882	-0.07168076	0.02833014	0.034815183	0.07444209	0.04972862	0.024789198								
KONE   P12303	5.37695376	0.01430568	0.621465314	0.05897538	0.00582195	0.171884122	0.170854438	0.999965506	-0.081375796	-0.21787067	-0.21479811	0.13630117	-0.13342314	0.003878957								
TUBB2A   Q13885	2.79434075	0.043926061	0.050439634	0.997788467	0.828223094	0.078201476	0.262715051	0.909692463	-0.333837907	-0.02308429	-0.105453147	0.031794778	0.22925495	-0.08148888								
HGB2   P69891	2.25295572	0.08382284	0.233398654	0.996664385	0.204942977	0.326337367	0.999957594	0.296652441	-0.578733517	-0.062464459	-0.564271108	0.516269058	0.014406409	0.051862649								
PTPRN   Q16849	0.1731928	8.78E-08	0.017484038	4.04E-06	3.10E-07	0.168408852	0.060094991	0.975106675	0.226128735	0.380843967	0.410657289	0.154715232	0.184528554	0.029813322								
PROX   P22891	3.12730435	0.025735865	0.17773384	0.984733685	0.249027098	0.076820141	0.992235961	0.111102034	-0.275612762	0.046583736	-0.29048001	0.322196498	0.036564761	-0.08561737								
TXNRD1   Q16881	19.7034908	3.96E-11	0.999997784	3.34E-07	2.55E-06	4.24E-07	3.16E-06	0.942802903	0.000658334	-0.198036136	-0.179122837	-0.19869447	-0.179781171	0.018913299								
KL   P05038	0.42398439	0.736040894	0.149381059	0.968405932	0.96405792	0.999997713	0.77723881	0.771290903	-0.016611907	-0.01956299	0.038112578	0.000655614	0.032924484	0.021268801								
SAMK20   Q13557	5.70238058	0.00093624	0.35950196	0.00371395	0.002485157	0.284338126	0.262186952	0.999999904	-0.288179122	-0.169332336	-0.169609172	-0.087632214	-0.087900051	-0.00276836								
CDH21   Q9U199	3.49020873	0.01684444	0.999081092	0.106969372	0.07121249	0.153144226	0.10672173	0.999350435	0.006752235	0.10930156	0.114918741	0.10249325	0.10816056	0.0056178								
PZP   Q95996	6.72393878	0.000248894	0.99245238	0.006362914	0.005189632	0.017261548	0.017461385	0.999998513	0.025571081	0.2948631	0.293486272	0.269292019	0.267915191	-0.0013799828								
LYVE1   Q9Y577	4.6161647	0.003863998	0.997289146	0.02496649	0.045316852	0.047106316	0.081889631	0.991395353	0.009448008	0.133047787	0.119998992	0.123599778	0.110550983	-0.013048795								
LBPI   P18428	1.75809814	0.07145533	0.953431479	0.359482908	0.879524547	0.141160726	0.578465723	0.77145071	-0.052247291	0.159261026	0.075042006	0.211508319	0.127789297	-0.088719022								
PARR2   Q99969	0.85511378	0.465498461	0.63639113	0.999937737	0.759922419	0.588992036	0.994136328	0.71173424	-0.055763692	0.00254873	-0.044203342	0.058312421	0.01156035	-0.046752072								
ADAMTS1   Q75173	1.71846864	0.061720683	0.676437998	0.853883046	0.260584761	0.985484131	0.012158802	0.483192152	0.040127663	0.02387734	0.07549906	-0.012254263	0.035481397	0.04775566								
FWAHB   P15146	16.7177057	1.18E-09	0.999999035	0.00121256	6.81E-07	0.00132597	8.18E-07	0.117102184	0.001823657	0.264647362	-0.326549876	-0.56471289	-0.32385733	0.06189264								
PDIA6   Q15084	0.50516098	0.679186465	0.747216872	0.997904784	0.813558064	0.834630182	0.988218552	0.892809403	0.027708878	0.004847117	0.032168814	-0.02861671	-0.004540084	0.018321697								
VLDR   P98155	1.45763698	0.227615908	0.95212659	0.999642679	0.47547768	0.202928932	0.20295286	0.52476053	-0.02511433	0.004617229	0.06531371	0.029731558	0.009228064	0.06349691								
EPHA10   Q51273	0.77161331	0.00023403	0.00982704	0.007211501	0.000175643	0.999999658	0.782993171	0.73083873	0.218655169	0.219324681	0.281262708	0.00060692	0.062670889	0.061938028								
PS90A81   P08238	2.55239057	0.057414974	0.840700386	0.132858265	0.080672022	0.558793984	0.937575264		-0.055203353	-0.140863012	-0.152858958	-0.08565969	-0.07482155	-0.01182496								
SKP1   P63208	9.99693486	3.87E-06	0.169943955	0.06489533	0.045811821	5.59E-05	2.55E-05	0.999820956	0.080373755	-0.094415314	-0.097301333	-0.174789069	-0.17675088	-0.002886019								
HYAL1   Q12794	2.51494588	0.05785267	0.143081059	0.999917794	0.397367251	0.118837707	0.906112191	0.345646805	-0.119264827	0.032873062	0.083086807	0.122572189	0.036178287	0.008398901								
CDH11   P12830	4.24560729	0.00703752	0.175706032	0.088102633	0.02154728	0.081110728	0.789101172	0.398859591	-0.280854192	-0.04704728	-0.059671472	0.30952447	0.112329041	-0.00237041								
ADAM11   Q75078	1.34261732	0.261965991	0.50876628	0.955667183	0.93840123	0.224404154	0.819448689	0.676231912	-0.074410591	0.026821029	-0.029416582	0.10132162	0.04949941	-0.056237211								
GRF2   P12802	1.98327377	0.118019229	0.999897435	0.545095285	0.10765632	0.51624151	0.19361922	0.973438512	-0.00276444	0.052074057	0.054701954	0.05470502	0.078095799	0.023435297								
PRK1   Q12821	2.78751931	0.042034442	0.294271542	0.274726995	0.02451419	0.999999785	0.75362661	0.371100562	0.064386485	0.06404079	0.099275541	-0.000302407	0.034889056	0.035191463								
DNER   Q8N78	6.39714495	0.000379844	0.795780836	0.425516154	0.01067362	0.03767929	0.00043575	0.37489049	-0.03556623	0.057493256	0.11557783	0.003959779	0.151145256	0.05808477								
CDH11   P12830	1.51269151	0.674022687	0.999986314	0.931128971	0.715228267	0.94325636	0.743572325	0.969722988	0.001101993	0.019252607	0.032984264	0.018123074	0.031882271	0.013759197								
CDH11   P12830	1.51269151	0.674022687	0.999986314	0.931128971	0.715228267	0.94325636	0.743572325	0.969722988	0.001101993	0.019252607	0.032984264	0.018123074	0.031882271	0.013759197								
CDH11   P12830	1.51269151	0.674022687	0.999986314	0.931128971	0.715228267	0.94325636	0.743572325	0.969722988	0.001101993	0.019252607	0.032984264	0.018123074	0.031882271	0.013759197								
CDH11   P12830	1.51269151	0.674022687	0.999986314	0.931128971	0.715228267	0.94325636	0.743572325	0.969722988	0.001101993	0.019252607	0.032984264	0.018123074	0.031882271	0.013759197								
CDH11   P12830	1.51269151	0.674022687	0.999986314	0.931128971	0.715228267	0.94325636	0.743572325	0.969722988	0.001101993	0.019252607	0.032984264	0.018123074	0.031882271	0.013759197								
CDH11   P12830	1.51269151	0.674022687	0.999986314	0.931128971	0.715228267	0.94325636	0.743572325	0.969722988	0.001101993	0.019252607	0.032984264	0.018123074	0.031882271	0.013759197								
CDH11   P12830	1.51269151	0.674022687	0.999986314	0.931128971	0.715228267	0.94325636	0.743572325	0.969722988	0.001101993	0.019252607	0.032984264	0.018123074	0.031882271	0.013759197								
CDH11   P12830	1.51269151	0.674022687	0.999986314	0.931128971	0.715228267	0.94325636	0.743572325	0.969722988	0.001101993	0.019252607	0.032984264	0.018123074	0.031882271	0.013759197								
CDH11   P12830	1.51269151	0.674022687	0.999986314	0.931128971	0.715228267	0.94325636	0.743572325	0.969722988	0.001101993	0.019252607	0.032984264	0.018123074	0.031882271	0.013759197								
CDH11   P12830	1.51269151	0.674022687	0.999986314	0.931128971	0.715228267	0.94325636	0.743572325	0.969722988	0.001101993	0.019252607	0.032984264	0.018123074	0.031882271	0.013759197								
CDH11   P12830	1.51269151	0.674022687	0.999986314	0.931128971	0.715228267	0.94325636	0.743572325	0.969722988	0.001101993	0.019252607	0.032984264	0.018123074	0.031882271	0.013759197								
CDH11   P12830	1.51269151	0.674022687	0.999986314	0.931128971	0.715228267	0.94325636	0.743572325	0.969722988	0.001101993	0.019252607	0.032984264	0.018123074	0.031882271	0.013759197								
CDH11   P12830	1.51269151	0.674022687	0.999986314	0.931128971	0.715228267	0.94325636	0.743572325	0.969722988	0.001101993	0.019252607	0.032984264	0.018123074	0.031882271	0.013759197								
CDH11   P12830	1.51269151	0.674022687	0.999986314	0.931128971	0.715228267	0.94325636	0.743572325	0.969722988	0.001101993	0.019252607	0.032984264	0.018123074	0.031882									

Gene ID   Uniprot ID	F-Value	Pr[F]	ANOVA p-values with Tukey Adjustment										Difference (AD - CT)									
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-AA	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs CT-AA
COR01A   P31146	5.39810778	0.00139167	0.821791327	0.67045576	0.001247605	0.995264203	0.026924077	0.042282682	-0.042692786	-0.05421169	-0.17642225	-0.011518905	-0.133729639	-0.122201735								
SEMA3C   Q99985	1.44100095	0.232308426	0.203192448	0.649783117	0.03129515	0.830585735	0.962538467	0.978801466	-0.133490246	-0.076802873	-0.101914821	-0.056687372	-0.031575424	-0.025111948								
CH3L2   Q5J5782	3.7348953	0.01232743	0.083442704	0.858767587	0.020567727	0.357899441	0.977945678	0.143126015	-0.192837429	-0.062166934	-0.224123132	0.130670495	-0.031283893	-0.161954388								
ITP19   Q9N515	8.1174771	0.026802	0.034879037	0.72045368	0.08531242	0.31161854	0.961581147	0.55863418	-0.099274198	-0.037654414	-0.082169256	0.061619784	0.017104941	-0.045148481								
AP181   Q10567	0.09541592	0.962476933	0.998395885	0.96749868	0.99999221	0.91449644	0.99854269	0.965788092	-0.033901091	-0.038063861	-0.00134922	-0.02416277	0.012866169	0.037289393								
PGY8   P12116	4.79028882	0.501361828	0.421419297	0.889220616	0.904398452	0.838603844	0.772314872	0.998005566	-0.171715236	-0.079165852	-0.070780615	0.092548385	0.100934622	0.008385237								
TFEMI328   Q140DG7	0.23699674	0.00355977	0.04751865	0.13307021	0.001802222	0.55926826	0.800344057	0.046203661	0.193521788	0.157034396	-0.058296679	-0.036487392	0.064774891	0.011262283								
MAG   P20916	1.58016894	0.195675969	0.980653114	0.99993056	0.275122962	0.970067519	0.512434557	0.233905934	0.016451083	-0.002406569	0.073381913	-0.018857652	0.05693803	0.075788427								
CSG   Q15828	3.84744306	0.01061545	0.1258892	0.951225617	0.216172697	0.33412575	0.98285734	0.908134055	0.137034961	-0.032172417	0.114988584	-0.169207378	-0.022049107	0.075788427								
LG1   Q09570	0.9999905	0.3941108	0.643997366	0.995557091	0.759147866	0.487140157	0.994580643	0.60060585	-0.05872888	0.01132735	-0.046789921	0.070100238	0.011982966	-0.058117272								
MOG   Q16553	1.33017709	0.26921743	0.489884116	0.304797723	0.335655117	0.992151982	0.997599768	0.999612581	0.064179884	0.0767499	0.072412264	0.012570017	0.00823238	-0.00433637								
IAG1   Q78504	6.81039062	0.00025052	0.47846832	0.990225576	0.00025675	0.33412575	0.98285734	0.908134055	0.052765515	0.113746042	-0.052765515	0.14624404	0.06980526	0.093358909								
PNOC   Q13519	13.0567842	8.99E-08	0.320165016	1.26E-05	1.36E-06	0.011928875	0.002296495	0.982671487	0.126033737	0.350623225	0.376087327	0.24584987	0.25003495	0.025465607								
EF1A1   P68104	0.56431422	0.639207312	0.939596829	0.944863461	0.56960956	0.999985594	0.905211358	0.882990246	-0.045429498	-0.042767486	-0.09705511	0.002662012	-0.051625612	-0.054287624								
YWHAQ   P61981	1.28730517	2.46E-30	0.897161425	1.23E-13	1.25E-13	1.14E-13	1.21E-13	0.928412186	0.033443816	0.471222261	-0.049317829	-0.504666077	-0.477361645	-0.027304431								
PLBD2   Q8NH98	2.14039348	0.09156707	0.166534382	0.922604542	0.171863946	0.450644783	0.999351026	0.874670205	-0.143327431	-0.042360163	-0.13521006	0.109697268	0.008117224	-0.092850044								
NOMD2   Q5JP67	1.57683785	0.196546373	0.246749321	0.999999094	0.862375935	0.22836605	0.649701316	0.849507318	-0.067293135	0.000477333	-0.026841493	0.067770467	0.040451642	-0.027318825								
EN1   P16152	5.81533521	0.000808305	0.425839009	0.011253445	0.000919161	0.41895973	0.120904163	0.907432651	-0.067108653	-0.13349898	-0.161368689	-0.066880335	-0.094260216	-0.027679881								
IGJ   P01591	0.3706348	0.72483197	0.94558536	0.998313335	0.771701885	0.99762427	0.900669961	0.852987868	-0.041709051	-0.023744715	-0.15298153	0.014363137	-0.11272478	0.012563815								
GFRA3   Q06079	1.21787808	0.30373753	0.305869461	0.946963174	0.996576169	0.609496186	0.384318493	0.984910011	-0.10654305	-0.032575078	-0.01240486	0.073967977	0.094138196	0.020170219								
SFRP4   Q6FH17	7.96852752	5.03E-05	0.001381524	0.991831439	0.041406662	0.000382513	0.591919215	0.015689954	-0.259868618	0.019318329	-0.175901231	0.279186947	0.08367387	-0.19219519								
ATP1B1   P05026	0.2190279	0.883108126	0.972975769	0.982268968	0.999947083	0.851185444	0.958842121	0.980753826	0.011904243	-0.010005466	-0.001383276	-0.021909709	-0.013287519	0.00862219								
CDH4   P55283	7.10227343	0.000152787	0.005523739	0.182009486	0.00012404	0.50657225	0.834646929	0.094434863	0.156113978	0.092124296	-0.04666731	-0.0103583	-0.00627934	-0.00360999								
LRN1   Q5JUX5	4.96288326	0.00245963	0.140187874	0.081661103	0.098808585	0.99797003	0.411298516	0.497229843	0.05743617	0.062125361	0.097152487	0.004689191	0.039716317	0.035027126								
PCDH9   Q95206	1.67811205	0.17323549	0.29887902	0.25288515	0.22350739	0.99969536	0.999858421	0.99994935	0.119528502	0.122737003	0.124329681	0.032038651	0.04801179	-0.0094794								
CDH9   Q9ULH4	6.18545008	0.000499783	0.10084792	0.935057594	0.00002836	0.67160074	0.93086995	0.770323973	-0.162203064	-0.024998224	0.077525062	0.05279516	0.011617892	0.036388332								
CD59   P13987	4.72711994	0.00342184	0.692085042	0.006653472	0.019692879	0.146870994	0.297983191	0.971859431	0.034264547	0.099856003	0.080755203	0.065591546	0.052810761	-0.1278074								
TFEMI327   Q6BIE7	0.66239229	0.503705	0.94524101	0.934857898	0.772492919	0.661136657	0.447153741	0.98237215	-0.023611685	0.024467411	-0.03750002	0.048079096	0.06961687	0.012882591								
CD200   P41217	0.21099711	0.000483493	0.882982264	0.001898844	0.012110556	0.023931408	0.103450269	0.913137432	0.043962697	0.212682433	0.175980185	0.168719734	0.132017488	-0.036202448								
TXNDC3   Q8RN85	0.07740383	0.972146799	0.999937077	0.998190546	0.981509546	0.98585723	0.97296132	0.996903084	0.001560263	-0.04666731	-0.0103583	-0.00627934	-0.01156993	-0.00360999								
CD28A1   Q2Y019	4.04947834	0.68633647	0.69753069	0.999827352	0.988049037	0.93368619	0.845877289	0.995129048	-0.10288832	-0.007185117	-0.02832527	0.09540325	0.047618125	-0.02114141								
CDK6B   Q9H7Y0	3.6530086	0.01361503	0.045793238	0.087541378	0.008648203	0.94484297	0.563176846	0.94536791	0.078684984	0.102742362	0.1337156	0.045405738	0.05052122	0.03094794								
SAAN1   P35542	4.14000295	0.24130094	0.756717883	0.925602991	0.997818507	0.180154078	0.800852241	0.570231333	-0.136184571	0.139673536	-0.06221478	0.275838107	0.109967093	0.165891015								
CDXN3   Q9ULH4	2.0791677	0.105451523	0.815538019	0.987306076	0.10803534	0.94238457	0.544015734	0.204400685	0.03176241	0.011679207	0.078051907	-0.020083204	0.046287788	0.066370992								
POLCB2   Q5KU26	0.68053925	2.11E-05	0.001048722	0.133513576	2.51E-05	0.31392911	0.890940833	0.05020409	0.105395605	0.058484822	0.024400537	-0.046910783	0.019006933	0.065917716								
GLDN   Q6ZM13	0.21388668	0.113521186	0.454414435	0.990805001	0.152431064	0.624547578	0.94511331	0.257420683	0.104590244	0.0204952	0.14248676	-0.084095044	0.037858516	0.12195356								
MAPT   P10636	61.28827534	4.34E-27	0.016223141	1.32E-12	1.73E-12	0	0	0.987438598	0.225459819	-0.583372134	-0.560003631	-0.08831953	-0.78552283	0.02303123								
DNM1   Q5J193	1.6275346	0.598171463	0.830926828	0.542500335	0.772497987	0.968365979	0.999897854	0.976187318	-0.046647182	-0.071324884	-0.050122129	-0.024677702	-0.060475008	0.021202694								
COL5A1   P12110	6.33878215	0.000415034	0.045793238	0.087541378	0.008648203	0.94484297	0.563176846	0.94536791	0.078684984	0.102742362	0.1337156	0.045405738	0.05052122	0.03094794								
IT5   P25774	1.12157196	0.24130094	0.756717883	0.925602991	0.997818507	0.180154078	0.800852241	0.570231333	-0.136184571	0.139673536	-0.06221478	0.275838107	0.109967093	0.165891015								
YWHAQ   Q04017	3.46047335	2.29E-19	0.999997518	2.10E-11	2.75E-12	1.12E-11	4.27E-12	0.9979795	0.000861521	-0.328237437	-0.33578335	-0.320908985	-0.336644871	-0.007545912								
CD43   Q5A329	5.40269329	0.001383374	0.123133157	0.164993438	0.000487027	0.997243455	0.942477733	0.21956449	0.094378071	0.086070398	0.162881229	-0.008037673	0.068503219	0.071680192								
SELL   P14151	0.2712355	0.846076057	0.986977285	0.981187474	0.979708837	0.999983803	0.883230661	0.857237211	-0.019023817	-0.021010094	0.02109767	-0.001986277	0.040093583	0.047207986								
EFNB2   P52799	6.1830129	0.00050136	0.026781087	0.013884458	0.000289343	0.99806713	0.645834263	0.71821121	0.10651104	0.11889725	0.014907352	0.005388684	0.042506113	0.037176277								
AGALG   Q9NFC4	0.56376953	0.6395491	0.9732																			



Gene ID	Uniprot ID	F-Value	P(=F)	ANOVA p-values with Tukey Adjustment								Difference (AD - CT)							
				AD-Cau vs AD-AA	CT-AA vs AD-AA	AD-AA vs AD-AA-CT	AD-AA-CT vs AD-AA-CT-Cau	AD-AA-CT-Cau vs AD-AA-CT	AD-AA-CT-Cau vs AD-AA-CT	AD-AA-CT-Cau vs AD-AA-CT	AD-AA-CT-Cau vs AD-AA-CT	AD-AA-CT-Cau vs AD-AA-CT	AD-AA-CT-Cau vs AD-AA-CT	AD-AA-CT-Cau vs AD-AA-CT	AD-AA-CT-Cau vs AD-AA-CT	AD-AA-CT-Cau vs AD-AA-CT	AD-AA-CT-Cau vs AD-AA-CT		
BRINP1	P06477	1.34008125	0.26363017	0.95075905	0.99629711	0.27655621	0.98792587	0.61217907	0.37755604	0.023259316	0.009362495	0.075569469	-0.014166821	0.052040153	0.062069749	0.000000000	0.000000000	0.000000000	0.000000000
TAH1	P09960	1.55227033	0.20255415	0.93782694	0.52838214	0.209433218	0.704737496	0.40048309	0.36512522	0.012975031	0.065719317	-0.088035575	-0.052742486	0.075005404	0.022316258	0.05005404	0.000000000	0.000000000	0.000000000
RTM2D	Q43300	0.51046751	0.02040887	0.04502114	0.009817095	0.009598397	0.984868938	0.719804584	0.467428128	0.118694033	0.03032006	0.164281367	0.015662447	0.045859194	0.061249361	0.000000000	0.000000000	0.000000000	0.000000000
FTM12	P28161	0.52704463	0.056243085	0.91266334	0.99028107	0.05949899	0.98298684	0.74007087	0.35699	0.051510033	0.00655219	0.0234201	0.006808104	0.05402314	0.03154299	0.000000000	0.000000000	0.000000000	0.000000000
FTM12	P28161	1.53891459	0.20293212	0.61564534	0.72434565	0.00908789	0.99087869	0.61297973	0.35699	0.051510033	0.00655219	0.0234201	0.006808104	0.05402314	0.03154299	0.000000000	0.000000000	0.000000000	0.000000000
SN1	Q00499	2.7306124	0.04257699	0.88362434	0.37707259	0.03712981	0.82514952	0.29867679	0.68594185	-0.047334625	0.03940779	-0.156761806	-0.050323256	-0.13028383	0.06296027	0.000000000	0.000000000	0.000000000	0.000000000
SEPIN1A	Q0UK55	1.96166758	0.121285938	0.97372625	0.35758078	0.98117208	0.17039643	0.119739843	0.17538955	-0.39858572	0.1482449	-0.033394943	0.18813062	0.006290779	-0.181839843	0.000000000	0.000000000	0.000000000	0.000000000
BGLN1	Q07572	1.89806394	0.03141265	0.16116179	0.88324587	0.09826065	0.98549524	0.63472258	0.32600789	0.038007372	0.02586739	0.075151462	-0.02138992	0.041143731	0.053462773	0.000000000	0.000000000	0.000000000	0.000000000
CTG1	Q09781	1.59893057	0.020044671	0.78958258	0.45048583	0.00152568	0.950235059	0.03996378	0.138204007	0.066715064	0.130367133	-0.2489574	-0.036752069	-0.182243236	0.000000000	0.000000000	0.000000000	0.000000000	0.000000000
FLYCN1A	Q08817	1.18677661	0.036121781	0.94095531	0.434536459	0.03458764	0.83052574	0.702112552	0.9366393	0.023886963	0.071459859	0.189110042	0.00472896	0.05323079	0.014054813	0.000000000	0.000000000	0.000000000	0.000000000
FLYCN1A	Q08817	0.97965053	0.4481266	0.00561477	0.00561477	0.00561477	0.00561477	0.00561477	0.00561477	0.00561477	0.00561477	0.00561477	0.00561477	0.00561477	0.00561477	0.00561477	0.00561477	0.00561477	0.00561477
POCXL	Q09432	0.5949885	0.03471789	0.85348626	0.88323162	0.02917948	0.97977463	0.22079672	0.16435141	0.048416284	0.03412963	0.16031006	-0.005283321	0.01191457	0.011797892	0.000000000	0.000000000	0.000000000	0.000000000
ADCMAP1	P18509	2.1927117	0.00966499	0.99995463	0.37761818	0.83126266	0.41466977	0.83047166	0.056946949	0.020320359	0.13580895	-0.07895425	0.15107849	-0.08177784	-0.23256823	0.000000000	0.000000000	0.000000000	0.000000000
FADY28	Q75063	0.48219287	0.02693591	0.43460191	0.07479292	0.04144028	0.819983079	0.51518261	0.58671144	0.04964354	0.077680813	0.17610202	0.028217359	0.05768069	0.08348249	0.000000000	0.000000000	0.000000000	0.000000000
NRN1	Q09077	9.2373662	8.86E-06	0.87358729	0.00079558	0.00015935	0.01283051	0.003682743	0.98801333	0.26757002	0.133793371	0.14555723	0.10703669	0.11779872	0.01762333	0.000000000	0.000000000	0.000000000	0.000000000
CSN8	Q09772	1.7436761	6.43E-10	1.31E-05	2.00E-05	3.07E-10	0.95928408	0.26939364	0.150492774	0.33017668	0.33342062	0.07457265	0.16145596	0.12598607	0.141943203	0.000000000	0.000000000	0.000000000	0.000000000
XLRI	Q09247	1.7786874	0.28334678	0.99726208	0.29645729	0.96908744	0.14182498	0.99442052	0.51896767	0.007642826	0.069442403	-0.071452246	0.068779957	-0.09089419	0.051990158	0.000000000	0.000000000	0.000000000	0.000000000
PCOLCE	Q09247	0.41097303	0.7453001	0.95644387	0.95644387	0.95644387	0.95644387	0.95644387	0.95644387	0.95644387	0.95644387	0.95644387	0.95644387	0.95644387	0.95644387	0.95644387	0.95644387	0.95644387	0.95644387
PL1	P01236	0.0884176	0.43211676	0.83450293	0.96176174	0.909870831	0.55821925	0.99999955	0.1034821	0.07663106	0.04074035	-0.07765204	0.11731434	-0.00348435	-0.117098639	0.000000000	0.000000000	0.000000000	0.000000000
ADAMTS13	P82987	1.82091647	0.14485998	0.44440759	0.99988587	0.24845324	0.4492009	0.99686736	0.28583314	-0.07852903	-0.00162102	-0.08019714	0.076908902	-0.016668394	-0.087577296	0.000000000	0.000000000	0.000000000	0.000000000
C2orf40	Q29048	0.70793739	0.30042706	0.06406493	0.97786146	0.14864784	0.011479948	0.08359011	-0.27489162	0.03405759	-0.20601574	0.15249236	0.05429636	0.08220128	0.246429108	0.000000000	0.000000000	0.000000000	0.000000000
METRL1	Q61403	0.40930295	0.00765997	0.00629731	0.84336569	0.21955161	0.05710962	0.94547304	0.68618631	-0.125723393	0.00626979	-0.069824662	0.095260414	0.055898731	0.039361683	0.000000000	0.000000000	0.000000000	0.000000000
PABP1	P05413	1.73549079	6.89E-32	0.29769309	1.23E-13	1.24E-13	9.86E-14	0.942614	0.927712499	0.098184267	-0.079964383	-0.074152024	-0.57014865	-0.6133647	-0.008881219	0.000000000	0.000000000	0.000000000	0.000000000
TCG1	P09039	1.94893034	0.01351517	0.94600285	0.06072785	0.05733732	0.98318628	0.97086790	0.16818017	-0.051947744	0.03174296	0.03175273	0.000000000	0.000000000	0.000000000	0.000000000	0.000000000	0.000000000	0.000000000
QSOX1	Q06043	0.5813439	0.62795311	0.67795311	0.67795311	0.67795311	0.67795311	0.67795311	0.67795311	0.67795311	0.67795311	0.67795311	0.67795311	0.67795311	0.67795311	0.67795311	0.67795311	0.67795311	0.67795311
CTG1	Q09772	2.5566709	0.07352164	0.13472198	0.99901238	0.97993391	0.11637441	0.90734843	0.49862004	0.15303939	0.07124998	0.10785201	-0.14830932	-0.05456189	0.098146239	0.000000000	0.000000000	0.000000000	0.000000000
SEMA6B	Q09733	4.1756213	0.00684025	0.99999994	0.093111029	0.045125198	0.989147534	0.04701408	0.99273384	-0.000277485	0.13486663	0.150066233	0.13514648	0.15301418	0.015199461	0.000000000	0.000000000	0.000000000	0.000000000
HIST2H2T	Q05906	0.5448837	0.114683058	0.931971083	0.990881254	0.96904859	0.98041588	0.68255851	0.94865444	0.009018593	0.04072881	-0.076472881	-0.046573228	-0.10447424	-0.113847197	0.000000000	0.000000000	0.000000000	0.000000000
PKP1	P04672	0.59125971	0.00072321	0.019741312	0.03120225	0.0004012395	0.995120314	0.76773803	0.959847648	0.121275278	0.113936302	0.16045739	0.008816456	0.038076337	0.04852109337	0.000000000	0.000000000	0.000000000	0.000000000
PKP1	P04672	1.60935101	0.17532466	0.99995304	0.934688358	0.218951798	0.948308049	0.23590446	0.930589229	0.004491034	0.05177808	0.165787445	0.047285773	0.16129641	0.014106373	0.000000000	0.000000000	0.000000000	0.000000000
CTG1	Q09772	0.60996706	0.2310001518	0.00015118	0.00015118	0.00015118	0.00015118	0.00015118	0.00015118	0.00015118	0.00015118	0.00015118	0.00015118	0.00015118	0.00015118	0.00015118	0.00015118	0.00015118	0.00015118
3GN7N	Q06722	2.4613337	0.06390397	0.077886142	0.059829724	0.31163683	0.20627949	0.83589955	0.06071366	0.09643963	0.01927761	0.05654547	0.077162201	0.01037897	0.046368304	0.000000000	0.000000000	0.000000000	0.000000000
CSG6	Q75144	1.3810613	3.30E-08	0.003016959	0.95455153	1.62E-06	0.005467951	0.37280272	0.331E-06	0.22924797	0.14844812	0.03048497	-0.112244637	0.01073937	0.315650338	0.000000000	0.000000000	0.000000000	0.000000000
CBN1	P23435	0.2952828	0.828775078	0.88891297	0.99999994	0.999486469	0.88313418	0.8266913	0.99952478	-0.044094904	0.000280084	0.0666365	0.04471078	0.051127494	0.006365146	0.000000000	0.000000000	0.000000000	0.000000000
CTA1	P06169	2.2763232	0.028312478	0.10957036	0.9331734	0.43371729	0.178512434	0.82318996	0.59249703	-0.152149684	-0.07594667	-0.096310959	0.13455501	0.0558878	-0.078162388	0.000000000	0.000000000	0.000000000	0.000000000
PTPR	Q12913	1.3551369	0.257998474	0.94472358	0.99514091	0.53037769	0.66882545	0.22478323	0.86438081	0.024551101	0.02457018	0.056364724	0.048953881	0.080815824	0.031857443	0.000000000	0.000000000	0.000000000	0.000000000
SPPR1	P07408	0.7207408	0.084665301	0.95128488	0.986885576	0.74173299	0.93981582	0.98400733	0.04899507	0.02072876	0.01725049	0.034354647	-0.09079611	0.017174707	0.031857443	0.000000000	0.000000000	0.000000000	0.000000000
CTG1	Q09772	2.6776125	0.04846263	0.99999994	0.99999994	0.99999994	0.99999994	0.99999994	0.99999994	0.99999994	0.99999994	0.99999994	0.99999994	0.99999994	0.99999994	0.99999994	0.99999994	0.99999994	0.99999994
FLN1	P08172	3.71641052	0.01253497	0.048464851	0.028632189	0.027177292	0.939439053	0.99980319	0.95992923	0.07120507	0.046654051	0.032366789	-0.00288993	0.020051807	-0.00213267	0.000000000	0.000000000	0.000000000	0.000000000
BAGN1A	Q07691	1.1479414	0.031106953	0.97312894	0.88241925	0.98186607	0.26889572	0.68838747	0.67364491	0.070867864	0.046459841	0.023068987	-0.115523245	-0.047798175	0.072721447	0.000000000	0.000000000	0.000000000	0.000000000
CHN1	Q08936	0.35155437	0.78067041	0.94467189	0.96902662	0.99868174	0.74218392	0.9402923											

Gene ID   Uniprot ID	F-Value	Pr(>F)	ANOVA p-values with Tukey Adjustment								Difference (AD - CT)							
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA
AK1   P00568	1.64864607	0.204057025	0.606784367	0.484752464	0.149498796	0.998749535	0.848044487	0.050460585	-0.09133875	-0.102383507	-0.149318452	-0.011044756	-0.057979702	-0.046934946	0.762991784	0.000236673	0.000769368	0.988817514
FOU1   P15328	1.52691001	0.07712601	0.52245062	0.87769076	0.059072906	0.915999604	0.704127969	0.280182235	0.051072772	0.027194605	0.098926129	-0.023878707	0.038753356	0.060352064	0.19640038	0.3125054	0.535061164	0.29072279
DYI   P01178	1.67190838	0.172870186	0.607127221	0.76310701	0.996371908	0.122588294	0.442607517	0.856283115	-0.0596812	0.04313558	0.009755238	0.09911678	0.056343358	-0.03376832	0.00856133	0.000589225	0.015139815	0.020393458
SPR331   Q06083	0.05860132	0.000589225	0.01539815	0.020393458	0.000378602	0.998023635	0.803673684	0.680240344	0.197929419	0.169340317	0.23148783	-0.010389102	0.051758413	0.062147515	0.00856133	0.000589225	0.015139815	0.020393458
CTN51   Q94779	0.597199278	0.000695297	0.01782386	0.023779728	0.002348102	0.788200918	0.990548746	0.905422921	0.242277195	0.181700862	0.223103377	-0.060576334	0.019146818	0.041429516	0.00856133	0.000589225	0.015139815	0.020393458
KOP1   P03950	1.18840738	3.74E-07	0.000350239	0.97559415	9.23E-05	0.000565091	0.999457383	0.000515977	-0.268857044	-0.011280238	-0.27609411	0.256748807	-0.007234367	-0.263983174	0.00856133	0.000589225	0.015139815	0.020393458
PLAUR   Q03405	1.32620309	0.268897517	0.307421081	0.325031072	0.147545622	0.999398484	0.863821831	0.884105069	0.122791217	0.11894031	0.06964003	-0.003847204	0.0053150814	-0.04930361	0.00856133	0.000589225	0.015139815	0.020393458
PLAGL5   Q8NCV3	0.12250114	0.946744719	0.998939704	0.982162074	0.989114427	0.954052383	0.967565004	0.999882745	-0.005776141	0.014616839	0.01203429	0.02029497	0.01780957	0.002852522	0.00856133	0.000589225	0.015139815	0.020393458
SAINT15   Q8N371	0.048373294	0.008107216	0.600856551	0.530405607	0.289134693	0.049199556	0.967304003	0.00033802	0.003117988	-0.09865062	0.12640627	-0.191813049	0.033205689	0.225105689	0.00856133	0.000589225	0.015139815	0.020393458
UBE2L3   P08036	19.006671	8.67E-11	0.805909185	3.61E-06	1.45E-08	0.00024852	2.31E-06	0.7494127	-0.026728693	-0.149705776	-0.17525284	-0.122977082	-0.150796591	-0.027819508	0.00856133	0.000589225	0.015139815	0.020393458
NPOC1   Q9NQX5	5.75895752	0.000870219	0.097779683	0.175793937	0.000301275	0.988136441	0.329838053	0.161180546	0.11066593	0.095339082	0.188813898	-0.015326849	0.078147968	0.093474817	0.00856133	0.000589225	0.015139815	0.020393458
UCLH1   P09936	90.433007	4.56E-36	0.708965133	8.82E-14	8.70E-14	1.10E-13	1.07E-13	0.999436016	-0.053010109	-0.586173492	-0.580785114	-0.533163383	-0.527775005	-0.035888378	0.00856133	0.000589225	0.015139815	0.020393458
MAMDC2   Q72304	11.1512983	9.22E-07	0.000203163	0.113617676	1.45E-06	0.161980426	0.810911788	0.014177874	-0.207567626	-0.107151244	-0.24936716	0.100416382	-0.041829534	-0.142245916	0.00856133	0.000589225	0.015139815	0.020393458
UBE2L3   P08036	37.6369246	4.91E-19	0.9647717	2.90E-11	7.53E-11	2.97E-12	7.32E-12	0.985699892	0.017837776	-0.270846647	-0.288664423	-0.276504574	-0.012179849	-0.012179849	0.00856133	0.000589225	0.015139815	0.020393458
AD23A   Q94779	5.6581447	0.000991754	0.999999992	0.027219191	0.01739702	0.024875902	0.019214526	0.99999545	0.000128806	-0.130597701	-0.131673764	-0.130726507	-0.11802571	-0.001070683	0.00856133	0.000589225	0.015139815	0.020393458
ENG3   Q70700	14.8000332	1.12E-08	0.15865201	0.043342498	0.00056467	2.47E-05	3.46E-08	0.567841356	-0.129339713	-0.159051697	-0.23371134	-0.28839143	-0.363050667	-0.074659437	0.00856133	0.000589225	0.015139815	0.020393458
CYC5   P99999	1.1464108	0.34445536	0.965812937	0.730934366	0.940194373	0.442066128	0.998827298	0.349538309	0.020261939	-0.043020919	-0.03519208	-0.063664038	0.003257269	0.066921307	0.00856133	0.000589225	0.015139815	0.020393458
SLA   P06280	0.9170847	0.182325645	0.091027209	0.836035048	0.960713738	0.662337571	0.967230364	0.994293917	0.901419297	0.769220364	-0.088215037	-0.030647915	-0.046310989	-0.057567122	0.00856133	0.000589225	0.015139815	0.020393458
AP0A18P   Q8NCW5	2.88462492	0.03707888	0.63046249	0.68095667	0.467548475	0.098164126	0.039927853	0.988784111	-0.047820645	-0.043381839	-0.05286915	-0.09120484	-0.10310756	-0.01905077	0.00856133	0.000589225	0.015139815	0.020393458
IGSF1   Q8NC65	4.64395334	0.003726096	0.999954202	0.640675841	0.907549475	0.881177502	0.106883137	0.17198805	0.002279081	0.052011077	0.139028879	-0.049913996	-0.136759127	0.087027131	0.00856133	0.000589225	0.015139815	0.020393458
BAI3   Q06242	0.80333765	0.493467076	0.926857584	0.840617231	0.95210432	0.472472473	0.651527971	0.987915972	-0.029113965	0.038164571	0.03776137	0.067278536	0.025850102	-0.014284344	0.00856133	0.000589225	0.015139815	0.020393458
SAL1   Q75468	2.80364826	0.037108561	0.998884827	0.992542382	0.974598095	0.063466028	0.147984329	0.999999999	-0.012805012	0.023602027	0.197675808	0.036405309	0.021408013	0.17405503	0.00856133	0.000589225	0.015139815	0.020393458
CTN51   Q94779	39.2374568	1.13E-19	0.537466085	4.97E-09	2.73E-11	3.43E-12	1.35E-13	0.860054946	-0.048272404	-0.04043152	-0.058378207	-0.07466555	-0.054801611	-0.037935055	0.00856133	0.000589225	0.015139815	0.020393458
TPR555   Q8H353	2.8085385	0.041074696	0.460370167	0.79311631	0.027485266	0.942698267	0.556133215	0.272357316	-0.115134655	-0.071619953	-0.214404894	0.043514702	-0.099035039	-0.14280541	0.00856133	0.000589225	0.015139815	0.020393458
RMOJ3   Q967C7	0.60306	0.613441414	0.94538906	0.98830563	0.576698933	0.994923917	0.901419297	0.769220364	0.023413017	0.013289041	0.051417183	-0.010213977	0.028004615	0.03812842	0.00856133	0.000589225	0.015139815	0.020393458
GF2   P01344	1.82487859	0.144139921	0.381357078	0.992047787	0.22692198	0.535738689	0.995948495	0.333765308	-0.07084135	-0.01219693	-0.08083453	0.058582705	-0.005999408	-0.068186613	0.00856133	0.000589225	0.015139815	0.020393458
VNN1   Q95497	1.72156234	0.164084402	0.981396165	0.150390529	0.982976663	0.321108805	0.987361487	0.468337327	0.053654496	0.29204395	-0.086875533	0.23887899	0.045203037	-0.191384862	0.00856133	0.000589225	0.015139815	0.020393458
KPMAP   Q9HDC9	1.71343854	0.165759399	0.959384193	0.90135726	0.14609764	0.998121647	0.386857327	0.462777246	0.044804864	0.060203982	0.182300824	0.015395521	0.137499752	0.122104231	0.00856133	0.000589225	0.015139815	0.020393458
TAOLN1   P07802	5.59211921	0.00114722	0.229739676	0.311914669	0.00044137	0.991781068	0.904543722	0.799213613	-0.089508621	-0.090821175	-0.15569891	0.016086385	-0.108617337	-0.124748802	0.00856133	0.000589225	0.015139815	0.020393458
TAOLN1   Q9H15	8.86057534	1.70E-05	0.873944089	0.002093864	0.029007097	0.000147835	0.02059823	0.77244725	0.004023354	-0.02563729	-0.04878207	-0.253587083	-0.02123362	-0.054657271	0.00856133	0.000589225	0.015139815	0.020393458
MGP   P08493	2.3443888	0.074452848	0.140229333	0.140918112	0.117458304	0.999916854	0.999995515	0.999985816	-0.154322522	-0.149994679	-0.15277614	0.004327843	0.002050908	-0.002276935	0.00856133	0.000589225	0.015139815	0.020393458
LOXJ3   P58215	0.16851084	0.917488313	0.982364001	0.999998494	0.986628396	0.994293917	0.901419297	0.769220364	-0.023704499	0.00099275	-0.02029266	0.042697249	0.043997195	0.019299946	0.00856133	0.000589225	0.015139815	0.020393458
THSD7A   Q9U0Z6	0.91371136	0.435732909	0.997894991	0.978991272	0.6632242	0.939477155	0.784364033	0.38838917	0.008797776	-0.018538124	0.052523978	-0.027359501	0.04726201	0.071062102	0.00856133	0.000589225	0.015139815	0.020393458
ADAM9   Q13443	4.1468095	0.00713891	0.01886023	0.997287885	0.970510577	0.00077682	0.139266991	0.963728886	-0.0990338	0.006438938	-0.029524708	-0.105472738	0.06977902	-0.035693464	0.00856133	0.000589225	0.015139815	0.020393458
LRP4   Q75096	0.06810535	0.615997893	0.957206895	0.663301679	0.959596144	0.999999893	0.911817965	0.908379977	0.02673603	0.092136839	0.040511373	-0.000536764	0.051625466	0.051625466	0.00856133	0.000589225	0.015139815	0.020393458
HHN1   Q5465	2.0486621	0.108246166	0.085137946	0.311914669	0.00044137	0.991781068	0.904543722	0.799213613	-0.089508621	-0.090821175	-0.15569891	0.016086385	-0.108617337	-0.124748802	0.00856133	0.000589225	0.015139815	0.020393458
CTN51   Q94779	2.6694984	0.097117413	0.629108839	0.002093864	0.029007097	0.000147835	0.02059823	0.77244725	0.004023354	-0.02563729	-0.04878207	-0.253587083	-0.02123362	-0.054657271	0.00856133	0.000589225	0.015139815	0.020393458
ENGGT1   Q95841	1.53091753	0.001481382	0.010014279	0.643696054	0.004415376	0.175637246	0.99975662	0.115138853	-0.124963768	-0.045252819	-0.128309896	0.079710949	-0.003346128	-0.08057077	0.00856133	0.000589225	0.015139815	0.020393458
EMUN3   Q9NT72	0.7398476	0.361398861	0.614392871	0.999620606	0.52265114	0.665694448	0.999679052	0.564196315	0.06677015	0.050419206	-0.016510899	0.005608606	0.069481905	0.056945705	0.00856133	0.000589225	0.015139815	0.020393458
SRB2   P62993	0.9573245	0.465181748	0.442490759	0.993146002	0.964072152	0.594041415	0.700724034	0.996949689	0.048384260	0.008480425	0.014673778	-0.039903781	-0.033710148	-0.060193363	0.008			



Gene ID   Uniprot ID	F-Value	Pr(<F)	ANOVA p-values with Tukey Adjustment								Difference (AD - CT)							
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA
ERPA4   Q85256	2.17224307	0.092788126	0.109738492	0.99697169	0.629537935	0.15694287	0.644772818	0.746726419			-0.084604131	-0.007421702	-0.024779548	0.077182429	0.042133183	-0.035049247		
FAH1   P69390	0.28791119	0.834080002	0.844868534	0.955295853	0.856666666	0.988260458	0.999891010	0.999891010			-0.062695077	-0.038343287	-0.057705442	0.024351791	0.004939658	-0.019412133		
SLO1   Q04760	27.1871732	1.30E-14	0.48729584	2.46E-06	8.29E-08	2.10E-09	3.85E-11	0.939598072			0.059043334	-0.212157618	-0.244445751	-0.271200953	-0.293489086	-0.022288133		
HNVS-51   A0A0C4D3H8	1.15532668	0.32829514	0.875940991	0.697850175	0.956380147	0.259140626	0.71091745	0.858719899			-0.098525076	0.134896164	0.034938664	0.230795402	0.13079454	-0.099490583		
LUR1   P01310	7.3415295	0.00012301	0.230720153	0.037586894	0.791201669	4.59E-05	0.22183181	0.244110414			-0.088219559	0.121886116	0.040804297	0.210105675	0.129033856	-0.081081819		
BLL1   Q09173	6.94304148	0.000187585	0.003846231	0.99978956	0.027480079	0.002403863	0.852317602	0.018615481			-0.158271234	0.003733524	-0.122756628	0.162004757	0.035514965	-0.126489793		
ENP4   Q9V6X5	1.9524655	0.12247526	0.826170334	0.511248649	0.808386064	0.116622771	0.289077445	0.951166700			0.052713872	-0.082663854	-0.052135238	-0.135377726	-0.10484911	-0.030528616		
CD44   P16070	5.15874169	0.001901732	0.098994262	0.715124095	0.235785872	0.004638004	0.950312804	0.01429615			0.080754332	-0.03597457	0.062756391	-0.116728901	-0.07199794	0.098730961		
MP1   P35449	0.73280536	0.533655833	0.961244252	0.774380437	0.99938542	0.474503147	0.942608247	0.783697191			0.023282587	-0.044208315	-0.002505948	0.067409002	-0.025788535	-0.041702367		
CRIM1   Q9NZV1	1.18636026	0.318274753	0.997709738	0.999610544	0.400461365	0.999752648	0.520799652	0.436563991			-0.021974127	-0.011818655	-0.173178847	0.010155472	-0.15120472	-0.161360192		
PCN1   Q15293	1.85522179	0.144005233	0.369424492	0.977716683	0.955949183	0.262673497	0.130262017	0.988006838			-0.066274107	0.007392353	0.01984529	0.37666551	0.086117487	0.012450936		
WSP1   O75076	5.81125627	0.00071149	0.005320149	0.970652619	0.01337301	0.030518872	0.967104629	0.071914068			-0.196952605	-0.036373734	-0.17100919	0.160578871	0.025943415	-0.134635456		
HNRPNA2B1   P22626	1.62699571	0.185432982	0.165037779	0.970577305	0.680018323	0.35397887	0.703463865	0.913218155			-0.244204532	-0.051548794	-0.123771396	0.192655737	0.120433135	-0.072226202		
TR1   Q70L00	4.45216864	0.716090304	0.736403426	0.95715805	0.999941797	0.923234869	0.744487655	0.98151699			-0.06505042	-0.022386645	-0.08260611	0.034112775	0.053644809	-0.019526034		
SVEP1   Q4LE05	0.38089514	0.766900249	0.955306741	0.76287326	0.998158745	0.967941602	0.984055874	0.8375501			-0.046994666	-0.088026941	-0.051329076	-0.041032775	0.031665589	0.072697864		
JAM2   P57087	1.26105068	0.28898674	0.479091926	0.303708433	0.403181459	0.993358668	0.99951978	0.99579391			0.044314491	0.052415584	0.054832504	0.008101093	0.001518013	-0.00658308		
LSR   Q80K29	2.61287468	0.05268917	0.804000961	0.039611759	0.293764539	0.309169271	0.85133767	0.71383727			0.031238559	0.090389254	0.008117472	0.059150694	0.026878913	-0.032271782		
DC11   Q80K74	5.02086743	0.66845137	0.994628089	0.689037552	0.995724072	0.825770453	0.998801515	0.728507637			-0.019580788	0.087142539	0.008210355	0.0567961751	-0.051319463	-0.07893184		
SEMA5   O15041	1.0623614	0.3659858	0.996980804	0.998079964	0.54052416	0.64354164	0.689162356	0.99902933			0.031659662	0.043409405	0.031329323	0.112746743	0.11137957	-0.01070172		
LAMP2   P13473	1.56557236	1.19246677	0.91486005	0.625501617	0.90278272	0.253028703	0.9995541	0.232122975			0.029696066	-0.05337377	0.027490034	-0.083054283	-0.002206872	0.080847132		
FAM69C   Q0P602	18.6324854	0.1302669	0.00011084	0.997732527	6.52E-08	0.000170777	0.53230365	1.03E-07			0.224519995	0.009222320	0.20956622	0.215297692	0.064663627	0.28173432		
WSCD1   Q6S8N2	3.25227561	0.022974761	0.0360387	0.996437636	0.91493435	0.0482385	0.116051472	0.971822331			-0.133743054	-0.010116782	-0.029825698	0.13262673	0.103913486	-0.019721786		
HRNR   Q80K73	0.95891477	0.450991325	0.995328069	0.446279587	0.61780057	0.939546373	0.61780057	0.939546373			-0.114986429	-0.685341703	-0.03277073	-0.570843056	-0.278272086	-0.01958864		
DYML1   Q96F12	13.7779908	3.78E-08	0.055979165	0.013225982	0.034389135	4.19E-07	1.55E-06	0.974689104			0.081061318	-0.094877017	-0.082657652	-0.175938353	-0.16371897	0.012123965		
F3GALB   Q9Y274	0.92964605	0.427535644	0.671206475	0.960217923	0.994891919	0.360553404	0.740858783	0.709145369			-0.070915288	0.026766618	-0.036945342	0.101102774	0.061280936	-0.08921838		
CTD17   Q57636	1.76317608	0.156104824	0.386961024	0.957488078	0.710718567	0.178584917	0.932481134	0.420364649			-0.015221743	0.032174321	0.052390126	0.125217436	0.13715688	-0.0717688		
KAP12   Q02952	2.16379069	0.095620113	0.99925772	0.908307059	0.327021586	0.855124278	0.041035668	0.077373534			-0.015571189	0.08120699	-0.196784326	0.096778179	-0.181211317	-0.277991316		
MOXD1   Q9U6V6	1.52815249	0.001991174	0.570568302	0.065678045	0.595171357	0.055101917	0.055520037	0.551457193			-0.065577634	0.122559894	0.188137528	0.125406717	-0.276370577	-0.067370577		
CFHR3   Q02985	0.38552402	0.763556144	0.852432244	0.739356437	0.940249497	0.997601379	0.993068778	0.996360364			0.11552843	0.142254033	0.078145923	0.026723793	0.037382507	-0.06410648		
S10A9   P06702	0.00286074	0.993592476	0.999766132	0.999750448	0.99760194	0.99807351	0.992618638	0.996397062			0.023809326	-0.023644502	-0.047453829	-0.047453829	-0.073262589	-0.06280876		
PIR1283	1.86698789	0.18853396	0.113775712	0.715545627	0.416487264	0.579992049	0.795721049	0.716616167			-0.444749976	-0.193919351	-0.270953001	0.250830624	0.173766975	-0.07703365		
CDT17   Q80K73	8.32862075	3.108E-05	0.127611711	0.63507059	0.041062057	0.030838863	0.985763972	0.745E-05			-0.36634999	0.267665399	0.421786641	0.054003352	-0.055448036	-0.08921838		
OSY572	2.14632035	0.095920524	0.432860029	0.567428606	0.02985822	0.994158546	0.61675317	0.61675317			-0.009363411	-0.00773701	-0.01054997	0.027123701	0.07241748	-0.03778685		
TINAGL1   Q9GZM7	1.20354254	0.10108064	0.531133954	0.996924973	0.442415509	0.645554199	0.999852806	0.558013615			-0.080419873	-0.011864601	-0.084678638	0.06555272	-0.004258765	-0.072814036		
B3GAT3   Q94766	1.35812489	0.163433396	0.160935976	0.542703	0.25410371	0.853244907	0.986020953	0.96086429			-0.065514915	-0.04072258	-0.024791629	0.024791615	0.010374766	-0.04146849		
THB53   P49746	0.9781196	0.404580704	0.715243237	0.976299516	0.396625882	0.912331543	0.96098865	0.04560474			-0.077728959	-0.030274654	-0.111952205	0.047454305	-0.034222466	-0.08167551		
CRMB1   P24387	2.7329371	0.045306323	0.64920205	0.45249636	0.897271463	0.63476215	0.11073322	-0.088225774			0.10686279	-0.05905693	0.196904884	0.038320082	0.038320082	-0.0586402		
JAM1   Q80K67	1.29134586	0.27876908	0.914482701	0.580383038	0.986220557	0.222627229	0.740388657	0.761368032			-0.026068173	0.049521262	0.012976167	0.075589435	0.03900434	-0.036545095		
IRAP3   P50842	0.1508842	0.528496039	0.999876767	0.969742657	0.969742657	0.969742657	0.969742657	0.969742657			-0.063498189	0.037076925	0.037076925	0.037076925	0.037076925	-0.037076925		
SA2   P01310	2.18143479	0.01791562	0.617389917	0.12377174	0.97895617	0.93486528	0.898781398	0.124077535			-0.17597818	0.052319016	0.049218517	0.049218517	0.049218517	-0.049218517		
ULBP2   Q9ZM75	16.2245342	2.10E-09	3.84E-05	0.367807442	1.75E-08	0.011543956	0.539175715	6.41E-05			0.375070249	0.127657358	0.479214746	-0.474712892	0.104144696	0.35557388		
C14orf13   Q9B7Y3	1.95121488	0.004793836	0.230131547	0.10166316	0.002102515	0.98643698	0.380015621	0.996251806			-0.084959042	0.105191065	0.012381378	0.012381378	0.012381378	-0.012381378		
ADAM17   P78536	4.07846682	0.007807298	0.021892799	0.992728886	0.12967517	0.040953831	0.83300099	0.214004488			-0.127528547	-0.01177677	-0.091718657	0.11575087	0.03580899	-0.07994957		
SNAI2   P04899	0.42932477	0.73268278	0.72259433	0.85836321	0.812610654	0.994102064	0.99704294	0.99909041			-0.081893495	-0.066185844	0.020007651	0.020007651	0.020007651	-0.020007651		
SDCBP   O00560	0.04666524	0.986591432	0.988636574	0.993651513	0.98809593	0.99895848	0.99999008	0.999936126			0.033612463	0.026770732	0.032243305	-0.006841731	-0.001378157	-0.005465374		
ITGB1   Q15848	1.17980946	0.318765725	0.986714937	0.990200809	0.660336033	0.464240492	0.999950219	0.488555103			0.127784117	-0.033148892	0.122211338	-0.16939301	-0.005577297	0.155360374		
WNT1   P54417	2.38943603	0.070264244	0.263653595	0.808877905	0.06430834	0.764135439	0.942816211	0.377157662			0.092368544	0.043876666	0.119762093	-0.048491878	0.0			

Gene ID   Uniprot ID	F-Value	Pr[F]	ANOVA p-values with Tukey Adjustment										Difference (AD - CT)									
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs CT-AA
ISTN   P60881	4.14224603	0.0077141	0.040725571	0.06162664	0.00777964	0.993599739	0.967236884	0.874736987	-0.279645614	-0.252803094	-0.326755527	0.02684522	-0.047109913	-0.073952433								
BPGM   P07738	0.70322942	0.551704536	0.712739289	0.984307178	0.596041993	0.881924548	0.999793688	0.806071573	-0.25080299	-0.079019766	-0.269726471	0.171783224	-0.018923484	-0.190760704								
CLINTF5   Q9H0X0	1.388251	0.247800144	0.433962991	0.991089686	0.35627512	0.622398476	0.999733407	0.521964389	-0.085347587	-0.016565673	-0.090384092	0.068781914	-0.005036055	-0.073814915								
FCBR1   P12318	5.23947026	0.00711571	0.007568948	0.967671012	0.05333668	0.017607149	0.836688373	0.109426236	-0.29511662	-0.029124302	-0.218773	0.246017359	-0.073264361	-0.193753998								
PDI   P52209	5.62343104	0.001060367	0.043989312	0.271034711	0.000532049	0.805727259	0.621050913	0.12879062	-0.197643577	-0.284931897	-0.06605764	0.06065764	-0.07288321	-0.153354596								
REL1   Q96924	4.87389493	0.002891658	0.336285945	0.066889171	0.001437346	0.880839492	0.216005001	0.615720172	0.070739596	0.01385052	0.149175494	0.030645546	0.078435898	0.047790442								
CAPG   P40121	9.75524081	5.24E-06	0.593815809	0.916288505	0.000921337	0.226209129	0.482E-06	0.007563351	0.083193185	-0.041825695	-0.23056301	0.125018881	-0.032644986	-0.201236065								
INPEP   Q9UIQ6	1.4703547	0.224086673	0.916633875	0.75820158	0.175065242	0.988977425	0.533027217	0.716737009	-0.036120582	-0.053537791	-0.108647461	-0.017417209	-0.072526879	-0.055215841								
MDK1   P21744	0.1941508	0.900528699	0.95915739	0.98342621	0.996142593	0.000347152	0.91522183	0.980422357	-0.016366642	-0.013990533	0.008319075	0.002376109	-0.024685717	-0.02309608								
ADIR1   U15847	2.69742405	0.048295698	0.87664458	0.245228986	0.050555626	0.655156682	0.234667036	0.887351578	-0.059798876	-0.149534538	-0.204641398	-0.089555662	-0.144842522	-0.05528686								
MDK1   P21744	9.01031368	1.34E-05	0.25018837	0.032718477	0.440154666	4.49E-05	0.960768897	0.000118132	0.085774961	-0.13807894	0.07274347	-0.233852855	-0.02303149	-0.21082355								
PLD2   Q9U9P5	4.9304282	7.88E-06	0.99407321	0.007095157	0.004982706	0.000347152	0.002314392	0.924507014	0.010837708	-0.180175291	-0.135551271	-0.170112999	-0.146388979	-0.02464202								
SLR2A2   Q9U9P5	0.97702268	0.405074802	0.940758331	0.847788209	0.894892222	0.996367667	0.573858626	0.398225621	0.047837674	0.056373281	-0.05453344	0.017889607	-0.103237018	-0.112126625								
HHP   Q9H008	2.67982819	0.048322251	0.941038198	0.043139032	0.413556621	0.177366806	0.787150661	0.635068068	-0.023648126	-0.107037846	-0.060936791	-0.083389721	-0.037288665	-0.046101055								
SCRN1   Q12765	13.0461802	1.01E-07	0.995786023	0.00132764	2.94E-05	0.000559819	1.02E-05	0.834799093	0.01381501	-0.21133838	-0.25835417	-0.226319838	-0.27153568	-0.045215841								
CTRH2   Q9H251	2.55149037	0.057203552	0.96296504	0.629651021	0.500240505	0.900041811	0.239178328	0.041058057	-0.038689343	-0.089893133	0.102994102	-0.05206679	-0.138963445	-0.191030236								
FMN193   Q725A7	1.1042609	0.348714051	0.321502166	0.625675909	0.500924411	0.947088177	0.977226495	0.998583564	0.066373412	0.04541565	0.051182406	-0.020918448	-0.015191006	-0.005470484								
PGC1M1   Q00264	0.92150925	0.431551898	0.886932287	0.897175442	0.899528322	0.48454762	0.477154466	0.999996382	-0.018575645	0.017398541	0.016883304	0.035914186	0.035417979	-0.000510207								
PXD1   Q9Z626	1.1827624	0.318064529	0.987974591	0.892250522	0.02473937	0.91134018	0.496591741	0.668334363	-0.014442196	-0.027163782	-0.071464605	-0.012721586	-0.005970420	-0.004982623								
DLK2   Q9U171	6.41576761	0.000370922	0.077995714	0.052254542	0.000118484	0.999706246	0.270501712	0.291637004	0.123317003	0.128020042	0.21245792	0.00470309	0.089140919	0.08443788								
PMPL1   Q5SGD2	0.44759608	0.719336222	0.995364622	0.999613901	0.735718698	0.999039146	0.876633721	0.78840205	0.017746707	0.040710713	0.212737604	-0.010335993	0.054309088	0.064726891								
SYT1   P21579	4.83197148	0.002961176	0.168031532	0.773004006	0.48862101	0.104021257	0.002734722	0.970314389	0.091446009	0.041279214	-0.059721396	-0.132725223	-0.151167405	-0.018442182								
PLG1   Q3641	4.01529273	0.008554178	0.93082146	0.11311484	0.01452895	0.336690639	0.071933192	0.980461243	0.036569532	0.141450121	0.18623647	0.104808089	-0.156669616	-0.03166825								
GHV3-1   QAO0B4I1V9	4.1111083	0.007480913	0.069497425	0.99995742	0.05666222	0.066828145	0.999599584	0.062583922	-0.32082837	-0.002888039	-0.307821165	0.317940332	0.013007206	-0.304931678								
FMN1   Q95490	3.94477251	0.020827566	0.561623979	0.01513866	0.11494708	0.34031366	0.82221373	0.15038791	0.078311713	0.178698298	0.12856711	0.105085195	0.050255404	-0.05329791								
THSD4   Q6ZMP0	1.99277825	0.116598653	0.948140404	0.892250522	0.007716053	0.96805619	0.440589304	0.163477526	-0.031027803	-0.002406744	-0.113335521	0.028621059	-0.082305719	-0.119296776								
PI01721	10.752921	1.51E-06	0.002828934	0.772606439	0.009922875	5.87E-05	0.97846807	0.000117625	-0.443587067	-0.11698643	-0.395489744	0.560573498	0.048097323	-0.512476175								
SPINK5   Q9N38	0.06590646	0.977887936	0.998892657	0.995792693	0.96129173	0.982158731	0.982667448	0.999991961	0.011713123	-0.017853587	-0.06989808	-0.02956671	-0.000953779	-0.000953779								
ANGPT14   Q9B7Y6	4.2105423	0.006574005	0.873545278	0.518281158	0.00660696	0.142484157	0.007180222	0.681183188	0.04781139	-0.084611286	-0.150437242	-0.13242676	-0.19824863	-0.06825957								
PI01619	4.9747563	0.005379555	0.02978591	0.999825982	0.038665674	0.032713215	0.995254623	0.04449512	-0.417395554	-0.101442375	-0.381112	0.05953179	0.04284354	-0.37166825								
PI00748	0.91005777	0.43725795	0.981988828	0.99842383	0.556717815	0.949470827	0.801707633	0.439107296	-0.045431283	0.018845393	-0.15109853	0.064276677	-0.10566747	-0.169943924								
NA   P00558	5.9911628	0.00084639	0.005173997	0.133520783	0.00071304	0.58396613	0.981743952	0.131710639	-0.15664163	0.098429284	0.173573707	0.028631338	0.03391744	-0.070108415								
NA1616   Q9N428	1.4898995	0.22731898	0.712183263	0.892250522	0.007716053	0.96805619	0.440589304	0.163477526	-0.047884373	0.031650548	-0.034652139	0.097549321	0.082346924	-0.002812003								
CTSO   P43234	1.092475	0.353624411	0.959774053	0.506263123	0.995235463	0.81993203	0.876111623	0.331168968	-0.02160692	-0.058918599	0.00949112	-0.037311679	0.031456032	0.068677111								
MT1   P25713	1.8924491	0.33371771	0.980182107	0.123003583	0.887472607	0.278906146	0.98889765	0.39537717	0.023034377	0.128117259	0.040624621	0.105082882	0.017590244	-0.00492638								
MESDC2   Q14696	0.34441703	0.79320472	0.911472711	0.98922453	0.993786076	0.75986038	0.97346555	0.934106308	-0.030775127	0.014229642	-0.011557093	0.045040769	0.019218034	-0.025786735								
CTRH2   Q9H251	6.32786203	0.00045663	0.0263318	0.541545393	0.998187084	0.000198507	0.026639798	0.40660605	-0.112295447	0.050606388	0.006372614	0.162091835	0.105922834	-0.05979002								
PVR   P15151	12.871945	1.12E-07	2.18E-06	0.10261025	0.236E-06	0.042176997	0.984478398	0.029250566	0.248691358	0.10576337	0.023536884	-0.142927821	-0.016514474	-0.126773347								
FCBLD1   Q9H0D2	5.44775523	0.00134321	0.407800451	0.983410116	0.08140909	0.213952178	0.90058178	0.16998859	-0.06263106	-0.012862984	0.028631338	0.009713151	0.13936154	-0.06646415								
FMN1   Q95490	1.14334738	0.33922224	0.360219941	0.998028654	0.77390362	0.44641791	0.87373686	0.859177048	-0.109124394	-0.011654591	-0.034652139	0.097549321	0.082346924	-0.002812003								
FMN1   Q95490	6.778331	0.000232008	0.053699506	0.042271519	7.27E-05	0.99996797	0.29004137	0.274902182	0.134473009	0.135542193	0.22300558	0.01069185	0.08942755	0.088358365								
RAB14   P61106	0.2379423	0.86980895	0.999523528	0.987469342	0.865236032	0.965614284	0.166996911	0.377175203	-0.003725402	-0.019048605	-0.024793572	-0.00723203	-0.021068169	-0.01384667								
SLRX   P35754	0.40845821	0.007745089	0.999495172	0.127561343	0.04654484	0.105020507	0.037177356	0.981654151	0.004083607	-0.077509599	-0.09077551	-0.082034562	-0.094881114	-0.012846556								
GBPL1   Q9BXX7	3.07011937	0.029124327	0.494203694	0.615079769	0.015921102	0.95893898	0.439079038	0.283516721	-0.099710001	-0.08383022	-0.101795805	-0.15826979	-0.102085804	-0.117912783		</						



Gene ID   Uniprot ID	F-Value	Pr(>F)	ANOVA p-values with Tukey Adjustment								Difference (AD - CT)								
			AD-Cau vs AD-AA	CT-AA vs AD-AA	AD-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau
SPR56   Q9Y653	3.68472922	0.013064887	0.700469855	0.158963975	0.747138352	0.009615251	0.151538834	0.653573326	0.065625408	-0.123468461	-0.057851767	-0.189093868	-0.123471735	0.065616693					
LRP2   P98164	0.97346385	0.407547275	0.802719747	0.885011106	0.33143104	0.997308505	0.868008983	0.075019866	0.083566099	0.06597424	0.152075786	-0.10759186	0.068511487	0.086013446					
SELM   Q8WVX9	1.50420833	0.214939892	0.873651137	0.898921802	0.169619221	0.999813957	0.595902173	0.518405779	0.035121556	0.031453866	0.09095063	-0.00366769	0.055829073	0.059496764					
ESTO1   P78417	2.34181315	0.074664528	0.152341485	0.510861371	0.072344654	0.863656542	0.996339705	0.7226235	-0.15065918	-0.09565781	-0.155603674	0.054700136	-0.149137144	-0.069673788					
SLC5A5   Q92911	0.65769471	0.567188849	0.983282057	0.881050549	0.936650921	0.984027451	0.774013595	0.523138779	-0.036258863	-0.071402844	0.055145059	-0.095143982	0.091399372	0.125643353					
FAM19A2   Q8NH30	7.86446355	5.75E-05	0.000207159	0.064092013	0.00026431	0.258459346	0.992464028	0.35254896	0.375413236	0.215005365	0.351698448	-0.160407872	-0.023714788	0.136693084					
HTSH1E   P10412	0.15105903	0.9386873	0.947832773	0.957461927	0.9990979	0.999320082	0.999923562	0.10525879	0.094138271	0.084340433	-0.01117608	-0.020915446	-0.009797839						
LAMP5   Q9JUG1	6.60546301	0.00290081	0.519985805	0.977362961	0.000578409	0.755274525	0.06266006	0.002211552	-0.070058806	-0.020194771	-0.193300289	0.049864035	-0.123244183	-0.171055518					
FCGR3A   P08637	4.00234313	0.008614705	0.19510083	0.153904417	0.009082829	0.999912174	0.542561319	0.50801943	-0.118432332	-0.122091272	-0.134799792	-0.003659388	-0.073655889	-0.07206201					
CIGAL1   Q9NSU0	3.4364128	0.010609815	0.940426285	0.072396021	0.882114817	0.01627432	0.550308764	0.27840326	-0.026178487	0.108939853	0.032077042	0.135118341	0.058255529	0.076862812					
NME2   P22392	32.406212	6.99E-17	0.99999999	0.54402E-08	4.19E-12	6.30E-08	7.15E-12	0.41120758	0.000134561	-0.26590602	-0.331099788	-0.266049023	-0.33124435	-0.065193722					
FAM171A1   Q5VUB5	1.04104077	0.375659315	0.99923682	0.980693753	0.95068583	0.95602354	0.6896237	0.341865219	0.004936042	-0.01433484	0.02169525	0.040637583	0.05907208						
PSMA4   P25789	12.182303	3.14E-07	0.99973818	0.000247578	0.000216242	0.000168459	0.000145506	0.999999232	0.002985734	-0.29937553	-0.298489807	-0.302363267	-0.301475541	0.000087726					
NRG3   P56975	1.36497531	0.255135186	0.720916287	0.289377813	0.03450808	0.889961486	0.90760671	0.999915931	0.084044986	0.140574582	0.135879214	0.056529596	0.051834227	-0.00469368					
DLFML2B   Q8BBL8	18.9968162	3.19E-11	5.00E-08	0.885765041	8.23E-07	1.13E-06	0.824301014	1.79E-05	-0.301113597	-0.035324564	-0.259735363	0.265789033	0.041378234	-0.224410799					
LRTM2   Q8N967	9.53107801	6.94E-06	0.025547965	0.000166012	9.30E-06	0.52820533	0.21105363	0.938309809	0.19857688	0.291943837	0.329751517	0.093366149	0.031173469	0.03870732					
PFM3   P06753	9.26780516	1.16E-05	0.045896071	0.000168327	2.22E-05	0.371187787	0.12790575	0.97562034	-0.179360233	-0.288301305	-0.315245313	-0.108941052	-0.13589426	-0.026953208					
RTT3   P61304	11.4346043	7.06E-07	0.557420025	9.95E-05	9.76E-06	0.14866195	0.002647857	0.957051326	-0.06352574	-0.207200545	-0.2308084	-0.143677971	-0.166058927	-0.023897856					
EMMAA   Q9H551	0.33236011	0.80195746	0.831091789	0.946061619	0.97907227	0.99148896	0.881428948	0.987611654	-0.076976555	-0.025152428	-0.04963644	0.024824227	0.062013191	0.037188964					
BGN3T8   Q277M8	4.4136586	0.005035729	0.244608577	0.907522807	0.04683398	0.053890844	0.977065194	0.01151937	-0.118815	0.041551234	-0.143740182	0.160366234	-0.024926082	-0.185292316					
PLAGT7   Q13093	0.53621495	0.65807347	0.970957482	0.99991497	0.68683021	0.97564937	0.924074628	0.709453444	-0.029773455	-0.003990023	0.037017295	0.025783416	-0.04053484	-0.006372526					
GLA3S1   P17391	3.75187303	0.01196719	0.297315201	0.580168062	0.603732404	0.01408773	0.930802482	0.905605898	-0.078061611	0.05059226	-0.05225885	0.133158731	0.025805576	-0.107348115					
PSMA5   P28066	1.5076646	0.02836842	0.99989634	0.434375207	0.057491284	0.45634937	0.063119448	0.738749439	-0.003823261	-0.175456149	-0.256015246	-0.153632889	-0.252228003	-0.098595115					
MB   P02144	3.31096237	0.021282704	0.38989658	0.996889483	0.07644145	0.270386012	0.878939629	0.039863845	-0.301369392	0.038153363	-0.43785434	0.339527525	-0.136489448	-0.476007703					
HTSH1D   P53758	0.00296832	0.4817604	0.94390567	0.541386789	0.548903497	0.903612014	0.912057104	0.99977704	-0.03251284	-0.16969519	0.133272778	0.137446731	0.100749017	0.03674194					
HTSH1D   P16402	0.35784622	0.47126017	0.931487218	0.943018995	0.940480717	0.884080677	0.999991836	0.951695889	-0.04119983	0.083713487	-0.045359565	0.124931317	-0.024977296	0.129097051					
MERTK   Q12866	8.13319633	4.08E-05	0.000184967	0.282734215	0.00045323	0.053473787	0.968520775	0.117567603	0.171866913	0.070602149	0.154211767	-0.101804765	-0.17655147	0.084140618					
HPD1   P10809	1.23991493	0.081836416	0.0724607	0.400590622	0.16624484	0.821665369	0.986766769	0.984651941	-0.373136677	-0.243747021	0.239896632	0.050255945	-0.07137111						
GHV1-18   A0A0C4DH31	2.50572133	0.062707245	0.21164072	0.89465563	0.983586755	0.042608353	0.370390737	0.701930976	-0.15842969	0.054713571	-0.028364078	0.213143262	0.130065612	-0.08307765					
NLG3N1   Q9N294	1.65252697	0.1773244	0.199920118	0.986551581	0.996229977	0.343377141	0.266561365	0.999269532	-0.1070003	-0.018568367	-0.11839261	0.092311663	0.098860769	0.00672106					
NSG1   P42857	0.52211511	0.667590176	0.931286765	0.999519203	0.926171072	0.958373866	0.604679414	0.879243255	-0.024441543	-0.004353775	0.0238528	0.020087767	0.048294343	0.028206576					
FWY1   P04216	2.56345772	2.36E-05	0.849802566	0.000132236	0.001369923	0.803357375	0.04849125	0.951681769	-0.032527885	-0.16996519	0.133272778	0.137446731	0.100749017	0.03674194					
E100AT   Q11511	0.8446623	0.47126017	0.974142514	0.976861384	0.99961017	0.850480677	0.965238679	0.931621011	-0.234352211	-0.08362345	-0.024977296	0.137446731	0.100749017	0.03674194					
LN2   P80188	0.09709535	0.961542965	0.975607885	0.999709339	0.999580077	0.956580886	0.986453281	0.997332006	0.042001626	-0.009160937	0.009386467	-0.051162563	-0.03263316	0.018524033					
CD74   P04233	2.58572323	0.054569432	0.803126682	0.404188094	0.597159303	0.969521156	0.135186362	0.984651287	-0.03746855	0.062959699	0.04921561	0.100428249	0.08667906	-0.03749189					
ARGHDG   P52566	1.93671451	0.125262057	0.909844338	0.999997985	0.18410767	0.899416681	0.551570822	0.160061973	-0.038830881	0.001007198	-0.112951229	0.039883079	-0.074084349	-0.113922428					
PIR1284	0.7582843	7.99E-10	4.01E-07	0.515190779	3.75E-07	0.000129508	0.992236367	0.000162223	-0.737862046	-0.175739855	-0.702399042	0.562122191	0.035463004	-0.512665187					
EPB4121   Q43491	2.11137378	0.02674316	0.96544808	0.994861303	0.126226678	0.995700274	0.340875015	0.232026799	-0.043693662	-0.022295554	-0.193329892	0.021398108	-0.14963623	-0.171034383					
ICP2   P11117	0.36889418	0.775320197	0.803097061	0.999997985	0.999997985	0.999997985	0.999997985	0.999997985	-0.032769868	-0.099973673	0.099973673	0.099973673	0.099973673	0.099973673					
ICP2   P11117	0.36889418	0.775320197	0.803097061	0.999997985	0.999997985	0.999997985	0.999997985	0.999997985	-0.032769868	-0.099973673	0.099973673	0.099973673	0.099973673	0.099973673					
ICP2   P11117	0.36889418	0.775320197	0.803097061	0.999997985	0.999997985	0.999997985	0.999997985	0.999997985	-0.032769868	-0.099973673	0.099973673	0.099973673	0.099973673	0.099973673					
ICP2   P11117	0.36889418	0.775320197	0.803097061	0.999997985	0.999997985	0.999997985	0.999997985	0.999997985	-0.032769868	-0.099973673	0.099973673	0.099973673	0.099973673	0.099973673					
ICP2   P11117	0.36889418	0.775320197	0.803097061	0.999997985	0.999997985	0.999997985	0.999997985	0.999997985	-0.032769868	-0.099973673	0.099973673	0.099973673	0.099973673	0.099973673					
ICP2   P11117	0.36889418	0.775320197	0.803097061	0.999997985	0.999997985	0.999997985	0.999997985	0.999997985	-0.032769868	-0.099973673	0.099973673	0.099973673	0.099973673	0.099973673					
ICP2   P11117	0.36889418	0.775320197	0.803097061	0.999997985	0.999997985	0.999997985	0.999997985	0.999997985	-0.032769868	-0.099973673	0.099973673	0.099973673	0.099973673	0.099973673					
ICP2   P11117	0.36889418	0.775320197	0.803097061	0.999997985	0.999997985	0.999997985	0.999997985	0.999997985	-0.032769868	-0.099973673	0.099973673	0.099973673	0.099973673	0.099973673					
ICP2   P11117	0.36889418	0.775																	

Gene ID   Uniprot ID	F-Value	Pr(F)	ANOVA p-values with Tukey Adjustment										Difference (AD - CT)									
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs CT-AA
JNCSD1 Q6UJX2	4.46261564	0.20472354	0.028640884	0.123668883	0.003785918	0.912735019	0.957531919	0.618463096	0.170882118	0.131365394	0.20061129	-0.039516724	0.029729172	0.060254896	0.029729172	0.060254896	0.029729172	0.060254896	0.029729172	0.060254896	0.029729172	0.060254896
HDSD1 Q9H0R4	10.3784168	2.404626	0.261564282	0.012302087	0.061725986	1.166E-05	0.00014994	0.910632584	0.086405649	-0.141727441	-0.112490574	-0.22813309	-0.198896237	-0.029236867	-0.029236867	-0.029236867	-0.029236867	-0.198896237	-0.198896237	-0.198896237	-0.198896237	-0.198896237
HEBP2 Q9Y524	7.9459574	5.42E-05	0.038095956	0.3723439	0.17289876	0.000142549	0.866913598	0.00127682	0.156558124	0.091068103	0.113371314	-0.247626227	-0.04320929	-0.04320929	-0.04320929	-0.04320929	-0.04320929	-0.04320929	-0.04320929	-0.04320929	-0.04320929	-0.04320929
NTSE1 P21589	1.65555834	0.18132974	0.225097882	0.9996696	0.99071775	0.25820105	0.28708991	0.99730661	0.20618724	-0.010215048	-0.029311884	0.196303675	0.17727319	-0.01902636	-0.01902636	-0.01902636	-0.01902636	0.196303675	0.196303675	0.196303675	0.196303675	0.196303675
ELC12 P43004	3.38766153	0.01925674	0.10068304	0.957502378	0.992847181	0.02547604	0.04125332	0.99544806	0.112678714	-0.02408711	-0.012699811	-0.136765824	-0.125378525	-0.013872929	-0.013872929	-0.013872929	-0.013872929	-0.136765824	-0.136765824	-0.136765824	-0.136765824	-0.136765824
S10A08 P05109	0.02690248	0.94025736	0.99754881	0.997917148	0.99250193	0.999998724	0.999838798	0.999693079	0.045577878	0.041984447	0.063215607	-0.00359343	0.017637729	0.02123116	0.02123116	0.02123116	0.02123116	0.045577878	0.045577878	0.045577878	0.045577878	0.045577878
SEMA6C Q9H372	4.23542082	0.006358094	0.87354727	0.999760848	0.01766638	0.872872331	0.14263675	0.011487821	0.038753818	-0.004347736	-0.004347736	-0.004347736	-0.004347736	-0.004347736	-0.004347736	-0.004347736	-0.004347736	-0.004347736	-0.004347736	-0.004347736	-0.004347736	-0.004347736
PLXND1 Q9Y407	1.20810116	0.308394015	0.676606231	0.888319132	0.973821485	0.252357905	0.88003556	0.637351084	-0.049167179	0.030719967	-0.017804908	0.979887471	0.033162271	-0.048524876	-0.048524876	-0.048524876	-0.048524876	-0.049167179	-0.049167179	-0.049167179	-0.049167179	-0.049167179
AO3 Q16853	0.03209265	0.992904478	0.9998603	0.980393934	0.999538631	0.998643444	0.999867453	0.999316551	0.003719952	-0.01875982	-0.01875982	-0.022515772	0.007665921	0.007665921	0.007665921	0.007665921	0.007665921	-0.01875982	-0.01875982	-0.01875982	-0.01875982	-0.01875982
GPC5 P78533	2.5323126	0.07588335	0.250777189	0.662671403	0.060179806	0.875635104	0.951267919	0.53265558	-0.13475401	-0.08048947	-0.17202312	0.054264963	-0.037258302	-0.037258302	-0.037258302	-0.037258302	-0.037258302	-0.08048947	-0.08048947	-0.08048947	-0.08048947	-0.08048947
TRTA1 Q1QYR7	1.42510566	0.236880825	0.9181038	0.997791884	0.531347181	0.838388199	0.19093875	0.637878942	-0.00076577	0.008563959	0.061561567	0.03933173	0.092327337	-0.05995607	-0.05995607	-0.05995607	-0.05995607	0.008563959	0.008563959	0.008563959	0.008563959	0.008563959
TBCA1 Q75347	13.7206064	6.95E-08	0.792811038	2.43E-05	0.001317176	0.000463095	0.99725104	-0.03938337	-0.17070666	-0.17070666	-0.17070666	-0.17070666	-0.17070666	-0.17070666	-0.17070666	-0.17070666	-0.17070666	-0.17070666	-0.17070666	-0.17070666	-0.17070666	-0.17070666
SNAP25 P06880	2.57461408	0.051821129	0.99909309	0.075976956	0.58659214	0.09914727	0.66854484	0.56091273	-0.010197496	-0.18530802	-0.090794484	-0.17510586	-0.080596988	0.094513598	0.094513598	0.094513598	0.094513598	-0.18530802	-0.18530802	-0.18530802	-0.18530802	-0.18530802
TMED4 Q7Z7H5	2.15931997	0.094341133	0.328353962	0.899154755	0.997460242	0.078830468	0.209767638	0.952416886	0.063991037	-0.02548092	-0.060903934	-0.089471529	-0.070894971	0.018756558	0.018756558	0.018756558	0.018756558	-0.02548092	-0.02548092	-0.02548092	-0.02548092	-0.02548092
ELC012 P05997	1.84218799	0.142823139	0.955585808	0.716405073	0.094695344	0.996153404	0.733709486	0.574696654	0.070946277	0.058655073	0.126600608	-0.012291024	0.055653809	0.067945012	0.067945012	0.067945012	0.067945012	0.058655073	0.058655073	0.058655073	0.058655073	0.058655073
LC010 Q5UCU4	7.70714103	7.03E-05	0.00703244	0.071836478	0.31495305	0.804543297	0.60568487	0.121434988	0.155093293	0.11301907	0.211474872	-0.042074223	0.056381579	0.099455802	0.099455802	0.099455802	0.099455802	0.155093293	0.155093293	0.155093293	0.155093293	0.155093293
SLC12A1 Q9H209	2.107275	0.05631641	0.626064484	0.236314526	0.08782143	0.92420568	0.70477698	0.967974351	0.069672346	0.105070581	0.129571015	0.035398255	0.059896601	0.042500434	0.042500434	0.042500434	0.042500434	0.105070581	0.105070581	0.105070581	0.105070581	0.105070581
FEA15 Q15121	5.46510504	2.42E-25	0.753323773	1.32E-13	2.09E-13	1.23E-13	1.23E-13	0.923618454	0.039503994	-0.33971316	-0.161448539	-0.379217155	-0.355952533	0.023264622	0.023264622	0.023264622	0.023264622	-0.33971316	-0.33971316	-0.33971316	-0.33971316	-0.33971316
FRP1 Q8N474	1.52637608	0.00919838	0.982359598	0.064952495	0.007821166	0.124822414	0.028064975	0.92347788	-0.020784055	-0.142199104	-0.171672543	-0.12145049	-0.150888489	-0.029473439	-0.029473439	-0.029473439	-0.029473439	-0.020784055	-0.020784055	-0.020784055	-0.020784055	-0.020784055
ADM1 P35318	1.73799346	0.07452623	0.360015034	0.464971068	0.127367093	0.99610193	0.96557855	0.889652209	0.060347997	0.052276039	0.077005499	-0.008071958	0.016662553	0.02473451	0.02473451	0.02473451	0.02473451	0.060347997	0.060347997	0.060347997	0.060347997	0.060347997
BDNF P23560	1.52741297	1.61E-07	0.088937839	1.72E-05	5.127E-07	0.085731302	0.014155029	0.923145974	0.173488138	0.345440758	0.078833094	0.17195262	0.21544566	0.043492336	0.043492336	0.043492336	0.043492336	0.088937839	0.088937839	0.088937839	0.088937839	0.088937839
HLA-DRA P01093	2.77643365	0.04264632	0.097540596	0.987250005	0.180934538	0.182271716	0.977557131	0.31722922	0.196028459	0.027382246	0.163108709	-0.168646213	-0.032919751	0.135726462	0.135726462	0.135726462	0.135726462	0.097540596	0.097540596	0.097540596	0.097540596	0.097540596
SPG6 Q99Y86	0.02960986	0.92060119	0.632749565	0.999263687	0.999595779	0.954048653	0.636027352	0.99782851	-0.07162859	0.007431805	0.007431805	0.007431805	0.007431805	0.007431805	0.007431805	0.007431805	0.007431805	-0.07162859	-0.07162859	-0.07162859	-0.07162859	-0.07162859
PTXK1 Q92844	0.6134284	0.60767597	0.99762228	0.904741302	0.750806444	0.830967598	0.651596851	0.990830911	-0.014382757	0.05030495	0.071912788	0.06489077	0.086300309	0.021405299	0.021405299	0.021405299	0.021405299	-0.014382757	-0.014382757	-0.014382757	-0.014382757	-0.014382757
NUTS1 Q10XJ9	0.81300651	0.488112209	0.666837583	0.515023528	0.56682743	0.994986183	0.9996461	0.99943421	-0.07707325	-0.05981873	0.083448676	0.037144965	0.006716111	0.007368854	0.007368854	0.007368854	0.007368854	-0.05981873	-0.05981873	-0.05981873	-0.05981873	-0.05981873
CSK5 Q15620	1.6468488	0.0206611	0.91312256	0.996845058	0.99717274	0.970691348	0.998155004	0.99122661	-0.024973567	-0.07880802	-0.018460355	0.017092745	-0.00513212	-0.010579534	-0.010579534	-0.010579534	-0.010579534	-0.024973567	-0.024973567	-0.024973567	-0.024973567	-0.024973567
GK4V1 P01632	8.58855131	2.28E-05	0.000807514	0.999997631	0.00873353	0.000687799	0.815530895	0.0778969	-0.52378078	-0.024455262	-0.409744065	0.521325254	0.114036715	0.047788099	0.047788099	0.047788099	0.047788099	-0.52378078	-0.52378078	-0.52378078	-0.52378078	-0.52378078
DMN1 Q6U0U4	5.36700501	0.001449181	0.006484369	0.986647985	0.005434052	0.015649423	0.823484089	0.106024068	0.25748181	0.025731642	-0.021750167	-0.065016423	0.166737744	0.005016423	0.005016423	0.005016423	0.005016423	0.006484369	0.006484369	0.006484369	0.006484369	0.006484369
WFCD1 Q9H557	1.95093935	0.12294411	0.291321122	0.999996383	0.970225668	0.268676262	0.109249176	0.974643444	-0.157894853	0.001874072	0.037087637	0.159768294	0.19498249	0.035213566	0.035213566	0.035213566	0.035213566	0.291321122	0.291321122	0.291321122	0.291321122	0.291321122
H6S72 Q9GMM7	1.12510203	0.30648042	0.65378477	0.393175137	0.00272861	0.980559941	0.963468812	0.999762682	0.099188935	0.132112148	0.138340611	0.032933013	0.09511676	0.008218663	0.008218663	0.008218663	0.008218663	0.65378477	0.65378477	0.65378477	0.65378477	0.65378477
FNH3 Q15768	4.1209853	0.00564662	0.00958446	0.429886152	0.022543234	0.315780811	0.970664712	0.578235152	-0.026631835	0.198913629	0.02504053	0.036646933	0.143446897	0.079506545	0.079506545	0.079506545	0.079506545	-0.026631835	-0.026631835	-0.026631835	-0.026631835	-0.026631835
GLV9-49 AD00841Y8	0.09591869	0.962112264	0.968311096	0.985250327	0.964734895	0.999419684	0.9999992	0.999418344	-0.110628218	-0.08254077	0.077477444	0.03016306	0.014702464	-0.22576903	-0.22576903	-0.22576903	-0.22576903	0.968311096	0.968311096	0.968311096	0.968311096	0.968311096
CSRP1 P12129	2.93657925	0.03464469	0.70410578	0.636918063	0.38134488	0.111015355	0.870664712	0.578235152	-0.026631835	0.198913629	0.02504053	0.036646933	0.143446897	0.079506545	0.079506545							



Gene ID   Uniprot ID	F-Value	Pr(>F)	ANOVA p-values with Tukey Adjustment										Difference (AD - CT)									
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-AA
KLK7   P49862	20.945422	9.99E-12	8.45E-08	0.973832396	4.70E-05	5.67E-09	0.36459212	4.55E-06					-0.541301947	0.07866326	-0.398291572	0.579168274	0.14301095	-0.436158078				
LAP3   P08625	0.5750665	0.632726257	0.68915364	0.83268255	0.98685687	0.99419191	0.767621862	0.894908965					0.097654215	0.07557807	0.034912967	0.022076408	0.083262948	-0.06128654				
SUGT1   Q92220	1.62754641	0.186305912	0.9712426	0.448172964	0.215264094	0.723017679	0.4452173	0.974421503					-0.0366738	-0.12089842	-0.153057246	-0.084211062	-0.116389866	-0.032158803				
PSMB1   P20618	6.18132459	0.000378879	0.901807232	0.00601193	0.05550237	0.00829752	0.27766039	0.401645882					-0.040018103	-0.223893004	-0.139805412	-0.183814901	-0.099787309	0.084087592				
ENOPH1   Q9UHY7	10.4302104	4.73E-06	0.714476233	0.041119595	0.00311193	0.001758517	2.17E-05	0.746741931					0.099925841	-0.248361349	-0.335904536	-0.348287189	-0.358303777	-0.087543188				
FABP4   P15090	3.73074827	0.012424558	0.877068161	0.175027074	0.80937931	0.033202509	0.999714103	0.01528352					-0.108196151	0.286823689	-0.121128828	0.39501984	-0.012932677	-0.407952517				
TNFRSF1A   P19438	1.49382828	0.217706593	0.34184954	0.923145406	0.27502454	0.70771235	0.99997972	0.64034604					0.07448877	0.02720936	0.07631422	-0.04777841	0.001852544	0.049132385				
SCPEP1   Q9H840	3.12905307	0.0021439	0.049131195	0.945579163	0.16765318	0.143924788	0.889474587	0.429500463					-0.244298669	-0.04987031	-0.180891308	0.194411636	0.06331761	-0.131094005				
DH1   Q43323	0.40363189	0.182299849	0.019165383	0.978563132	0.73846524	0.195964642	0.895703395	0.949738495					-0.162866145	0.040390471	-0.033435653	0.203266616	0.068530692	-0.134726124				
S100A1   P26447	1.88328621	0.134189142	0.430923508	0.9980361	0.354648006	0.334981299	0.999982415	0.022139386					-0.19007135	0.019061679	-0.194508087	0.209132029	-0.004429489	-0.215652158				
S   P01593	3.15932746	0.025931939	0.345097037	0.963700327	0.171913403	0.137146703	0.990633906	0.054009468					-0.17305007	0.048411762	-0.203070147	0.221461832	-0.02997078	-0.25141891				
PHL1   Q13642	1.68938084	0.17224298	0.99808051	0.690513946	0.05865113	0.59579806	0.22738566	0.90257167					0.020163129	-0.121413849	-0.195074607	-0.141576978	-0.215327375	-0.073660757				
CDH3   P22223	2.46173198	0.064026347	0.144293276	0.999280176	0.292035995	0.17399597	0.963943358	0.349316886					-0.16596441	-0.009518659	-0.130319701	0.156455752	0.035644709	-0.128001403				
NME1   P15531	12.4676758	3.74E-07	0.994089959	0.001197995	1.46E-05	0.003261749	4.26E-05	0.70309903					-0.022399438	-0.328914984	-0.16551949	-0.306515545	-0.394152511	-0.087689695				
VIT   Q6UJX7	7.12646419	0.000148101	0.019508095	0.999961393	0.002979192	0.019569714	0.97287255	0.028556469					-0.194938733	-0.003069596	-0.222651651	0.138691337	-0.027627422	-0.219465559				
RAB4A   P20338	0.40011165	0.766529589	0.795242355	0.78644121	0.92971398	0.999999343	0.984470008	0.984570886					-0.062647795	-0.061828737	-0.095353399	0.000819058	0.023294935	-0.02245338				
RYL2   Q9H185	2.28523399	0.08013599	0.08348647	0.269174484	0.158177487	0.922885128	0.976970535	0.995300443					-0.145305541	-0.107672013	-0.12174186	0.037678528	0.023913156	-0.013747172				
CA11   Q5493	3.11078976	0.027623057	0.963950686	0.082208847	0.083306238	0.240874579	0.248818562	0.999990974					0.031932721	0.15559272	0.151644251	0.123659999	0.11971153	-0.003944669				
3   P01593	3.82921696	0.010816269	0.96790445	0.12664471	0.008812696	0.824762083	0.234999663	0.97534627					0.09467005	0.156710671	0.02949099	0.062040621	0.13322044	0.071717982				
TAC1   P20366	5.99857635	0.000636997	0.999713478	0.183462552	0.003274521	0.159270872	0.00276249	0.468942606					-0.005616055	0.1193306	0.2013462	0.12480936	0.206962075	0.083252715				
MCFD2   Q9H122	1.0981128	0.353881809	0.316426294	0.973848638	0.95828121	0.54831157	0.584632103	0.999735115					-0.063113672	-0.01523751	-0.03373475	0.04787162	0.04477897	-0.003097225				
NHR3F1   Q5J537	1.78534864	0.150268638	0.77311296	0.545276322	0.967149410	0.11000584	0.471997662	0.75338636					-0.054626305	0.073847127	0.024893148	0.128473431	0.07946553	-0.049007978				
SHS5A   Q9H114	0.5282234	2.01E-06	6.12E-05	0.999048627	0.005791985	8.08E-05	0.48566043	0.007665169					0.160410364	0.004769435	0.111897942	-0.155640928	-0.048512421	0.07128507				
CTD1   Q9H040	6.21764802	0.00047934	0.022365907	0.003849307	0.000551512	0.96424931	0.78458163	0.966771453					0.280650221	0.32620595	0.368362148	0.045570374	0.087711927	0.042415533				
BRAXIN   Q9H813	9.67497291	6.12E-06	0.002778167	0.642715421	0.065805547	2.30E-05	0.589253162	0.00128974					-0.28586675	-0.02005971	-0.188795244	-0.177874646	-0.097073431	0.28801215				
VAPA   Q9P010	2.99415888	0.032147578	0.322838036	0.10919071	0.02107607	0.957097137	0.718923872	0.9468867					-0.06848607	-0.08855441	-0.109112015	-0.200660824	-0.040623408	-0.025056584				
C6orf48   Q5L98	12.0676121	2.99E-07	0.000131984	0.000125639	3.30E-07	0.999555422	0.07378123	0.61312122					0.327555942	0.31992245	0.405654329	-0.07963697	0.78097481	0.080661178				
ALCA   P06881	2.92372359	0.03289309	0.090542306	0.999714636	0.394615816	0.66589638	0.812393366	0.302526828					-0.219532867	0.00841177	-0.139941609	0.227947044	0.795951259	-0.148535785				
ITGB4   P16144	2.06264255	0.061928053	0.963846742	0.167567556	0.837149598	0.059902094	0.557855053	0.591466595					0.037635967	-0.156373791	-0.003512812	-0.194009758	-0.101147789	0.092860979				
GAS1   P54826	0.54902014	0.789266281	0.96801283	0.977908631	0.979055586	0.999955422	0.97025588	0.800573818					-0.054714599	-0.02049016	-0.028665583	0.057921626	0.029256043	-0.225985093				
CTD1   Q9H040	6.21764802	0.00047934	0.022365907	0.003849307	0.000551512	0.96424931	0.78458163	0.966771453					0.18909917	0.18520627	-0.0406947	0.16638705	-0.059601387	-0.225985093				
PPV1   Q15415	10.0093005	8.04E-07	0.84320409	0.00971621	0.00385144	0.00848913	0.00137771	0.95774995					0.088193341	-0.07897918	0.35564443	-0.38801621	-0.45757474	-0.048512421				
TW12   Q9H050	10.3325381	3.24E-06	0.483621593	0.00687064	0.00168666	0.444E-05	0.00212877	0.988120049					0.067975659	-0.148962799	-0.134703332	-0.16938459	-0.022678991	0.041254967				
SHBGRL1   Q9H299	12.9263171	1.05E-07	0.883991216	0.183248921	1.20E-05	0.033536112	4.43E-07	0.022573794					0.027609185	-0.074210078	-0.175811861	-0.101819263	-0.203421064	-0.101601783				
GPIIIB   P07359	0.60437064	0.750968151	0.91452474	0.881621222	0.99801243	0.730021637	0.996823374	0.84968268					-0.03455412	0.08854394	0.098544686	0.123098514	0.024713552	-0.098384962				
RFG   Q9Y644	1.46804969	0.225982816	0.34628322	0.679718456	0.213659597	0.938044824	0.977120308	0.947844908					-0.101005145	-0.066320944	-0.112730631	0.034682402	-0.011725486	-0.046089976				
HLA-DPA1   P20336	0.79372898	0.498799388	0.777887573	0.737986092	0.92845486	0.40555366	0.736394913	0.971361858					0.04704257	-0.115997175	-0.06798941	-0.163039744	-0.11493721	0.048102534				
TUBB3   Q9H045	2.13322961	0.07483638	0.153782259	0.713303731	0.09164788	0.69303651	0.999311997	0.576472391					0.1777885	0.057665413	0.12464362	-0.060122936	0.006677014	0.066799948				
CLN4   Q9U177	12.1126578	1.41E-05	0.00077785	2.41E-05	0.00077785	2.41E-05	0.00077785	2.41E-05					0.73907781	-0.03787185	0.13970776	-0.03787185	-0.03787185	-0.03787185				
UBF1   Q9H164	6.8134019	0.000229275	0.00564347	0.00028877	0.00168666	0.923008574	0.711080672	0.943581702					0.153992742	0.22106169	0.19219491	-0.068057327	0.024062048	-0.028871289				
TM2A   Q43736	2.96099432	0.036001069	0.103092281	0.984698453	0.65218944	0.0397255	0.600033554	0.413691135					-0.18494331	0.017808706	-0.066681423	0.136303037	0.066181298	-0.074490129				
IGHV4   Q2A0ACDH34	13.7373785	6.14E-08	0.000484421	0.991490202	8.52E-06	0.000889594	0.879958012	1.90E-05					-0.561601085	-0.034597383	-0.061317506	0.527003702	-0.097169421	-0.674901292				
SERPINC1   P50453	2.18929114	0.09046147	0.35331931	0.065498857	0.27855109	0.857411611	0.99980188	0.879818526					-0.132388846	-0.194967085	-0.18868977	-0.062578239	-0.006308302	0.056277408				
METRN   Q9UHI8	1.49365809	0.21752231	0.99504884	0.73562398	0.228005569	0.86926588	0.36195371	0.81765268					0.011773291	0.048626834	0.036853543	0.07678897	0.039914354	-0.00969948				
ILIRAP1   Q9H271	6.5606492	0.000314883	0.006305918	0.13525485	0.000387201	0.357250465	0.844238334	0.096330884					0.220018165	0.111206425	0.255914826	-0.108811174	0.03					

Gene ID   Uniprot ID	F-Value	Pr[F]	ANOVA p-values with Tukey Adjustment										Difference (AD - CT)									
			AD-Cau vs AD-AA	CT-AA vs AD-AA	AD-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-Cau vs AD-Cau	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-Cau vs AD-Cau
G1P01703	0.3734054	0.77228881	0.866689107	0.999967039	0.913050089	0.840103195	0.99876263	0.890836706		-0.097474432	0.005472394	-0.078912268	0.102947376	0.018562164	-0.084385212							
GNAS1	0.165597985	0.178082904	0.518162476	0.893562416	0.87191012	0.158773036	0.902019278	0.439847903		-0.072254959	0.03629985	-0.07456657	0.10854809	0.034778302	-0.073756507							
STN3N1	0.74821767	0.00310181	0.015842037	0.016553081	0.000640085	0.999672113	0.998790099	0.994040027		0.149810563	0.145505284	0.157012713	-0.004760279	0.00702125	0.011962429							
CDH4	0.04646415	0.727121218	0.999170617	0.99014254	0.864851117	0.974034111	0.921166539	0.690561369		0.06680057	-0.038142236	0.06680057	-0.038142236	0.055712824	0.09386405							
CEND1	0.74711613	9.86E-05	0.39678998	0.035756345	0.012575532	0.000170492	0.921662925	0.833886454		0.086769911	-0.14602532	-0.102922631	-0.234021543	-0.190521642	0.043679901							
PP3CA	0.2273759	1.70E-10	0.642285772	7.00E-05	1.134E-05	4.69E-07	0.647E-08	0.991630776		0.089056734	-0.331416756	-0.351487304	-0.42047439	-0.440544037	-0.02070548							
AT1P35611	3.0085014	0.03706347	0.994952768	0.332101645	0.123489814	0.216640064	0.07072553	0.948299162		0.040614084	-0.27596462	-0.36184604	-0.31675846	-0.40248688	0.05194239							
PN02	0.121565	0.508005673	0.950686054	0.97157183	0.807623728	0.757871189	0.462416167	0.966689094		-0.063171675	0.051975345	0.103012752	0.11514702	0.166188928	0.051490127							
ALB03	0.05062	0.371089618	0.96653298	0.856971261	0.545831742	0.740470214	0.406232669	0.969724039		-0.039348642	0.145021585	-0.22898231	0.184370227	0.268330855	0.09860627							
B3GNT7	0.12981028	0.21394522	0.21374552	0.858724228	0.372214686	0.650207904	0.972394518	0.858471593		-0.151499007	-0.060778829	-0.119029438	0.080710716	0.03246954	-0.058241176							
ROBO4	0.080775	0.15733382	0.753132213	0.302838033	0.142097413	0.890472826	0.698025349	0.964363695		0.05417384	0.09262597	-0.111175567	0.034632516	0.057001727	0.01854921							
CA13T4	0.02667	0.371089618	0.96653298	0.856971261	0.545831742	0.740470214	0.406232669	0.969724039		-0.039348642	0.145021585	-0.22898231	0.184370227	0.268330855	0.09860627							
ITGAM1	0.121125	9.58740398	7.29E-06	0.15197983	0.039349782	0.117602771	2.57E-05	0.000124776	0.948277721	0.158093634	-0.12599007	-0.155691271	-0.315083704	-0.313784905	0.037298799							
NME3	0.132322	2.41872343	0.06768571	0.793943432	0.972170102	0.194043899	0.522402315	0.742727429	0.066161189	0.033883899	-0.015618953	0.069730478	-0.049502851	0.035846579	0.08534943							
MKRA7	0.184157	0.421803083	0.006581058	0.04432426	0.999993904	0.104992755	0.035520635	0.963290457	0.086909777	-0.155449315	0.001459492	-0.128152747	0.156908002	0.027292068	-0.129616739							
SLC39A14	0.125043	9.58740398	7.29E-06	0.15197983	0.039349782	0.117602771	2.57E-05	0.000124776	0.948277721	0.158093634	-0.12599007	-0.155691271	-0.315083704	-0.313784905	0.037298799							
ENM3D3	0.095205	1.05447777	0.030986135	0.123952176	0.944611917	0.160142546	0.033257372	0.67723375	0.266776205	-0.209008161	0.049268774	-0.106626146	0.258276935	0.013282015	-0.155894927							
STP1	0.131948	2.81939876	0.041416403	0.542539615	0.860011663	0.029960833	0.94029579	0.56030688	0.20399277	-0.133619282	-0.076335815	-0.259085785	0.057283467	-0.125466503	-0.18274997							
TGFB2	0.161823	6.33693943	0.000419498	0.03447396	0.707109107	0.184173088	0.000982712	0.836605562	0.009323296	-0.196543022	0.05705093	-0.13585841	0.271548114	0.057957611	-0.213595053							
AC6G	0.090190	0.62608283	0.5998051	0.999977889	0.753622485	0.994200864	0.742494755	0.99688605	0.959219887	-0.007239136	0.177159864	-0.004755139	0.184399	-0.037516035	-0.22195034							
PCDHGA3	0.035910	0.2160857	0.88512546	0.98565991	0.99707043	0.99909962	0.95802561	0.89039138	0.99637993	-0.041602572	-0.011651211	0.000276539	0.299551361	0.041870435	-0.01919074							
CSMD2	0.072408	4.2773152	0.06276955	0.95704292	0.136962384	0.137945718	0.368081073	0.377281539	0.999938483	0.035489257	0.147090803	0.143471711	0.111601545	0.107981915	-0.003619631							
FLT3	0.136888	4.9867878	0.02669213	0.94079873	0.997904162	0.70247581	0.02585892	0.001772075	0.821311503	-0.377820008	0.024343085	0.046005889	0.402163093	0.116250524	-0.116250524							
TNXCND7	0.098492	0.82551649	0.48133079	0.999934166	0.81347036	0.554009307	0.847949655	0.601925147	0.974948625	-0.003193905	-0.048288204	-0.07385602	-0.045088899	-0.067191697	-0.022107798							
SPNK1	0.09095	1.33859031	0.258681073	0.58016224	0.309102645	0.287558239	0.95845293	0.945840329	0.999933294	-0.15564249	-0.230104379	-0.37533303	0.0796195	-0.077808074	-0.00742849							
CA5G	0.094175	0.45849175	0.004742694	0.10740654	0.88524936	0.00539035	0.474741175	0.77894042	0.995727992	0.103729732	0.03855392	0.145415578	-0.064874341	0.041681845	-0.00556186							
GXYT1	0.04148	0.106468572	0.367081497	0.641518386	0.543151839	0.99999785	0.999353238	0.640897981	0.540526551	-0.098207318	-0.10829519	-0.00148338	-0.10051862	0.096748979	0.106800841							
TNME25	0.080313	1.17130617	0.22384701	0.240156415	0.588782634	0.290191879	0.910767253	0.969643343	0.6175362	0.113689966	0.074205417	-0.0176074	-0.039484549	-0.012592226	-0.005759233							
CKX12	0.148061	3.98415554	0.008832043	0.027017764	0.41295815	0.012324889	0.539624775	0.999392153	0.419684809	-0.189706123	-0.101078828	-0.197442212	0.088627295	-0.007716003	-0.09634298							
PR523	0.059084	0.39884403	0.88512546	0.98565991	0.99707043	0.99909962	0.95802561	0.89039138	0.99637993	-0.041602572	-0.011651211	0.000276539	0.299551361	0.041870435	-0.01919074							
CA14	0.09147	0.7760016	0.508865088	0.998276602	0.994037144	0.633255458	0.973455031	0.519497812	0.780720426	-0.007421711	0.011083331	0.049723284	0.018505043	0.057144995	0.038693953							
IGF1R	0.040405	2.01078249	0.14213081	0.211605818	0.99016212	0.818588649	0.115993352	0.64590881	0.64067598	-0.364286007	0.052169393	0.15549819	0.1414524	0.208656415	-0.00758558							
CKX12	0.148061	3.98415554	0.008832043	0.027017764	0.41295815	0.012324889	0.539624775	0.999392153	0.419684809	-0.189706123	-0.101078828	-0.197442212	0.088627295	-0.007716003	-0.09634298							
RAB6B	0.090190	0.62608283	0.5998051	0.999977889	0.753622485	0.994200864	0.742494755	0.99688605	0.959219887	-0.007239136	0.177159864	-0.004755139	0.184399	-0.037516035	-0.22195034							
SUMF1	0.098313	2.4994465	0.067362895	0.95776334	0.0594011	0.87712655	0.176305414	0.972634511	0.331703924	0.033313711	0.166078193	0.050239723	0.132764482	0.02681302	-0.10955147							
VAT1L	0.09147	1.13321626	0.336952156	0.297541244	0.551847007	0.594370565	0.963282278	0.935414276	0.999643431	-0.110024682	-0.080384461	-0.07548201	0.029642021	0.035476481	0.000836259							
P03631	7.14451331	0.001447	0.003769136	0.717739639	0.000743548	0.068368975	0.993067885	0.92896777	0.02896777	-0.56745593	-0.167912311	0.379833262	-0.042595324	-0.116250524	-0.116250524							
B3GAT1	0.092977	0.91100409	0.438359693	0.99898308	0.760099984	0.932717744	0.846551991	0.884584531	0.36022872	-0.017158995	-0.076710972	0.04594251	-0.065181977	0.057470245	0.122652222							
NA	0.040405	2.01078249	0.14213081	0.211605818	0.99016212	0.818588649	0.115993352	0.64590881	0.64067598	-0.364286007	0.052169393	0.15549819	0.1414524	0.208656415	-0.00758558							
SPR180	0.080313	1.17130617	0.22384701	0.240156415	0.588782634	0.290191879	0.910767253	0.969643343	0.6175362	0.113689966	0.074205417	-0.0176074	-0.039484549	-0.012592226	-0.005759233							
SLC12A2	0.055011	0.22041378	0.882054234	0.999317207	0.992516052	0.953689556	0.979618199	0.981287078	0.987713907	0.009799386	-0.021939552	0.038893941	-0.037138938	0.029194554	0.060923493							
FZD8	0.09461	1.48952082	0.2201369	0.969552695	0.517736308	0.226679732	0.813657855	0.459505454	0.946779132	0.045490952	0.132507716	0.07835789	0.087011763	0.137884836	0.009673073							
FAP	0.121884	0.67849214	0.51258804	0.999098677	0.972412479	0.608455015	0.941490128	0.530284695	0.848911372	-0.01436711	0.044242723	0.13291296	0.058069435	0.138279671	0.079620737							
EFNA3	0.052797	0.21541831	0.000517666	0.070426329	0.843535106	0.000718761	0.340537373	0.460732217	0.00922244	0.168234981	0.05951683	0.26592406	-0.112303297	0.067899079								



Gene ID   Uniprot ID	F-Value	Pr(>F)	ANOVA p-values with Tukey Adjustment								Difference (AD - CT)							
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau
JDL07   Q08722	3.10077679	0.032039113	0.377133119	0.787405143	0.487856252	0.055252756	0.99237052	0.075298557	-0.108361965	0.061053182	-0.090361613	0.169415147	0.018000052	-0.15415095				
UB02L1   Q08H9D	3.00776002	0.338197082	0.744207033	0.998746792	0.530051295	0.039312229	0.043922655	0.045928557	-0.071545949	0.010537898	-0.08901062	0.082083846	-0.017355113	-0.09943866				
DBP2A   Q09Y56	13.4031775	1.76E-07	1.32E-06	0.158194247	1.25E-05	0.003670911	0.830698751	0.026062162	-0.196650555	-0.446028017	-0.121830842	0.750625238	0.174819713	-0.575802825				
TF1S118   Q9Y275	0.78650278	0.49825669	0.513130933	0.61313829	0.641890205	0.994110652	0.989125611	0.999941817	-0.14937344	0.08517689	-0.083083414	-0.019119655	-0.02285393	-0.03734275				
PSMB7   Q09436	14.5775138	2.35E-08	0.625913993	0.000542209	0.000844162	2.71E-06	4.51E-06	0.99862704	0.10774902	-0.352810237	-0.340329066	-0.460559257	-0.448078086	-0.012481171				
PMCH   P20382	0.40135561	0.752280287	0.999974895	0.895092043	0.98827118	0.910943825	0.983086156	0.704138354	-0.003330506	-0.055677888	0.024804366	-0.052347383	0.028170871	0.080518254				
RRAP1   P03533	0.7257858	0.538126024	0.982544897	0.999898688	0.749350842	0.97616074	0.51296867	0.746955818	-0.026757918	0.008271732	0.002212124	0.028879042	0.095029651	0.086510609				
TFE2F2   Q09IK5	1.4654804	0.030373764	0.120181867	0.971295541	0.890898108	0.26507521	0.367753267	0.994488841	0.146527806	0.028240667	0.043628332	-0.118287319	-0.102899474	0.015387665				
SERPIN2   P20848	0.86262639	0.706474771	0.797349254	0.957005401	0.699258787	0.93739257	0.999355336	0.939694363	-0.067195686	0.038315451	0.079797901	0.030831545	-0.00802215	-0.0394376				
PDGFRA   P16234	1.1204174	0.342575745	0.996444385	0.525292596	0.990254761	0.664881698	0.952158556	0.310318812	0.014920882	0.091937831	-0.020168809	0.07701995	-0.035089691	-0.11210646				
ENY2   Q08257	2.76090564	0.04538476	0.061213771	0.366131235	0.999948088	0.784749457	0.740510048		-0.285730732	-0.294513476	-0.181427908	-0.008727243	0.014042804	0.01308547				
MYL6   P06060	0.58024892	0.628945106	1	0.99935823	0.705786009	0.999360022	0.705859455	0.765769773	-9.85E-06	-0.01052682	0.008390521	-0.010516972	-0.089389673	-0.078872701				
GUS8   P08236	0.36002951	0.781949088	0.901098964	0.987790973	0.99999908	0.741124563	0.89500135	0.985039065	-0.059327198	0.027488853	-0.000854324	0.08682605	0.058472874	-0.028353176				
MYOG1   Q0869H	0.54054789	0.65510561	0.772192289	0.999664731	0.999070644	0.737539961	0.659344249	0.995942201	-0.04754976	0.002220669	0.007238252	0.049770428	0.054788012	0.005071583				
ASPRV1   Q53RT3	0.14895842	0.930128559	0.989743046	0.990205083	0.995444104	0.999993721	0.946913579	0.943057774	-0.026099257	-0.023948539	0.01770193	0.002510717	0.043889402	0.041738685				
LUTP2   Q8ET4E	1.1740322	0.32145607	0.918405838	0.445847613	0.9545498	0.832211591	0.75305788	0.999206463	0.032546384	0.074757738	0.08109545	0.042211354	0.048505546	0.006294192				
CDCA1   P13598	2.6497783	0.05236442	0.998955803	0.082681215	0.380629001	0.12269429	0.480625989	0.825644103	0.006747547	0.109773961	0.071845518	0.103026413	0.065106971	-0.037919442				
NPC1   O15118	0.92202135	0.431620677	0.81635488	0.9964637	0.87048658	0.694240995	0.357272998	0.951613198	-0.073816549	0.017658995	0.059488709	0.091476444	0.133301258	0.041824814				
ECM2   P13431	1.82371108	0.146639986	0.99789657	0.587238019	0.380629001	0.48806175	0.861492216	0.98232569	-0.016317612	0.11267897	0.08306919	0.127440058	-0.066890328	-0.194337086				
GLV3-16   A0A075B6K0	9.25650964	9.81E-06	0.01098277	0.810774603	0.00782460	0.000429319	0.99994299	0.000226425	-0.556907509	0.154051818	-0.547633361	0.170595936	0.009271448	-0.701685178				
NEDD8   Q15843	12.0021758	3.99E-07	0.991908524	0.001187947	0.000129575	0.000439558	4.32E-05	0.945399086	0.14201468	-0.287069612	-0.196582054	-0.222070684	-0.05248863	-0.2133477				
YIPF3   Q9GZM5	3.5012684	0.016412041	0.329293947	0.1860284	0.008096208	0.993075837	0.487032046	0.64005096	0.08524413	0.067400595	0.105103984	0.009146156	0.047049571	0.037903414				
UFM1   P16360	6.17630993	0.000274887	0.977283798	0.031394934	0.008482435	0.012877044	0.003184745	0.985515824	0.019153252	-0.126212806	-0.143499877	-0.145366058	-0.025860129	-0.015286071				
YMO1   Q7Q550	0.35999008	0.78199014	0.964277234	0.869711663	0.755008508	0.991574128	0.959126532	0.979035295	0.072225083	0.14739963	0.143046458	0.04251478	0.070829515	0.028814795				
GLV3-10   A0A075B6K4	0.66402594	0.57515527	0.708390167	0.601733204	0.66047437	0.99902255	0.999991674	0.999318574	-0.170161947	-0.192039313	-0.021801967	0.021801967	0.03461495	-0.01640471				
CDP7   P48950	8.22661249	3.62E-05	0.770159435	0.114601096	0.006732946	0.000732454	0.00010042	0.642765944	-0.051293164	0.116357372	0.174850044	0.167650536	0.02738168	-0.058467632				
PFN2   P35080	27.2759333	1.65E-14	0.958155587	7.27E-08	1.14E-08	7.53E-09	1.07E-09	0.997817034	0.030205682	-0.348580465	-0.587476181	-0.378766181	-0.388949851	-0.010163703				
SLP3G1   Q084G4	2.79741684	0.043807536	0.3655649	0.754824499	0.58775551	0.055910945	0.97531159	0.11493496	-0.158203043	0.095118343	-0.118016358	0.253321386	0.004186685	-0.2133477				
TFE1F1   Q08YR6	4.23744703	0.006511824	0.003125565	0.541828109	0.254566338	0.119991627	0.279589843	0.961246147	0.179273286	0.007175229	0.090963161	-0.112089057	-0.088310153	0.023787904				
STB5A4   Q92187	1.7896709	0.152558523	0.466260212	0.812360917	0.990908051	0.104775155	0.608617973	0.69611961	-0.116629021	0.06833658	-0.02228975	0.184965601	0.094346466	-0.090619555				
SUCO   Q08B59	1.80943655	0.150305917	0.884092149	0.463622284	0.991734357	0.145444944	0.96150626	0.30585856	-0.067523917	0.125858137	-0.022840044	0.193377975	0.044684323	-0.148690312				
NW130   Q08D58	2.65426381	0.051969414	0.999048024	0.088951234	0.98177362	0.123047722	0.999111893	0.112379381	-0.041739474	-0.24069702	-0.025300228	0.025300228	0.014717691	-0.016346865				
CDP7   P48950	8.22661249	3.62E-05	0.770159435	0.114601096	0.006732946	0.000732454	0.00010042	0.642765944	-0.051293164	0.116357372	0.174850044	0.167650536	0.02738168	-0.058467632				
CAST   P20810	1.4446361	0.126508656	0.578481297	0.329478879	0.093258847	0.980908112	0.740136744	0.91572544	-0.129996287	-0.168217983	-0.30686457	-0.038221696	-0.100872171	-0.062650475				
SLC39A1   Q13433	3.0980574	0.02917785	0.08763511	0.11343531	0.03763574	0.95765277	0.989491797	0.984917437	0.159566931	0.203057379	-0.01414242	0.023350087	0.023350087	-0.023350087				
BMP1   P13497	0.8865973	0.44977772	0.828951578	0.985791301	0.431249623	0.935647834	0.929838014	0.96438753	0.062412842	0.024731224	0.104671004	0.037681617	0.042556243	0.07993982				
SMAP1   P09090	6.36287021	0.00039688	0.971128073	0.111115303	0.140695917	0.002159478	0.002796049	0.96641957	0.128867791	-0.124798858	-0.195965639	-0.343846649	-0.324568302	0.019283219				
NAGPA   Q9UK23	1.95168438	0.193993217	0.987229144	0.823394425	0.848244615	0.955132616	0.342571683	0.630442063	0.022442133	0.0563626	0.132726055	0.039320427	0.109854072	0.079933644				
CTC1   Q14960	0.47223882	0.004664722	0.220448658	0.088951234	0.98177362	0.123047722	0.999111893	0.112379381	-0.041739474	-0.24069702	-0.025300228	0.025300228	0.014717691	-0.016346865				
PDGFRA   Q9Y5G9	1.00046437	0.35999008	0.964277234	0.869711663	0.755008508	0.991574128	0.959126532	0.979035295	0.072225083	0.14739963	0.143046458	0.04251478	0.070829515	0.028814795				
HSIA6   Q9Z519	2.63668468	0.051525069	0.198865025	0.998004199	0.895720644	0.252477184	0.034531166	0.802274422	-0.06996991	-0.008321097	0.032608845	0.088675813	0.129605755	-0.040929942				
FIBIN   Q8CTA5	0.97832429	6.28E-05	0.00098353	0.96778753	0.004239711	0.024039711	0.018090616		-0.251136779	-0.028543443	0.222593337	0.039297082	-0.015962549	-0.024895293				
MAP2   P55001	0.60479157	0.613065813	0.76630646	0.999935274	0.99176986	0.78889395	0.565714646	0.985132557	-0.074819977	-0.004208398	0.020668955	0.070611578	0.095508472	0.024895293				
SABARAPL2   P60520	8.94078908	1.55E-05	0.950271164	0.000370923	0.003470924	0.01353222	0.009798016	0.987636957	-0.010695639	-0.178974546	-0.148459188	-0.168278907	-0.177635449	0.030513359				
GLV7-46   A0A075B6I9	5.16421206	0.00188802	0.05033558	0.965629837	0.079841583	0.012103287	0.988966934	0.019515888	-0.37467812	0.066105995	-0.330576054	0.440784115	0.044101615	-0.3966825				
LARG1   Q95461	7.97746461	5.67E-05	0.011013658	0.00387125	1.66E-05	0.993548928	0.478265101	0.346878102	0.246375101	0.266709214	0.353034622	0.000334213	0.014042804	0.01308547				
SKRGL1   Q7L266	3.23330726	0.02053022	0.979732544	0.855564969	0.076923014	0.624765183	0.025712228	0.342246356	0.045647786	-0.091702666	-0.277663053	-0.137368451	-0.323					

Gene ID   Uniprot ID	F-Value	Pr[F]	ANOVA p-values with Tukey Adjustment								Difference (AD - CT)							
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-AA	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-Cau vs AD-Cau	CT-Cau vs CT-AA
MPST   P25325	1.03211084	0.380811342	0.787277663	0.996785813	0.588042022	0.659102069	0.989371885	0.447519618	-0.089879174	0.020075098	-0.119107089	0.109954272	-0.029227915	-0.139182187	-0.039842733	-0.13850545	-0.13850545	-0.13850545
SQSTM1   Q13501	2.66087364	0.049699927	0.364739772	0.999913046	0.108874173	0.382866367	0.932047748	0.113770452	-0.105128913	-0.03968117	-0.142473566	0.101160797	-0.037444653	-0.137444653	-0.037444653	-0.137444653	-0.137444653	-0.137444653
RAMBP1   P43487	0.78352423	0.505102934	0.997906956	0.715166122	0.57342486	0.840144239	0.703435842	0.994604044	-0.011003238	-0.06063509	-0.04742682	-0.049600271	-0.06373582	-0.01673311	-0.06373582	-0.01673311	-0.06373582	-0.01673311
CTSB   P04080	1.2626082	0.289634227	0.99911448	0.84296456	0.3714599	0.816266861	0.34381925	0.85522716	-0.009397519	0.07069414	0.136330781	0.075465173	0.141786339	0.06631367	0.141786339	0.06631367	0.141786339	0.06631367
MASP2   O00187	10.2370874	2.74E-06	0.37118927	0.04917087	0.011318716	0.00152545	1.46E-05	0.96683117	-0.094324872	-0.13883153	-0.162602238	-0.23515605	-0.2560511	-0.023788705	-0.2560511	-0.023788705	-0.2560511	-0.023788705
IGKV1-5   P01602	0.59888586	0.616624152	0.990017101	0.89040874	0.950521168	0.980055919	0.834274925	0.564596678	-0.04929482	-0.110415755	0.080683869	-0.061120934	0.129978689	0.131099623	0.129978689	0.131099623	0.129978689	0.131099623
MFAP5   Q13361	10.7544966	1.51E-06	0.000198553	0.94658007	0.00019441	0.001288139	0.996566178	0.00137125	-0.64794216	-0.083075074	-0.616224289	0.56441912	0.032169927	-0.53149215	0.032169927	-0.53149215	0.032169927	-0.53149215
GLV2   B1A0A0758619	1.52662666	0.20938156	0.564210816	0.998045326	0.448970393	0.440303438	0.99941626	0.32705058	-0.106551726	0.14085299	-0.114595787	0.119737025	-0.008940661	-0.126881086	-0.008940661	-0.126881086	-0.008940661	-0.126881086
TMEM95   Q9H543	4.62272033	0.006302096	0.00452583	0.008008035	0.08309319	0.7632565	0.17176688	0.999840191	-0.694217527	-0.500118125	-0.485508864	0.194099043	-0.208708663	-0.041602621	-0.208708663	-0.041602621	-0.208708663	-0.041602621
TMEM95   Q9H543	0.60684125	0.578053224	0.991072905	0.742427885	0.611111178	0.900851905	0.831750022	0.959825925	0.014018484	0.046249568	0.053469112	0.032230884	0.039450628	0.007219745	0.039450628	0.007219745	0.039450628	0.007219745
RAMBP1   P43487	3.1813227	0.026151583	0.384856373	0.095828422	0.020093825	0.924532041	0.62361204	0.925193804	-0.189259946	-0.261650768	-0.329697374	-0.072406822	-0.140447428	-0.06840606	-0.329697374	-0.06840606	-0.329697374	-0.06840606
GLV4   B1A0A075861	6.6246965	0.00031167	0.408673623	0.186238782	0.265706132	0.002085259	0.996243746	0.000563344	-0.385059524	0.494574536	-0.437476857	0.88018406	-0.051867332	-0.051867332	0.88018406	-0.051867332	-0.051867332	0.88018406
MGAT4B   Q9UQ53	1.76491841	0.155711008	0.946912532	0.878057301	0.133771151	0.997722915	0.378545237	0.469387743	0.032167345	0.042813362	0.122407577	0.010646018	0.09024032	-0.079594215	0.010646018	0.09024032	-0.079594215	0.010646018
FAM38   P58499	1.83355548	0.144916813	0.132918711	0.425179333	0.277279741	0.888514735	0.9532025	0.906540504	-0.334659032	-0.225193887	-0.257831578	0.109465146	0.076827455	-0.032637691	-0.225193887	0.109465146	0.076827455	-0.032637691
PRND   Q9UKY0	1.63126256	0.210957386	0.995892878	0.433648626	0.981946025	0.372011833	0.993450994	0.201972374	0.010540152	-0.14945684	0.039558077	-0.159996992	0.025417926	0.185414918	-0.14945684	0.039558077	0.025417926	0.185414918
PLS2   Q9P052	1.7239228	0.10615875	0.30417074	0.338058886	0.159396255	0.999775956	0.990972074	0.998040191	-0.101989815	-0.07908067	-0.163849281	0.004909145	-0.01659467	-0.01659467	-0.07908067	0.004909145	-0.01659467	-0.01659467
CCDC8   P70696	1.0938265	0.354177008	0.726394142	0.39566748	0.38554999	0.962788743	0.960877225	0.999990281	-0.081118946	-0.118285563	-0.116135029	-0.037166617	-0.035010683	-0.002150534	-0.118285563	-0.037166617	-0.035010683	-0.002150534
AKCY   P23536	2.32373694	0.077321132	0.62849956	0.449173875	0.046256074	0.994528198	0.530336818	0.669997042	-0.120656956	-0.145440715	-0.323946072	-0.074897919	-0.132289116	-0.107493537	-0.145440715	-0.323946072	-0.074897919	-0.132289116
RNF167   Q9H577	1.35838489	0.259755005	0.95839731	0.33353399	0.487509195	0.915777274	0.692361154	0.981926386	-0.012831498	-0.090305817	-0.077418319	-0.055866821	-0.014837431	-0.014837431	-0.090305817	-0.077418319	-0.055866821	-0.014837431
CXCL10   P02778	2.47270581	0.066240759	0.59516817	0.865746108	0.477956184	0.945682221	0.597318829	0.220404068	-0.19071682	-0.08571457	-0.38260044	0.082145363	-0.19188727	-0.02742583	-0.08571457	-0.38260044	0.082145363	-0.19188727
PI3   P01718	1.3858074	0.100105258	0.167730248	0.578250867	0.99438422	0.005154688	0.231826922	0.980710473	-0.345979458	0.280611196	-0.040043547	0.305935912	-0.24810743	-0.24810743	-0.345979458	0.280611196	-0.040043547	0.305935912
FZD7   O75084	0.26025565	0.000193551	0.000251148	0.189361912	0.002968192	0.099575061	0.840521515	0.101122695	-0.248714567	-0.114689873	-0.200948019	0.12404694	0.047766548	-0.086258146	-0.114689873	-0.200948019	0.12404694	0.047766548
PM2   P07478	5.63039291	0.001075726	0.003237426	0.980168107	0.07270721	0.090189543	0.593259387	0.161010843	-0.249071406	-0.026648415	-0.163849281	0.222422991	0.085231029	-0.01731963	-0.026648415	-0.163849281	0.222422991	0.085231029
PROX1   P06044	2.33574393	0.074353598	0.734783207	0.719000564	0.440200603	0.999959596	0.98663593	0.426819389	-0.093712395	-0.091674594	-0.191508133	0.000237801	-0.12578944	-0.127827241	-0.093712395	-0.091674594	-0.191508133	-0.12578944
FAM81   P48551	1.48812871	0.219521015	0.82807966	0.418501495	0.193519172	0.91591769	0.699758198	0.991495401	0.030778009	0.064728079	0.08425287	0.07355071	0.045830278	0.017252084	0.030778009	0.064728079	0.08425287	0.07355071
GRK5   Q06055	0.33167828	0.022094789	0.02556109	0.552397494	0.046467104	0.380302913	0.4861953	0.60588243	-0.12367341	-0.230702025	-0.148666608	0.001453743	-0.107202864	-0.107202864	-0.12367341	-0.230702025	-0.148666608	0.001453743
TLN1   Q8WVA0	1.13512684	0.336869196	0.77820995	0.821785158	0.998446119	0.261386146	0.658019281	0.88118373	0.085271462	-0.075378139	-0.013951455	-0.160649601	-0.099221918	0.06142684	-0.075378139	-0.013951455	-0.160649601	-0.099221918
IGLV10-54   A0A0758614	0.26025565	0.000193551	0.000251148	0.189361912	0.002968192	0.099575061	0.840521515	0.101122695	-0.248714567	-0.114689873	-0.200948019	0.12404694	0.047766548	-0.086258146	-0.114689873	-0.200948019	0.12404694	0.047766548
CRISPLD1   Q9H336	1.63039291	0.001075726	0.003237426	0.980168107	0.07270721	0.090189543	0.593259387	0.161010843	-0.249071406	-0.026648415	-0.163849281	0.222422991	0.085231029	-0.01731963	-0.026648415	-0.163849281	0.222422991	0.085231029
LRP2   Q9B951	2.33574393	0.074353598	0.734783207	0.719000564	0.440200603	0.999959596	0.98663593	0.426819389	-0.093712395	-0.091674594	-0.191508133	0.000237801	-0.12578944	-0.127827241	-0.093712395	-0.091674594	-0.191508133	-0.12578944
SUMO1   P55854	1.48812871	0.219521015	0.82807966	0.418501495	0.193519172	0.91591769	0.699758198	0.991495401	0.030778009	0.064728079	0.08425287	0.07355071	0.045830278	0.017252084	0.030778009	0.064728079	0.08425287	0.07355071
PRNT1   Q9P946	1.6204212	0.188696887	0.994066374	0.273880088	0.07692142	0.223048421	0.91799683	0.42124594	-0.021870522	-0.142616407	-0.032019689	0.146466659	0.005200994	-0.112396717	-0.021870522	-0.142616407	-0.032019689	0.146466659
RAREX1   P49788	4.79951482	0.00354139	0.019721372	0.947779466	0.700821407	0.903298789	0.246677924	0.360443727	-0.449622635	-0.075960021	-0.162675238	0.529182656	0.286950097	-0.242325559	-0.449622635	-0.075960021	-0.162675238	0.529182656
MTF3   Q9H2K0	0.53463737	0.65909449	0.53446657	0.999197692	0.08898431	0.978547825	0.611202273	0.983797704	-0.024084422	-0.0058364	-0.030576307	-0.081514782	-0.025462479	-0.032649947	-0.024084422	-0.0058364	-0.030576307	-0.081514782
HST17H4   P64831	0.24369567	0.865744208	0.99873682	0.970223598	0.98167882	0.93609785	0.997604268	0.54061111	0.040687608	-0.004826152	-0.04836622	-0.045531376	0.007749014	-0.053262774	-0.040687608	-0.004826152	-0.04836622	0.007749014
ARL8B   Q9NV12	1.22759138	0.301510024	0.708233679	0.027299902	0.034847166	0.910511843	0.983662221	0.987903829	-0.167992765	-0.07503829	-0.108488935	0.000487915	-0.02418796	-0.02418796	-0.167992765	-0.07503829	-0.108488935	0.000487915
LAEP1   Q9B951	0.89740765	0.44443758	0.541798582	0.463535823	0.403079236	0.914540546	0.84209995	0.999841465	-0.248674988	-0.155327301	0.163129973	-0.093347687	-0.085545015	-0.07602673	-0.248674988	-0.155327301	0.163129973	-0.093347687
STGAL1   P15907	0.94727174	0.420050131	0.76803388	0.841495003	0.193519172	0.91591769	0.699758198	0.991495401	0.030778009	0.064728079	0.08425287	0.07355071	0.045830278	0.017252084	0.030778009	0.064728079	0.08425287	0.07355071
CNPY1   Q9N129	0.95637923	0.416545004	0.586194312	0.906431622	0.406278804	0.923543298	0.99775711	0.81973041	-0.097220117	-0.049670279	-0.110900519	0.047599344	-0.013680041	-0.061279745	-0.097220117	-0.049670279	-0.110900519	0.047599344
UBR4   Q57457	0.9299276	0.428823292	0.524216411	0.999277715	0.987081262	0.943168401	0.752211289	0.956189285	-0.304642104</									

Gene ID   Uniprot ID	F-Value	Pr(-F)	ANOVA p-values with Tukey Adjustment								Difference (AD - CT)							
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau
MMP16   P51512	3.97882697	0.00984643	0.131672162	0.47996704	0.005211538	0.866187099	0.65325579	0.210067069	0.149363694	0.097451726	0.226235733	-0.051911968	0.076872039	0.128784008	0.149363694	0.097451726	0.226235733	-0.051911968
UST1   Q9Y2C2	0.33151575	0.80287631	0.999471719	0.917339823	0.826153332	0.957896417	0.894229161	0.997029618	0.010560341	0.057422192	0.075184813	0.048661852	0.064624472	0.01776262	0.010560341	0.057422192	0.075184813	0.048661852
MEPE   Q9NQ76	2.92313445	0.035729415	0.067198117	0.314038455	0.04201736	0.86381024	0.999796275	0.807133563	0.292649525	0.201196669	0.302098849	-0.091452856	0.009449324	0.109092018	0.292649525	0.201196669	0.302098849	-0.091452856
PIANP1   Q8YU74	6.80078278	4.83E-05	0.003604114	0.000945108	6.80E-05	0.992680272	0.831419105	0.937341502	0.250276286	0.26903821	0.309144376	0.019627515	0.058868609	0.039240355	0.250276286	0.26903821	0.309144376	0.019627515
FZD3   Q9NPG1	1.14907748	0.333163262	0.546465447	0.845299914	0.991321448	0.951176991	0.347513761	0.663194607	0.115723257	0.06985492	-0.024234649	-0.045838078	-0.139958219	-0.094120141	0.115723257	0.06985492	-0.024234649	-0.045838078
H3S3T1   O14792	0.6589858	0.579115693	0.591058998	0.741275997	0.665928354	0.993374319	0.997765093	0.999716739	-0.0997741	-0.078883143	-0.085756183	0.020809057	0.014017917	-0.00687304	-0.0997741	-0.078883143	-0.085756183	0.020809057
ATP6B1E1   P36543	5.58427989	0.00131284	0.756772568	0.12164468	0.098187183	0.008032801	0.00532332	0.999990805	0.085639918	-0.191648312	-0.194054948	-0.27728823	-0.279694865	-0.002406636	0.085639918	-0.191648312	-0.194054948	-0.27728823
ATP1B1   Q9BWP8	1.21663644	0.306978126	0.915866089	0.36096338	0.041693383	0.75876937	0.801591174	0.99975736	-0.041948069	-0.103476671	-0.098180318	-0.061528602	-0.056232249	0.005296353	-0.041948069	-0.103476671	-0.098180318	-0.061528602
COLC11   Q9BWP8	3.52269022	0.017055811	0.187145486	0.656720594	0.990851481	0.008792388	0.208996361	0.527154941	-0.228863681	0.127932144	-0.487661004	0.356795825	-0.212848637	-0.143947188	-0.228863681	0.127932144	-0.487661004	0.356795825
SDC2   P34741	1.94775003	0.125771276	0.479943286	0.986258727	0.392737465	0.288542651	0.999662565	0.216736925	-0.082963456	0.018133502	-0.088060179	0.100696958	-0.005496723	-0.10613508	-0.082963456	0.018133502	-0.088060179	0.100696958
CLL18   P55774	5.28075738	0.001972055	0.166602649	0.934046133	0.037775576	0.037522363	0.936633051	0.005034438	-0.327981922	0.09564059	-0.177180216	0.421625981	-0.089736094	0.511362075	-0.327981922	0.09564059	-0.177180216	0.421625981
TSKJ   Q9BUA8	1.24330663	0.29749655	0.440335087	0.655339403	0.274623925	0.981150784	0.994253203	0.91369362	-0.163036315	-0.122386352	-0.189099186	0.040649963	-0.026872871	-0.067522834	-0.163036315	-0.122386352	-0.189099186	0.040649963
PLEKH2   Q9C57	6.19359178	0.000494533	0.005652829	0.186794814	0.000534762	0.502898958	0.962942029	0.203589437	0.187531624	0.110176182	0.213637379	-0.077355441	0.026105755	0.103461196	0.187531624	0.110176182	0.213637379	-0.077355441
TGFBF1   P36897	5.55670769	0.001304531	0.975623401	0.339792443	0.009142879	0.158711961	0.002311785	0.40897278	0.027255558	-0.108207987	-0.206831748	-0.135463544	-0.234087306	-0.098623761	0.027255558	-0.108207987	-0.206831748	-0.135463544
ACVR1   Q04771	1.33114797	0.266129889	0.281925983	0.988961707	0.627565937	0.444607729	0.893776528	0.81737879	-0.099227471	-0.016987158	-0.061719287	0.082240313	0.037508184	-0.044732129	-0.099227471	-0.016987158	-0.061719287	0.082240313
PDXP1   Q06G0	25.2026342	3.25E-13	0.889422056	2.43E-06	4.48E-08	7.13E-08	9.29E-10	0.871751992	0.059684652	-0.428883259	-0.487661004	-0.587789545	-0.547346457	-0.058778545	0.059684652	-0.428883259	-0.487661004	-0.587789545
BGLAP   Q02B18	7.84904911	6.39E-05	0.018601417	0.637280112	0.000217796	0.861929184	0.00139887	0.289645491	0.116103153	-0.11059597	0.216103153	-0.400795088	-0.07542338	0.327162749	0.116103153	-0.11059597	0.216103153	-0.400795088
NINL   Q9V216	0.30759835	0.819878383	0.992016681	0.97178741	0.972202073	0.888596446	0.999103483	0.84959124	0.034262491	-0.051495043	0.050047663	-0.085757534	0.015794572	0.101542106	0.034262491	-0.051495043	0.050047663	-0.085757534
CKK1   P06307	1.85360527	0.139294826	0.091907115	0.538475471	0.661142481	0.726213982	0.561127792	0.995248601	0.165804772	0.093116538	-0.072784382	-0.075682389	-0.08520389	-0.015832155	0.165804772	0.093116538	-0.072784382	-0.075682389
GLIV4   A0A007586H9	9.93833911	4.17E-06	0.03822886	0.852177374	0.001073131	0.002477263	0.795797892	2.80E-05	-0.446388795	0.127559653	-0.990177003	0.573948448	-0.143788208	-0.17736656	-0.446388795	0.127559653	-0.990177003	0.573948448
PSMA3   P25788	10.5799165	2.31E-06	0.99605648	0.000248814	0.002842814	0.000137858	0.001606712	0.888127546	0.015132637	-0.305619515	-0.247508999	-0.320752152	-0.262641635	0.058101516	0.015132637	-0.305619515	-0.247508999	-0.320752152
MAPRE1   C15691	6.79597356	0.000316814	0.85288332	0.012773286	0.000929201	0.108520979	0.015768808	0.902091849	-0.074656022	-0.287652698	-0.346585948	-0.211196676	-0.270129926	-0.05893253	-0.074656022	-0.287652698	-0.346585948	-0.211196676
ITGA7   Q13683	0.1265194	0.537671258	0.999948938	0.604219054	0.990852804	0.576243006	0.985311158	0.971481537	-0.004116431	0.095138402	0.099254833	0.026322655	-0.077932179	-0.026322655	-0.004116431	0.095138402	0.099254833	0.026322655
MGAT5B   Q3V5L5	2.41736567	0.070187316	0.136601699	0.999999494	0.91903287	0.134514759	0.868740363	0.417264173	0.202221011	0.001011949	0.133915774	-0.201209062	-0.068625327	0.133902825	0.202221011	0.001011949	0.133915774	-0.201209062
WNP29   Q09542	1.82028926	0.145452892	0.688901434	0.992270729	0.309536382	0.511600363	0.94496261	0.178975867	0.086055826	-0.021360296	0.127885252	-0.107416122	0.041822426	0.14034548	0.086055826	-0.021360296	0.127885252	-0.107416122
PCAT1   P55899	1.34666294	0.261547332	0.259256163	0.965340399	0.9909289	0.498315411	0.349944944	0.995581121	-0.121508705	-0.029820226	-0.09168479	0.105847074	0.014158594	0.014158594	-0.121508705	-0.029820226	-0.09168479	0.105847074
SPRCSB   Q9N2H0	0.80741029	0.491994523	0.880064444	0.627661832	0.999796112	0.972134213	0.8243188	0.532186209	-0.05367574	-0.084294268	0.005696138	-0.030618528	0.059371878	0.089990406	-0.05367574	-0.084294268	0.005696138	-0.030618528
HINT1   Q97773	9.03731166	1.52E-05	0.749970023	0.004911398	5.30E-05	0.077215763	0.002296127	0.68737548	-0.08707706	-0.295247026	-0.386873366	-0.208169965	-0.299796245	-0.09162628	-0.08707706	-0.295247026	-0.386873366	-0.208169965
HCR7   Q43612	2.53578677	0.058200416	0.88466981	0.27482537	0.683499038	0.059428905	0.25075324	0.877152939	-0.048086465	0.115501768	0.069469754	0.163588232	0.117556219	-0.046032013	-0.048086465	0.115501768	0.069469754	0.163588232
PDLIM5   Q96HC4	19.1647287	2.66E-10	0.279311368	0.000132287	0.000527743	2.92E-08	1.14E-07	0.945896819	0.130060251	-0.320915428	-0.450975679	-0.412722317	0.03825362	0.03825362	0.130060251	-0.320915428	-0.450975679	-0.412722317
LYN6   Q9Y819	0.4200244	0.730471497	0.850166343	0.993322719	0.99981264	0.71251189	0.795453306	0.997226507	-0.079895416	0.02512348	0.00749174	0.105018897	0.087144591	-0.01784306	-0.079895416	0.02512348	0.00749174	0.105018897
IMD8   Q9S542	1.24160463	0.297475195	0.244322121	0.619076315	0.521786318	0.904374025	0.930935449	0.999566426	-0.307986127	-0.133696479	0.144760627	0.074299648	0.0632355	-0.01064148	-0.307986127	-0.133696479	0.144760627	0.074299648
SHSAS   B4D577	8.07415979	6.56E-05	0.000805698	0.001867388	0.000227381	0.985858135	0.999788296	0.968953066	0.350490525	0.319611973	0.357768397	-0.30878551	0.007277872	0.015836424	0.350490525	0.319611973	0.357768397	-0.30878551
SULF1   Q8WU6	0.6024758	0.615802414	0.999756625	0.669737155	0.992686266	0.645592099	0.984754758	0.797350566	0.010186704	-0.126877196	-0.029155925	-0.1370639	-0.039942629	0.097272721	0.010186704	-0.126877196	-0.029155925	-0.1370639
LRP3   Q75074	0.06933453	0.976155333	0.972315094	0.9904159	0.998077811	0.998795779	0.992027145	0.999082441	0.05231945	0.034961505	0.019992605	-0.017357945	-0.032326845	-0.0149689	0.05231945	0.034961505	0.019992605	-0.017357945
INAFM1   Q9IUV0	3.55174292	0.015975541	0.023957968	0.234843597	0.028048534	0.755476092	0.997278278	0.835159885	0.25768261	0.168849452	0.240704258	-0.088833158	-0.016978351	-0.071854807	0.25768261	0.168849452	0.240704258	-0.088833158
ADA1   P00813	8.96822809	2.45E-05	0.035332005	0.695428998	0.007682204	0.001483084	0.994420461	0.000152227	0.338886716	-0.131854459	0.368101012	-0.470741175	0.029214296	0.499955471	0.338886716	-0.131854459	0.368101012	-0.470741175
HCN2   Q9UL51	0.63857982	0.591681813	0.597184491	0.86492955	0.646222421	0.963148929	0.9992636	0.982245346	0.101079059	0.062847182	0.091361833	-0.038231877	-0.009717227	0.028514651	0.101079059	0.062847182	0.091361833	-0.038231877
ELF2   Q15723	2.73602408	0.04092903	0.137176315	0.33893387	0.035440389	0.953580769	0.971396123	0.471180644	0.209238454	0.159500057	0.350204001	-0.049738397	0.04095547	0.090703944	0.209238454	0.159500057	0.350204001	-0.049738397
SAE1   Q9UBED	0.88635216	0.440723021	0.673974852	0.977291229	0.998740558	0.42945901												



**Table 6.4: SRM Peptide Coefficients of Variation**

Gene	Protein Accession	Peptide	ATneg CV Total Area Ratio	ATpos CV Total Area Ratio	CV Total Area Ratio
AHSG	P02765	EHAVEGDCDFQLLK	9.40%	6.70%	22%
ALB	P02768	LVNEVTEFAK	3.80%	1.90%	21.50%
ALB	P02768	LVTDLTK	3.60%	2.50%	21.20%
ALDOA	P04075	VLAAYYK	7.30%	5.60%	16.10%
APOA4	P06727	SLAPYAQDTQEK	5%	3%	21.30%
APOC1	P02654	QSELSAK	8.60%	12.70%	28.80%
APOC2	P02655	TAAQNLYEK	3.50%	4.40%	16.10%
APOE	P02649	ELQAAQAR	4.60%	1.90%	13.30%
C9	P02748	TSNFNAISLK	10.50%	8.50%	18.50%
C9	P02748	LSPYNLVPVK	9%	6.70%	17.40%
CALM2	P0DP24	EAFSLFDK	9.80%	5.20%	18.30%
CD44	P16070	TEAADLCK	20.10%	14.60%	13.20%
CD44	P16070	ALSIGFETCR	26.80%	13.80%	13.40%
CHI3L1	P36222	IASNTQSR	6.60%	5.40%	20.10%
CHI3L1	P36222	GNQWVGYDDQESVK	8.90%	7.10%	21.20%
CHI3L1	P36222	QLLLSAALSAGK	6.50%	14.80%	23.40%
CP	P00450	EVGPTNADPVCLAK	10.30%	9.60%	12.70%
CP	P00450	GEFYIGSK	4.50%	2.90%	13.10%
CST3	P01034	ASNDMYHSR	15.40%	9.40%	15.70%
DCN	P07585	VDAASLK	7.40%	7.20%	8.70%
DDAH1	O94760	EFFVGLSK	14.10%	9.40%	18%
DKK3	Q9UBP4	DQDGEILLPR	5.50%	2.70%	12.50%
ENO1	P06733	IEEELGSK	11.70%	8.80%	21.20%
ENO1	P06733	LNVTQEK	9.20%	8.50%	18.20%
ENO2	P09104	IEEELGDEAR	10.80%	9.90%	16.60%
F2	P00734	YTACETAR	16.50%	16%	18%
F2	P00734	TATSEYQTFNPR	7.10%	6.60%	18.20%
GAPDH	P04406	AAFNSGK	16.90%	14.70%	27.60%
GAPDH	P04406	YDNSLK	11.60%	8.70%	20.40%
GDA	Q9Y2T3	DHLLGVSDSGK	13.70%	12.30%	23.20%
GOT1	P17174	VGNLTVVGK	7.90%	7.90%	18.40%
GOT1	P17174	IGADFLAR	6.80%	8.50%	16.40%
GSN	P06396	AGALNSNDAFVLK	4.70%	3.80%	12.60%
HBA1	P69905	FLASVSTVLSK	5.50%	2.90%	97.40%
HBA1	P69905	VGAHAGEYGAEALER	11.70%	10.10%	93.90%
HBB	P68871	VNVDEVGGEALGR	4.40%	2.90%	97.20%
KNG1	P01042	EGDCPVQSGK	11.80%	10.80%	17.80%
KNG1	P01042	QVVAGLNFR	10.40%	5.50%	20.60%
KNG1	P01042	VQVVAGK	5%	2.20%	20.90%
L1CAM	P32004	GQLSFNLR	9.10%	16.10%	13.40%
LAMP1	P11279	VWVQAFK	11.80%	12.70%	16.90%
LAMP2	P13473	YLDFFFAVK	13.10%	12.80%	15.10%
LDHB	P07195	FIPIQVK	7.30%	5.90%	17.50%
LDHC	P07864	VIGSGCNLDSAR	7.30%	8.80%	23.60%
MDH1	P40925	GEFVTTVQQR	7.20%	5.50%	20%
NCAM1	P13591	GLGEISAASEFK	5.90%	7%	15.50%
NPTX2	P47972	VAELEDEK	10.50%	15.30%	19.60%
NPTXR	O95502	ELDLVLQGR	4.70%	3.10%	13.80%
NRXN1	P58400	LAIGFSTVQK	11.50%	9%	15.40%
OGN	P20774	LEGNPIVLGK	6.20%	3.10%	8.60%
OMG	P23515	LESPLAHLPR	8.50%	6.10%	14.90%
PARK7	Q99497	ALVILAK	7.70%	4.90%	18%
PEBP1	P30086	GNDISSGTVLSYVVGSGPPK	7.40%	7.40%	17.70%
PEBP1	P30086	LYELSGK	11.70%	8.20%	17.70%
PEBP1	P30086	VLTPQVK	5.60%	3.10%	14.20%
PGLYRP2	Q96PD5	TFLLDPK	5%	3.10%	20.30%
PKM	P14618	VVEVGSK	3.50%	5.90%	20%
PKM	P14618	GVNLPGAAVDLPVSEK	5.50%	5.90%	21.40%
PKM	P14618	GDLGIEIPAEK	6.20%	5.80%	17.70%
PKM	P14618	GDYPLEAVR	5.30%	4.40%	18.60%
PKMisoform		LFEELVR	5.30%	4.40%	20.60%
PON1	P27169	LLIGTVFHK	7.70%	10%	22.10%
PPIA	P62937	VSFELFADK	6.60%	9.80%	18.70%
PRDX2	P32119	QITVNDLPVGR	15.10%	14.20%	32.10%
PTPRZ1	P23471	AIIDGVESVSR	6.50%	3.70%	13%
PTPRZ1	P23471	DIEGAIVNPGR	5%	4.20%	12%
SCG2	P13521	IESQTQEEVR	8.10%	7.40%	19%
SCG2	P13521	SGQLGIQEEDLR	7.10%	6.90%	21.30%
SMOC1	Q9H4F8	AQALEQAK	13.30%	9.20%	27.20%
SOD1	P00441	AVCVLK	13.60%	9.60%	23.30%
SOD1	P00441	GDGPVQGIINFEQK	11.40%	11.10%	18.50%
SOD1	P00441	HVGDLGNVTADK	11.10%	7%	19.90%
SPP1	P10451	GDSVVYGLR	24.30%	13.80%	14.70%
SPP1	P10451	YPDAVATWLNPDPSQK	9.60%	8.30%	15.30%
SPP1	P10451	QETLPSK	6.70%	7.10%	18.80%
THY1	P04216	HVLFGTVGVPEHTYR	11.40%	10%	17.90%
TP1	P60174	IAVAQNCYK	20.90%	24.50%	18.60%
VGF	O15240	EPVAGDAVPGPK	3.90%	2%	24.20%
VGF	O15240	GLQEAAEER	5.10%	5.40%	24.50%
VTN	P04004	GQCYELDEK	10.50%	5.60%	20.50%
VTN	P04004	DVWGIEGPIDAAFR	8.70%	7%	20.80%
YWHAB	P31946	NLLSVAYK	8.30%	9%	26.70%
YWHAB	P31946	VISSIEQK	11.80%	6.40%	18.60%
YWHAG	P61981	YLAEVATGEK	17.10%	9.30%	29.50%
YWHAZ	P63104	VVSSIEQK	15.10%	14.10%	35.40%

**Table 6.5: SRM Ratio Abundances Post-Regression**

[illegible]

PT	PT01	PT02	PT03	PT04	PT05	PT06	PT07	PT08	PT09	PT10	PT11	PT12	PT13	PT14	PT15	PT16	PT17	PT18	PT19	PT20	PT21	PT22	PT23	PT24	PT25	PT26	PT27	PT28	PT29	PT30	PT31	PT32	PT33	PT34	PT35	PT36	PT37	PT38	PT39	PT40	PT41	PT42	PT43	PT44	PT45	PT46	PT47	PT48	PT49	PT50	PT51	PT52	PT53	PT54	PT55	PT56	PT57	PT58	PT59	PT60	PT61	PT62	PT63	PT64	PT65	PT66	PT67	PT68	PT69	PT70	PT71	PT72	PT73	PT74	PT75	PT76	PT77	PT78	PT79	PT80	PT81	PT82	PT83	PT84	PT85	PT86	PT87	PT88	PT89	PT90	PT91	PT92	PT93	PT94	PT95	PT96	PT97	PT98	PT99	PT100
AD	AD01	AD02	AD03	AD04	AD05	AD06	AD07	AD08	AD09	AD10	AD11	AD12	AD13	AD14	AD15	AD16	AD17	AD18	AD19	AD20	AD21	AD22	AD23	AD24	AD25	AD26	AD27	AD28	AD29	AD30	AD31	AD32	AD33	AD34	AD35	AD36	AD37	AD38	AD39	AD40	AD41	AD42	AD43	AD44	AD45	AD46	AD47	AD48	AD49	AD50	AD51	AD52	AD53	AD54	AD55	AD56	AD57	AD58	AD59	AD60	AD61	AD62	AD63	AD64	AD65	AD66	AD67	AD68	AD69	AD70	AD71	AD72	AD73	AD74	AD75	AD76	AD77	AD78	AD79	AD80	AD81	AD82	AD83	AD84	AD85	AD86	AD87	AD88	AD89	AD90	AD91	AD92	AD93	AD94	AD95	AD96	AD97	AD98	AD99	AD100
AG	AG01	AG02	AG03	AG04	AG05	AG06	AG07	AG08	AG09	AG10	AG11	AG12	AG13	AG14	AG15	AG16	AG17	AG18	AG19	AG20	AG21	AG22	AG23	AG24	AG25	AG26	AG27	AG28	AG29	AG30	AG31	AG32	AG33	AG34	AG35	AG36	AG37	AG38	AG39	AG40	AG41	AG42	AG43	AG44	AG45	AG46	AG47	AG48	AG49	AG50	AG51	AG52	AG53	AG54	AG55	AG56	AG57	AG58	AG59	AG60	AG61	AG62	AG63	AG64	AG65	AG66	AG67	AG68	AG69	AG70	AG71	AG72	AG73	AG74	AG75	AG76	AG77	AG78	AG79	AG80	AG81	AG82	AG83	AG84	AG85	AG86	AG87	AG88	AG89	AG90	AG91	AG92	AG93	AG94	AG95	AG96	AG97	AG98	AG99	AG100
AL	AL01	AL02	AL03	AL04	AL05	AL06	AL07	AL08	AL09	AL10	AL11	AL12	AL13	AL14	AL15	AL16	AL17	AL18	AL19	AL20	AL21	AL22	AL23	AL24	AL25	AL26	AL27	AL28	AL29	AL30	AL31	AL32	AL33	AL34	AL35	AL36	AL37	AL38	AL39	AL40	AL41	AL42	AL43	AL44	AL45	AL46	AL47	AL48	AL49	AL50	AL51	AL52	AL53	AL54	AL55	AL56	AL57	AL58	AL59	AL60	AL61	AL62	AL63	AL64	AL65	AL66	AL67	AL68	AL69	AL70	AL71	AL72	AL73	AL74	AL75	AL76	AL77	AL78	AL79	AL80	AL81	AL82	AL83	AL84	AL85	AL86	AL87	AL88	AL89	AL90	AL91	AL92	AL93	AL94	AL95	AL96	AL97	AL98	AL99	AL100
AM	AM01	AM02	AM03	AM04	AM05	AM06	AM07	AM08	AM09	AM10	AM11	AM12	AM13	AM14	AM15	AM16	AM17	AM18	AM19	AM20	AM21	AM22	AM23	AM24	AM25	AM26	AM27	AM28	AM29	AM30	AM31	AM32	AM33	AM34	AM35	AM36	AM37	AM38	AM39	AM40	AM41	AM42	AM43	AM44	AM45	AM46	AM47	AM48	AM49	AM50	AM51	AM52	AM53	AM54	AM55	AM56	AM57	AM58	AM59	AM60	AM61	AM62	AM63	AM64	AM65	AM66	AM67	AM68	AM69	AM70	AM71	AM72	AM73	AM74	AM75	AM76	AM77	AM78	AM79	AM80	AM81	AM82	AM83	AM84	AM85	AM86	AM87	AM88	AM89	AM90	AM91	AM92	AM93	AM94	AM95	AM96	AM97	AM98	AM99	AM100
AN	AN01	AN02	AN03	AN04	AN05	AN06	AN07	AN08	AN09	AN10	AN11	AN12	AN13	AN14	AN15	AN16	AN17	AN18	AN19	AN20	AN21	AN22	AN23	AN24	AN25	AN26	AN27	AN28	AN29	AN30	AN31	AN32	AN33	AN34	AN35	AN36	AN37	AN38	AN39	AN40	AN41	AN42	AN43	AN44	AN45	AN46	AN47	AN48	AN49	AN50	AN51	AN52	AN53	AN54	AN55	AN56	AN57	AN58	AN59	AN60	AN61	AN62	AN63	AN64	AN65	AN66	AN67	AN68	AN69	AN70	AN71	AN72	AN73	AN74	AN75	AN76	AN77	AN78	AN79	AN80	AN81	AN82	AN83	AN84	AN85	AN86	AN87	AN88	AN89	AN90	AN91	AN92	AN93	AN94	AN95	AN96	AN97	AN98	AN99	AN100
AO	AO01	AO02	AO03	AO04	AO05	AO06	AO07	AO08	AO09	AO10	AO11	AO12	AO13	AO14	AO15	AO16	AO17	AO18	AO19	AO20	AO21	AO22	AO23	AO24	AO25	AO26	AO27	AO28	AO29	AO30	AO31	AO32	AO33	AO34	AO35	AO36	AO37	AO38	AO39	AO40	AO41	AO42	AO43	AO44	AO45	AO46	AO47	AO48	AO49	AO50	AO51	AO52	AO53	AO54	AO55	AO56	AO57	AO58	AO59	AO60	AO61	AO62	AO63	AO64	AO65	AO66	AO67	AO68	AO69	AO70	AO71	AO72	AO73	AO74	AO75	AO76	AO77	AO78	AO79	AO80	AO81	AO82	AO83	AO84	AO85	AO86	AO87	AO88	AO89	AO90	AO91	AO92	AO93	AO94	AO95	AO96	AO97	AO98	AO99	AO100
AP	AP01	AP02	AP03	AP04	AP05	AP06	AP07	AP08	AP09	AP10	AP11	AP12	AP13	AP14	AP15	AP16	AP17	AP18	AP19	AP20	AP21	AP22	AP23	AP24	AP25	AP26	AP27	AP28	AP29	AP30	AP31	AP32	AP33	AP34	AP35	AP36	AP37	AP38	AP39	AP40	AP41	AP42	AP43	AP44	AP45	AP46	AP47	AP48	AP49	AP50	AP51	AP52	AP53	AP54	AP55	AP56	AP57	AP58	AP59	AP60	AP61	AP62	AP63	AP64	AP65	AP66	AP67	AP68	AP69	AP70	AP71	AP72	AP73	AP74	AP75	AP76	AP77	AP78	AP79	AP80	AP81	AP82	AP83	AP84	AP85	AP86	AP87	AP88	AP89	AP90	AP91	AP92	AP93	AP94	AP95	AP96	AP97	AP98	AP99	AP100
AR	AR01	AR02	AR03	AR04	AR05	AR06	AR07	AR08	AR09	AR10	AR11	AR12	AR13	AR14	AR15	AR16	AR17	AR18	AR19	AR20	AR21	AR22	AR23	AR24	AR25	AR26	AR27	AR28	AR29	AR30	AR31	AR32	AR33	AR34	AR35	AR36	AR37	AR38	AR39	AR40	AR41	AR42	AR43	AR44	AR45	AR46	AR47	AR48	AR49	AR50	AR51	AR52	AR53	AR54	AR55	AR56	AR57	AR58	AR59	AR60	AR61	AR62	AR63	AR64	AR65	AR66	AR67	AR68	AR69	AR70	AR71	AR72	AR73	AR74	AR75	AR76	AR77	AR78	AR79	AR80	AR81	AR82	AR83	AR84	AR85	AR86	AR87	AR88	AR89	AR90	AR91	AR92	AR93	AR94	AR95	AR96	AR97	AR98	AR99	AR100
AS	AS01	AS02	AS03	AS04	AS05	AS06	AS07	AS08	AS09	AS10	AS11	AS12	AS13	AS14	AS15	AS16	AS17	AS18	AS19	AS20	AS21	AS22	AS23	AS24	AS25	AS26	AS27	AS28	AS29	AS30	AS31	AS32	AS33	AS34	AS35	AS36	AS37	AS38	AS39	AS40	AS41	AS42	AS43	AS44	AS45	AS46	AS47	AS48	AS49	AS50	AS51	AS52	AS53	AS54	AS55	AS56	AS57	AS58	AS59	AS60	AS61	AS62	AS63	AS64	AS65	AS66	AS67	AS68	AS69	AS70	AS71	AS72	AS73	AS74	AS75	AS76	AS77	AS78	AS79	AS80	AS81	AS82	AS83	AS84	AS85	AS86	AS87	AS88	AS89	AS90	AS91	AS92	AS93	AS94	AS95	AS96	AS97	AS98	AS99	AS100
AT	AT01	AT02	AT03	AT04	AT05	AT06	AT07	AT08	AT09	AT10	AT11	AT12	AT13	AT14	AT15	AT16	AT17	AT18	AT19	AT20	AT21	AT22	AT23	AT24	AT25	AT26	AT27	AT28	AT29	AT30	AT31	AT32	AT33	AT34	AT35	AT36	AT37	AT38	AT39	AT40	AT41	AT42	AT43	AT44	AT45	AT46	AT47	AT48	AT49	AT50	AT51	AT52	AT53	AT54	AT55	AT56	AT57	AT58	AT59	AT60	AT61	AT62	AT63	AT64	AT65	AT66	AT67	AT68	AT69	AT70	AT71	AT72	AT73	AT74	AT75	AT76	AT77	AT78	AT79	AT80	AT81	AT82	AT83	AT84	AT85	AT86	AT87	AT88	AT89	AT90	AT91	AT92	AT93	AT94	AT95	AT96	AT97	AT98	AT99	AT100
AV	AV01	AV02	AV03	AV04	AV05	AV06	AV07	AV08	AV09	AV10	AV11	AV12	AV13	AV14	AV15	AV16	AV17	AV18	AV19	AV20	AV21	AV22	AV23	AV24	AV25	AV26	AV27	AV28	AV29	AV30	AV31	AV32	AV33	AV34	AV35	AV36	AV37	AV38	AV39	AV40	AV41	AV42	AV43	AV44	AV45	AV46	AV47	AV48	AV49	AV50	AV51	AV52	AV53	AV54	AV55	AV56	AV57	AV58	AV59	AV60	AV61	AV62	AV63	AV64	AV65	AV66	AV67	AV68	AV69	AV70	AV71	AV72	AV73	AV74	AV75	AV76	AV77	AV78	AV79	AV80	AV81	AV82	AV83	AV84	AV85	AV86	AV87	AV88	AV89	AV90	AV91	AV92	AV93	AV94	AV95	AV96	AV97	AV98	AV99	AV100
AW	AW01	AW02	AW03	AW04	AW05	AW06	AW07	AW08	AW09	AW10	AW11	AW12	AW13	AW14	AW15	AW16	AW17	AW18	AW19	AW20	AW21	AW22	AW23	AW24	AW25	AW26	AW27	AW28	AW29	AW30	AW31	AW32	AW33	AW34	AW35	AW36	AW37	AW38	AW39	AW40	AW41	AW42	AW43	AW44	AW45	AW46	AW47	AW48	AW49	AW50	AW51	AW52	AW53	AW54	AW55	AW56	AW57	AW58	AW59	AW60	AW61	AW62	AW63	AW64	AW65	AW66	AW67	AW68	AW69	AW70	AW71	AW72	AW73	AW74	AW75	AW76	AW77	AW78	AW79	AW80	AW81	AW82	AW83	AW84	AW85	AW86	AW87	AW88	AW89	AW90	AW91	AW92	AW93	AW94	AW95	AW96	AW97	AW98	AW99	AW100
AX	AX01	AX02	AX03	AX04	AX05	AX06	AX07	AX08	AX09	AX10	AX11	AX12	AX13	AX14	AX15	AX16	AX17	AX18	AX19	AX20	AX21	AX22	AX23	AX24	AX25	AX26	AX27	AX28	AX29	AX30	AX31	AX32	AX33	AX34	AX35	AX36	AX37	AX38	AX39	AX40	AX41	AX42	AX43	AX44	AX45	AX46	AX47	AX48	AX49	AX50	AX51	AX52	AX53	AX54	AX55	AX56	AX57	AX58	AX59	AX60	AX61	AX62	AX63	AX64	AX65	AX66	AX67	AX68	AX69	AX70	AX71	AX72	AX73	AX74	AX75	AX76	AX77	AX78	AX79	AX80	AX81	AX82	AX83	AX84	AX85	AX86	AX87	AX88	AX89	AX90	AX91	AX92	AX93	AX94	AX95	AX96	AX97	AX98	AX99	AX100
AY	AY01	AY02	AY03	AY04	AY05	AY06	AY07	AY08	AY09	AY10	AY11	AY12	AY13	AY14	AY15	AY16	AY17	AY18	AY19	AY20	AY21	AY22	AY23	AY24	AY25	AY26	AY27	AY28	AY29	AY30	AY31	AY32	AY33	AY34	AY35	AY36	AY37	AY38	AY39	AY40	AY41	AY42	AY43	AY44	AY45	AY46	AY47	AY48	AY49	AY50	AY51	AY52	AY53	AY54	AY55	AY56	AY57	AY58	AY59	AY60	AY61	AY62	AY63	AY64	AY65	AY66	AY67	AY68	AY69	AY70	AY71	AY72	AY73	AY74	AY75	AY76	AY77	AY78	AY79	AY80	AY81	AY82	AY83	AY84	AY85	AY86	AY87	AY88	AY89	AY90	AY91	AY92	AY93	AY94	AY95	AY96	AY97	AY98	AY99	AY100
AZ	AZ01	AZ02	AZ03	AZ04	AZ05	AZ06	AZ07	AZ08	AZ09	AZ10	AZ11	AZ12	AZ13	AZ14	AZ15	AZ16	AZ17	AZ18	AZ19	AZ20	AZ21	AZ22	AZ23	AZ24	AZ25	AZ26																																																																										





**SUPPLEMENTAL TABLE 11: SRM RATIO ABUNDANCES POST-REGRESSION**

[illegible]

**SUPPLEMENTAL TABLE 11: SRM RATIO ABUNDANCES POST-REGRESSION**

RA1	RA101	RA102	RA103	RA104	RA105	RA106	RA107	RA108	RA109	RA110	RA111	RA112	RA113	RA114	RA115	RA116	RA117	RA118	RA119	RA120	RA121	RA122	RA123	RA124	RA125	RA126	RA127	RA128	RA129	RA130	RA131	RA132	RA133	RA134	RA135	RA136	RA137	RA138	RA139	RA140	RA141	RA142	RA143	RA144	RA145	RA146	RA147	RA148	RA149	RA150	RA151	RA152	RA153	RA154	RA155	RA156	RA157	RA158	RA159	RA160	RA161	RA162	RA163	RA164	RA165	RA166	RA167	RA168	RA169	RA170	RA171	RA172	RA173	RA174	RA175	RA176	RA177	RA178	RA179	RA180	RA181	RA182	RA183	RA184	RA185	RA186	RA187	RA188	RA189	RA190	RA191	RA192	RA193	RA194	RA195	RA196	RA197	RA198	RA199	RA200	RA201	RA202	RA203	RA204	RA205	RA206	RA207	RA208	RA209	RA210	RA211	RA212	RA213	RA214	RA215	RA216	RA217	RA218	RA219	RA220	RA221	RA222	RA223	RA224	RA225	RA226	RA227	RA228	RA229	RA230	RA231	RA232	RA233	RA234	RA235	RA236	RA237	RA238	RA239	RA240	RA241	RA242	RA243	RA244	RA245	RA246	RA247	RA248	RA249	RA250	RA251	RA252	RA253	RA254	RA255	RA256	RA257	RA258	RA259	RA260	RA261	RA262	RA263	RA264	RA265	RA266	RA267	RA268	RA269	RA270	RA271	RA272	RA273	RA274	RA275	RA276	RA277	RA278	RA279	RA280	RA281	RA282	RA283	RA284	RA285	RA286	RA287	RA288	RA289	RA290	RA291	RA292	RA293	RA294	RA295	RA296	RA297	RA298	RA299	RA300	RA301	RA302	RA303	RA304	RA305	RA306	RA307	RA308	RA309	RA310	RA311	RA312	RA313	RA314	RA315	RA316	RA317	RA318	RA319	RA320	RA321	RA322	RA323	RA324	RA325	RA326	RA327	RA328	RA329	RA330	RA331	RA332	RA333	RA334	RA335	RA336	RA337	RA338	RA339	RA340	RA341	RA342	RA343	RA344	RA345	RA346	RA347	RA348	RA349	RA350	RA351	RA352	RA353	RA354	RA355	RA356	RA357	RA358	RA359	RA360	RA361	RA362	RA363	RA364	RA365	RA366	RA367	RA368	RA369	RA370	RA371	RA372	RA373	RA374	RA375	RA376	RA377	RA378	RA379	RA380	RA381	RA382	RA383	RA384	RA385	RA386	RA387	RA388	RA389	RA390	RA391	RA392	RA393	RA394	RA395	RA396	RA397	RA398	RA399	RA400	RA401	RA402	RA403	RA404	RA405	RA406	RA407	RA408	RA409	RA410	RA411	RA412	RA413	RA414	RA415	RA416	RA417	RA418	RA419	RA420	RA421	RA422	RA423	RA424	RA425	RA426	RA427	RA428	RA429	RA430	RA431	RA432	RA433	RA434	RA435	RA436	RA437	RA438	RA439	RA440	RA441	RA442	RA443	RA444	RA445	RA446	RA447	RA448	RA449	RA450	RA451	RA452	RA453	RA454	RA455	RA456	RA457	RA458	RA459	RA460	RA461	RA462	RA463	RA464	RA465	RA466	RA467	RA468	RA469	RA470	RA471	RA472	RA473	RA474	RA475	RA476	RA477	RA478	RA479	RA480	RA481	RA482	RA483	RA484	RA485	RA486	RA487	RA488	RA489	RA490	RA491	RA492	RA493	RA494	RA495	RA496	RA497	RA498	RA499	RA500	RA501	RA502	RA503	RA504	RA505	RA506	RA507	RA508	RA509	RA510	RA511	RA512	RA513	RA514	RA515	RA516	RA517	RA518	RA519	RA520	RA521	RA522	RA523	RA524	RA525	RA526	RA527	RA528	RA529	RA530	RA531	RA532	RA533	RA534	RA535	RA536	RA537	RA538	RA539	RA540	RA541	RA542	RA543	RA544	RA545	RA546	RA547	RA548	RA549	RA550	RA551	RA552	RA553	RA554	RA555	RA556	RA557	RA558	RA559	RA560	RA561	RA562	RA563	RA564	RA565	RA566	RA567	RA568	RA569	RA570	RA571	RA572	RA573	RA574	RA575	RA576	RA577	RA578	RA579	RA580	RA581	RA582	RA583	RA584	RA585	RA586	RA587	RA588	RA589	RA590	RA591	RA592	RA593	RA594	RA595	RA596	RA597	RA598	RA599	RA600	RA601	RA602	RA603	RA604	RA605	RA606	RA607	RA608	RA609	RA610	RA611	RA612	RA613	RA614	RA615	RA616	RA617	RA618	RA619	RA620	RA621	RA622	RA623	RA624	RA625	RA626	RA627	RA628	RA629	RA630	RA631	RA632	RA633	RA634	RA635	RA636	RA637	RA638	RA639	RA640	RA641	RA642	RA643	RA644	RA645	RA646	RA647	RA648	RA649	RA650	RA651	RA652	RA653	RA654	RA655	RA656	RA657	RA658	RA659	RA660	RA661	RA662	RA663	RA664	RA665	RA666	RA667	RA668	RA669	RA670	RA671	RA672	RA673	RA674	RA675	RA676	RA677	RA678	RA679	RA680	RA681	RA682	RA683	RA684	RA685	RA686	RA687	RA688	RA689	RA690	RA691	RA692	RA693	RA694	RA695	RA696	RA697	RA698	RA699	RA700	RA701	RA702	RA703	RA704	RA705	RA706	RA707	RA708	RA709	RA710	RA711	RA712	RA713	RA714	RA715	RA716	RA717	RA718	RA719	RA720	RA721	RA722	RA723	RA724	RA725	RA726	RA727	RA728	RA729	RA730	RA731	RA732	RA733	RA734	RA735	RA736	RA737	RA738	RA739	RA740	RA741	RA742	RA743	RA744	RA745	RA746	RA747	RA748	RA749	RA750	RA751	RA752	RA753	RA754	RA755	RA756	RA757	RA758	RA759	RA760	RA761	RA762	RA763	RA764	RA765	RA766	RA767	RA768	RA769	RA770	RA771	RA772	RA773	RA774	RA775	RA776	RA777	RA778	RA779	RA780	RA781	RA782	RA783	RA784	RA785	RA786	RA787	RA788	RA789	RA790	RA791	RA792	RA793	RA794	RA795	RA796	RA797	RA798	RA799	RA800	RA801	RA802	RA803	RA804	RA805	RA806	RA807	RA808	RA809	RA810	RA811	RA812	RA813	RA814	RA815	RA816	RA817	RA818	RA819	RA820	RA821	RA822	RA823	RA824	RA825	RA826	RA827	RA828	RA829	RA830	RA831	RA832	RA833	RA834	RA835	RA836	RA837	RA838	RA839	RA840	RA841	RA842	RA843	RA844	RA845	RA846	RA847	RA848	RA849	RA850	RA851	RA852	RA853	RA854	RA855	RA856	RA857	RA858	RA859	RA860	RA861	RA862	RA863	RA864	RA865	RA866	RA867	RA868	RA869	RA870	RA871	RA872	RA873	RA874	RA875	RA876	RA877	RA878	RA879	RA880	RA881	RA882	RA883	RA884	RA885	RA886	RA887	RA888	RA889	RA890	RA891	RA892	RA893	RA894	RA895	RA896	RA897	RA898	RA899	RA900	RA901	RA902	RA903	RA904	RA905	RA906	RA907	RA908	RA909	RA910	RA911	RA912	RA913	RA914	RA915	RA916	RA917	RA918	RA919	RA920	RA921	RA922	RA923	RA924	RA925	RA926	RA927	RA928	RA929	RA930	RA931	RA932	RA933	RA934	RA935	RA936	RA937	RA938	RA939	RA940	RA941	RA942	RA943	RA944	RA945	RA946	RA947	RA948	RA949	RA950	RA951	RA952	RA953	RA954	RA955	RA956	RA957	RA958	RA959	RA960	RA961	RA962	RA963	RA964	RA965	RA966	RA967	RA968	RA969	RA970	RA971	RA972	RA973	RA974	RA975	RA976	RA977	RA978	RA979	RA980	RA981	RA982	RA983	RA984	RA985	RA986	RA987	RA988	RA989	RA990	RA991	RA992	RA993	RA994	RA995	RA996	RA997	RA998	RA999	RA1000
-----	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	--------

[illegible]



155

**Appendix Table 6.6: Correlation Values Between SRM and TMT-MS**

Gene ID   Protein ID   Peptide Sequence	bicor	p
AHS6   P02765   EHAVEGDC[+57]DFQLLK	0.7623983	1.14E-35
ALB   P02768   LVNEVTEFAK	0.77247034	3.87E-37
ALB   P02768   LVTDLTK	0.77556186	1.33E-37
ALDOA   P04075   VLAAYVK	0.71463278	1.37E-29
APOA4   P06727   SLAPYAQDTQEK	0.78931886	9.04E-40
APOC1   P02654   QSELSAK	0.81232011	8.85E-44
APOC2   P02655   TAAQNLYEK	0.84048111	1.63E-49
APOE   P02649   ELQAAQAR	0.6667207	1.25E-24
C9   P02748   TSNFNAAISLK	0.77327779	2.93E-37
C9   P02748   LSPYNLVPVK	0.77415659	2.16E-37
CD44   P16070   TEADLC[+57]K	0.33081839	5.40E-06
CD44   P16070   ALSIGFETC[+57]R	0.31900572	1.20E-05
CHI3L1   P36222   IASNTQSR	0.71941149	3.84E-30
CHI3L1   P36222   GNQWVGYYDDQESVK	0.72160382	2.13E-30
CHI3L1   P36222   QLLLSAALSAGK	0.71404577	1.59E-29
CP   P00450   EVGPTNADPVC[+57]LAK	0.69862608	7.98E-28
CP   P00450   GEFYIGSK	0.70157352	3.85E-28
CST3   P01034   ASNDM[+16]YHSR	0.71430865	1.49E-29
DCN   P07585   VDAASLK	0.34992095	1.37E-06
DDAH1   O94760   EFFVGLSK	0.48536443	4.36E-12
DKK3   Q9UBP4   DQDGEILLPR	0.64903925	5.04E-23
ENO1   P06733   IEELGSK	0.41121196	8.90E-09
ENO1   P06733   LNVTEQEK	0.39346754	4.26E-08
ENO2   P09104   IEELGDEAR	0.47383191	1.61E-11
F2   P00734   YTAC[+57]ETAR	0.66718198	1.13E-24
F2   P00734   TATSEYQTFNPR	0.7185046	4.90E-30
GAPDH   P04406   AAFNSGK	0.82854423	5.90E-47
GAPDH   P04406   YDNSLK	0.8186034	5.68E-45
GDA   Q9Y2T3   DHLLGVSDSGK	0.78616363	2.93E-39
GOT1   P17174   VGNLTVVGK	0.76070551	1.97E-35
GOT1   P17174   IGADFLAR	0.71338808	1.89E-29
GSN   P06396   AGALNSNDAFVLK	0.32361528	8.84E-06
HBA1   P69905   FLASVSVLTSLK	0.83492507	2.68E-48
HBA1   P69905   VGHAGEYGAEALER	0.76278902	1.00E-35
HBB   P68871   VNVDEVGGEALGR	0.80742692	6.99E-43
KNG1   P01042   EGDG[+57]PVQSGK	0.75355351	1.93E-34
KNG1   P01042   QVVAGLNFR	0.8176424	8.71E-45
KNG1   P01042   QVVVAGK	0.79004004	6.89E-40
L1CAM   P32004   GLSFLNLR	0.41209368	8.22E-09
LAMP1   P11279   VVVQAFK	0.38645987	7.72E-08
LAMP2   P13473   YLDFVFAVK	0.26890252	0.00025192
LDHB   P07195   FIIPQIVK	0.58318093	7.04E-18
MDH1   P40925   GEFVTVVQQR	0.71399458	1.62E-29
NCAM1   P13591   GLGEISAASEFK	0.76507851	4.70E-36
NPTX2   P47972   VAELEDEK	0.82254472	9.61E-46
NPTXR   O95502   ELDVLQGR	0.86521236	1.48E-55
NRXN1   P58400   LAIGFSTVQK	0.50862443	2.67E-13
OGN   P20774   LEGNPVLGK	0.2992511	4.27E-05
OMG   P23515   LESLPAHLPR	0.70425667	1.97E-28
PARK7   Q99497   ALVILAK	0.68806487	1.01E-26
PEBP1   P30086   GNDISSGTVLSDYVSGPPK	0.61326383	4.43E-20
PEBP1   P30086   LYEQLSGK	0.5461355	1.84E-15
PEBP1   P30086   VLTPTQVK	0.62020993	1.27E-20
PGLYRP2   Q96PD5   TFTLLDPK	0.75042625	5.11E-34
PKM   P14618   VVEVGSK	0.79626334	6.31E-41
PKM   P14618   GVNLPGAAVDLPVSEK	0.81283689	7.09E-44
PKM   P14618   GDLGIEIPAEK	0.7631657	8.84E-36
PKM   P14618   GDYPLEAVR	0.74440429	3.20E-33
PON1   P27169   LLIGTVFHK	0.85372793	1.30E-52
PPIA   P62937   VSFELFADK	0.42243149	3.15E-09
PRDX2   P32119   QITVNDLPVGR	0.5266618	2.63E-14
PTPRZ1   P23471   AIIDGVESVSR	0.59743528	6.82E-19
PTPRZ1   P23471   DIEEGAIVNPGR	0.55556383	4.76E-16
SCG2   P13521   IESQTQEEVR	0.83392878	4.38E-48
SCG2   P13521   SGQLGIQEEELR	0.69455479	2.15E-27
SMOC1   Q9H4F8   AQALEQAK	0.60304712	2.63E-19
SOD1   P00441   AVC[+57]VLK	0.64804803	6.15E-23
SOD1   P00441   GDGVPVQGIINFEQK	0.52708324	2.49E-14
SOD1   P00441   HVGDLGNVTADK	0.60438204	2.09E-19
SPP1   P10451   GDSVVYGLR	0.40604161	1.42E-08
SPP1   P10451   YPDVAATWLNPDPSQK	0.57766062	1.69E-17
SPP1   P10451   QETLPSK	0.53791195	5.78E-15
THY1   P04216   HVLFGTVGVPEHTYR	0.55672045	4.02E-16
TP11   P60174   IAAVAQNC[+57]YK	0.36815258	3.42E-07
VGf   O15240   EPVAGDAVPGPK	0.91564949	9.22E-73
VGf   O15240   GLQEAAEER	0.89844556	6.87E-66
VTN   P04004   GQYC[+57]YELDEK	0.73038636	1.88E-31
VTN   P04004   DVWGIQEPIDAAFTR	0.79647096	5.82E-41
YWHAB   P31946   NLLSVAYK	0.45898158	8.12E-11
YWHAB   P31946   VISSIEQK	0.41491193	6.35E-09
YWHAG   P61981   YLAEVATGEK	0.6193641	1.48E-20
YWHAZ   P63104   VVSSIEQK	0.61819486	1.83E-20

**Appendix Table 6.7: SRM Culled Protein List**

Gene ID   Protein ID   Peptide Sequence	Short Name
AHSG   P02765   EHAVEGDC[+57]DFQLLK	AHSG
ALB   P02768   LVTDLTk	ALB
ALDOA   P04075   VLAADVYK	ALDOA
APOA4   P06727   SLAPYAQDTQEK	APOA4
APOC1   P02654   QSELSAK	APOC1
APOC2   P02655   TAAQNLYEK	APOC2
APOE   P02649   ELQAAQAR	APOE
C9   P02748   LSPIYNLVPVK	C9
CALM2   P0DP24   EAFSLFDK	CALM2
CD44   P16070   TEAADLC[+57]K	CD44
CHI3L1   P36222   GNQWVGYYDDQESVK	CHI3L1
CP   P00450   GEFYIGSK	CP
CST3   P01034   ASNDM[+16]YHSR	CST3
DCN   P07585   VDAASLK	DCN
DDAH1   O94760   EFFVGLSK	DDAH1
DKK3   Q9UBP4   DQDGEILLPR	DKK3
ENO1   P06733   IEEELGSK	ENO1
ENO2   P09104   IEEELGDEAR	ENO2
F2   P00734   TATSEYQTFFNPR	F2
GAPDH   P04406   AAFNSGK	GAPDH
GDA   Q9Y2T3   DHLLGVSDSGK	GDA
GOT1   P17174   VGNLTVVGK	GOT1
GSN   P06396   AGALNSNDAFVLK	GSN
HBA1   P69905   FLASVSTVLTSK	HBA1
HBB   P68871   VNVDEVGGEALGR	HBB
KNG1   P01042   QVVAGLNFR	KNG1
L1CAM   P32004   GQLSFNLR	L1CAM
LAMP1   P11279   VWVQAFK	LAMP1
LAMP2   P13473   YLDFVFAVK	LAMP2
LDHB   P07195   FIIPQIVK	LDHB
LDHC   P07864   VIGSGC[+57]NLDSAR	LDHC
MDH1   P40925   GEFVTTVQQR	MDH1
NCAM1   P13591   GLGEISAASEFK	NCAM1
NPTX2   P47972   VAELEDEK	NPTX2
NPTXR   O95502   ELDVLQGR	NPTXR
NRXN1   P58400   LAIGFSTVQK	NRXN1
OGN   P20774   LEGNPIVLGK	OGN
OMG   P23515   LESLPAHLPR	OMG
PARK7   Q99497   ALVILAK	PARK7
PEBP1   P30086   VLTPTQVK	PEBP1
PGLYRP2   Q96PD5   TFTLLDPK	PGLYRP2
PKM   P14618   GVNLPGAADVLPVSEK	PKM
PKMisoform   NA   LFEELVR	PKMisoform
PON1   P27169   LLIGTVFHK	PON1
PPIA   P62937   VSELFADK	PPIA
PRDX2   P32119   QITVNDLPVGR	PRDX2
PTPRZ1   P23471   AIIDGVESVSR	PTPRZ1
SCG2   P13521   IESQTQEEVR	SCG2
SMOC1   Q9H4F8   AQALEQAK	SMOC1
SOD1   P00441   AVC[+57]VLK	SOD1
SPP1   P10451   YPDAVATWLNPDPSQK	SPP1
THY1   P04216   HVLFGTVGVPEHTYR	THY1
TPI1   P60174   IAVAAQNC[+57]YK	TPI1
VGf   O15240   EPVAGDAVPGPK	VGf
VTN   P04004   DVWGIEGPIDAAFTR	VTN
YWHAB   P31946   NLLSVAYK	YWHAB
YWHAG   P61981   YLAEVATGEK	YWHAG
YWHAZ   P63104   VVSSIEQK	YWHAZ

Appendix Table 6.8: SRM ANOVA Table

Gene ID   Protein ID   Peptide Sequence	F-Value	Pr(>F)	ANOVA p-values with Tukey Adjustment						Difference (AD - CT)					
			AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs CT-AA	AD-Cau vs AD-AA	CT-AA vs AD-AA	CT-Cau vs AD-AA	CT-AA vs AD-Cau	CT-Cau vs AD-Cau	CT-Cau vs CT-AA	CT-Cau vs CT-AA
AHSG   P02765   EHVLEDCQ<+57>DFQLLK	1.3396216	0.2628129	0.474086776	0.567944286	0.231890054	0.998878903	0.974327169	0.940159403	0.160646479	0.144026653	0.208064444	-0.016619826	0.047417985	0.064037811
ALB   P02748   LVDTLTK	1.4734736	0.2231127	0.560749882	0.999833888	0.386011551	0.52910704	0.993836008	0.361096177	0.151464229	-0.008969364	0.181759163	-0.160433593	0.030294934	0.190728526
ALDOA   P04075   VLAAYVK	10.174229	3.01E-06	0.017180245	0.05510928	0.891608328	1.06E-06	0.001827786	0.25670715	0.254410371	-0.218243155	-0.060023526	-0.47265526	-0.31443898	0.158219629
AP0A4   P06727   SLAPVQDQTEK	7.068182	0.0001573	0.001073693	0.68240995	0.001938129	0.043786257	0.99626835	0.06896345	0.487403173	0.142354234	0.459208662	-0.345048939	-0.028194511	0.316854428
AP0C1   P02654   QSELSAK	4.7228839	0.0033382	0.023895768	0.604700618	0.005179218	0.383820323	0.971300003	0.169970479	0.32883891	0.141953217	0.379702922	-0.186885693	0.050864012	0.237749705
AP0C2   P02655   TAAQNLYEK	4.0879524	0.0076726	0.055752971	0.220193185	0.005539559	0.92884694	0.883475114	0.530546559	0.355718941	0.268897924	0.458573753	-0.086821017	0.102854812	0.189675828
AP0C4   P02649   ELQAAQAR	5.4560937	0.0012788	0.015879176	0.999320335	0.022145615	0.026818767	0.998585772	0.036804745	0.25881093	0.010664937	0.245113456	-0.248145993	0.013697474	0.23448519
C9   P02748   LSPYNYLVVK	0.3536492	0.7864062	0.797378492	0.995145015	0.999989941	0.928382144	0.815237848	0.993873772	0.110681286	0.035160214	0.003615085	-0.075521072	-0.107065201	-0.031545129
CALM2   P00P24   EAFSLFDK	9.8850152	4.33E-06	0.08035563	0.13775141	0.923610412	2.09E-06	0.001020972	0.416682532	0.265238542	-0.177851995	-0.050690164	-0.443090538	-0.315928707	0.127161831
CD44   P16070   TEADLCQ<+57>K	3.6944437	0.012848	0.044301701	0.955066897	0.896731038	0.012139633	0.215171448	0.627379969	0.172513572	-0.033772955	0.045092249	-0.206286527	-0.127421323	0.078865204
CH13L1   P36222   QGVGVVQDQESVK	16.294013	1.80E-09	0.035954989	0.000155743	0.631102228	4.93E-10	0.000842457	0.011343493	0.27185023	-0.430802889	-0.117652276	-0.702653119	-0.389502506	0.313150612
CP   P00405   GFYFIQSK	0.5886242	0.6231626	0.553090124	0.943543602	0.878079104	0.880110799	0.938062504	0.998145304	0.135882844	0.057830795	0.075790988	-0.078052049	-0.060091856	0.017960193
CST3   P01834   ASNDML<+16>YHSR	6.2114283	0.0004776	0.001854471	0.999845797	0.108796562	0.003097524	0.490328835	0.141738964	0.320772007	0.006611731	0.195918623	-0.314160275	-0.189306892	0.189306892
DCN   P07585   VDAASLK	0.8397242	0.4736246	0.641646728	0.999388245	0.628956628	0.727773387	0.999999999	0.71754541	-0.05695656	-0.005778465	-0.057018131	0.051178095	-4.16E-05	-0.051239666
DDAH1   P04760   EFVVLGSK	8.7911555	1.73E-05	0.030486889	0.076283343	0.981165867	4.93E-06	0.01070231	0.176587153	0.198120554	-0.172840243	-0.026491617	-0.370960797	-0.224612171	0.146348626
DK3   C09J94   DDQDGLLPR	4.1153167	0.0074023	0.018359658	0.94923062	0.065689771	0.087007876	0.957243976	0.233183281	0.276084605	0.05042026	0.228441757	-0.225664345	-0.047642847	0.178021497
END1   P06733   IEEELGSK	17.030119	7.64E-10	0.794881612	3.32E-06	0.00755116	6.49E-08	2.48E-05	0.543841784	0.069798944	-0.39360421	-0.291935805	-0.463403154	-0.361734749	0.101668405
END2   P09104   IEEELDEAR	5.7336845	0.00089	0.53270156	0.040546901	0.570576586	0.000652094	0.048143582	0.503654161	0.097334969	-0.192713168	-0.091566684	-0.290048137	-0.189016564	0.101146484
F2   P00734   TATSEVQTFNPR	0.1261265	0.9445471	0.94197397	0.999667166	0.99956457	0.967770879	0.967778778	0.999999851	0.064195398	0.011052583	0.011900774	-0.053142815	-0.025229464	0.000848191
GAPDH   P04406   AAFNFSK	18.541109	1.34E-10	0.586856703	1.65E-05	1.97E-05	6.66E-08	0.96662968	0.15650007	-0.597993413	-0.540178962	-0.754494114	-0.696679663	-0.057814451	-0.057814451
GDA   Q0Y273   DHIILGVSDSGK	14.390617	1.72E-08	0.00285772	0.012872102	0.884658982	4.63E-09	0.000207764	0.092110587	0.33830207	-0.294112343	-0.06882872	-0.632414413	-0.407130348	0.225284064
GOT1   P17174   VGNLTVGVK	8.5114058	2.46E-05	0.042023181	0.07467602	0.924504692	8.45E-06	0.007251447	0.276854869	0.245745412	-0.223849661	-0.056715579	-0.469595073	-0.302461002	0.167134071
GSN   P06396   IAGALNSNDAPVLK	3.6466483	0.0136775	0.066301657	0.884672384	0.923939872	0.010244588	0.243378466	0.54948093	0.181281559	-0.053412143	0.043753808	-0.234693703	-0.137527751	0.097169591
HBA1   P06905   FLASVTVLSK	1.8404758	0.1412143	0.688225108	0.99826558	0.237297623	0.597738457	0.876431725	0.185494127	-0.600484676	0.092247722	-1.010991307	0.692731896	-0.410566631	-1.103738527
HBB   P68871   VNVDEVGGALGR	2.32807	0.0759095	0.471441228	0.999654801	0.154500976	0.43019762	0.924425675	0.137617472	-0.974579116	0.064394448	-1.396414228	1.041018564	-0.421835112	-1.462853676
KNG1   P01042   QVAVGLNFR	0.5385811	0.6564125	0.820225454	0.99799112	0.877461765	0.733563444	0.999148893	0.799653101	-0.113986756	0.023313687	-0.096423811	0.137300443	0.017562945	-0.119377498
LICAM   P32004   GVLGFNLNR	0.093145	0.9637523	0.999912402	0.985270534	0.998071967	0.992183337	0.995469588	0.954191413	0.003282144	-0.01838678	-0.009084311	0.015106534	-0.012366455	-0.027472889
LAMP1   P11279   VVWVQAFK	5.3514801	0.0014662	0.132341239	0.234292876	0.987930909	0.000534872	0.253359955	0.125649981	0.158505253	-0.137629474	0.023387568	-0.296134728	-0.135117686	0.161017042
LAMP2   P13473   YLDFVFAVK	2.3746803	0.0714969	0.345176041	0.841812692	0.709686326	0.072737613	0.928418795	0.245171595	0.138832849	-0.068927313	0.087620352	-0.207760162	-0.051212497	0.156547665
LDHB   P07195   RHPQVVK	10.870453	1.26E-06	0.102383459	0.024141047	0.088770791	5.98E-06	4.59E-05	0.950273544	0.189724771	-0.236247714	-0.191794518	-0.425971985	-0.381518788	0.04453197
LDHC   P07684   VIGSGCQ<+57>NLDASR	26.440708	2.38E-14	0.313834644	2.04E-05	8.79E-08	7.92E-09	1.31E-11	0.728779159	0.182827987	-0.507006002	-0.617322064	-0.689833989	-0.800150051	-0.110316062
MDH1   P40925   GEPVTVVQQR	17.570267	4.09E-10	0.052687709	0.000269633	0.022401882	2.28E-09	1.25E-06	0.550228699	0.207863584	-0.336972637	-0.229624758	-0.544836219	-0.437488342	0.107347877
NCAM1   P13591   GIGESASSEFK	9.6567936	5.77E-06	0.000205891	0.999998366	0.004881501	0.000306986	0.800774727	0.006464913	0.369088176	0.001441961	0.289621508	-0.367464214	-0.079465667	0.288180547
NPTX2   P47972   VAELEDEK	14.320392	1.87E-08	0.002246385	3.24E-05	1.28E-08	0.718761312	0.052388836	0.43646447	0.318446168	0.41332353	0.546955533	0.094877361	0.228509364	0.133632003
NPTXR   Q95502   ELVDLQGR	11.374712	6.74E-07	0.002975649	0.009208332	1.77E-07	0.986898328	0.138725346	0.063263917	0.289343027	0.261256179	0.467467578	-0.028086848	-0.178145551	0.206211399
NRXN1   P58400   LAIGFSTVQK	4.3790295	0.0052388	0.012728391	0.873131688	0.038550944	0.108061632	0.973889804	0.239541207	0.293541207	0.072319195	0.252659369	-0.221222101	-0.040881838	0.180340174
OGN   P20774   LEGNPVVLGK	1.3252112	0.2674555	0.971176757	0.82314577	0.511753895	0.57672992	0.27948397	0.960333897	0.029861415	-0.05847352	-0.092052756	-0.088334935	-0.129194171	0.037952936
OMG   P23515   LESLPAHLPR	7.1426892	0.0001428	0.011393561	0.999947435	0.003000718	0.016066064	0.985147457	0.00457736	0.278102215	0.00470359	0.309589204	-0.273398625	0.031486989	0.304885614
PARK7   Q99497   ALVILAK	15.790007	3.26E-09	0.443539456	0.000865847	0.000183232	2.36E-06	3.21E-07	0.987579629	0.121302854	-0.314064558	-0.340988963	-0.435367412	-0.262921818	-0.026924406
PEPFI   P30086   VLPTTQVK	8.8334042	1.64E-05	0.031720403	0.085660362	0.88176623	6.56E-06	0.003447763	0.358837809	0.213046555	-0.183073685	-0.05599928	-0.396120241	-0.269045835	0.127074406
PGLYBP2   Q96P05   TFFLLDLPK	6.5011868	0.0003278	0.000324031	0.049125468	0.00481251	0.443481747	0.858580524	0.886556143	0.495458115	0.312335988	0.400024045	-0.185122127	-0.09543407	0.087688057
PKM   P14618   GVNLPQAADVPAVSEK	16.384755	1.62E-09	0.008241931	0.002054457	0.27652835	1.29E-09	9.04E-06	0.254093124	0.293431272	-0.331099883	-0.1616406	-0.624531255	-0.455071872	0.169459383
PKMisoform   NA   ILEEVLR	12.424908	1.84E-07	0.083047304	0.044530663	0.146173467	3.09E-07	8.00E-05	0.568463751	0.202033174	-0.2877427	-0.177769226	-0.489775874	-0.379802399	0.099373475
PON1   P27169   LUIGTVFHK	0.0470855	0.9864194	0.995868664	0.989097202	0.987424468	0.999762047	0.999651238	0.999999578	0.033217628	0.046251968	0.047803852	0.013034339	0.014586224	0.001551884
PP1A   P26937   VSFELFADK	13.936988	2.96E-08	0.79909781	0.000348451	0.000302146	1.05E-05	8.52E-06	0.999991365	0.068196327	-0.302190515	-0.300057591	-0.370386842	-0.368253918	0.002132924
PRDX2   P32119   QITVNDLPVGR	0.2401885	0.8682331	0.984968071	0.998648294	0.965715813	0.997463739	0.849693359	0.927358961	0.05207842	0.023039088	-0.068259202	-0.029038511	-0.120337621	-0.09129911
PTPRK1   P23471   AIDGVESVSR	9.1786459	1.06E-05	0.001394099	0.797703029	0.050130676	5.40E-05	0.639316624	0.003861135	0.27026657	-0.066060796	0.18441715	-0.336327366	-0.085849421	0.250477945
SCG2   P13521   IESCTQEEVR	11.717683	4.42E-07	0.004065574	0.00067309	1.78E-07	0.960998419	0.114335644	0.301663141	0.410032442	0.469947613	0.679866002	0.059951571	0.26983556	0.209918389
SMOIC   Q9H4F8   AQALAEQAK	26.504979	2.23E-14	0.000487828	8.39E-05	0.02751479	7.22E-14	1.01E-09	0.338657408	0.385011458	-0.42690301	-0.265408394	-0.811914468	-0.650419852	0.161484616
SOD1   P00441   AVCG<+57>VLK	1.7527405	0.1576797	0.259590964</											

Appendix Table 6.9: ROC-AUC Analysis Table

Gene ID   Protein ID   Peptide Sequence	AUC			P Value			AUC 95% Confidence Interval (CI)			Accuracy		Sensitivity		Specificity	
	Cau ADvsCT	AA ADvsCT	ADvsCT	Cau ADvsCT	AA ADvsCT	ADvsCT	Cau ADvsCT	AA ADvsCT	ADvsCT	Cau ADvsCT	AA ADvsCT	Cau ADvsCT	AA ADvsCT	Cau ADvsCT	AA ADvsCT
AHSG   P02765   EHAEVGGC(+57)DFQLLK	51.74%	58.41%	45.95%	0.617745687	0.076453495	0.164882231	0.4-0.6349	0.4686-0.6995	0.3782-0.5408	0.567	0.622	0.518	0.681	0.902	0.98
ALB   P02768   LVTDLTK	49.15%	49.90%	48.70%	0.444029899	0.494326325	0.376979717	0.3751-0.6079	0.3811-0.6168	0.4052-0.5687	0.526	0.582	0.533	0.574	0.804	0.949
ALDOA   P04075   VLAAYVK	71.11%	66.37%	66.79%	0.000179953	0.002655286	2.57E-05	0.6052-0.817	0.555-0.7725	0.5924-0.7434	0.711	0.653	0.631	0.532	0.804	0.439
APOA4   P06727   SLAPYADQTQEK	55.02%	56.70%	47.75%	0.198172405	0.127605798	0.2399845	0.4332-0.6672	0.4505-0.6834	0.3961-0.5589	0.608	0.602	0.508	0.638	0.647	0.408
APOC1   P02654   QSELSAK	51.49%	57.82%	54.33%	0.601122951	0.091794971	0.148168722	0.3974-0.6323	0.4638-0.6926	0.4619-0.6248	0.577	0.582	0.559	0.532	0.667	0.469
APOC2   P02655   TAAQNLVEK	53.36%	59.91%	57.68%	0.2854767	0.045961561	0.032059364	0.4171-0.6501	0.4846-0.7136	0.4964-0.6572	0.577	0.602	0.585	0.383	0.569	0.5
APOE   P02649   ELQAAQAR	49.79%	48.52%	50.19%	0.487043435	0.601024933	0.482878941	0.3816-0.6141	0.3693-0.6011	0.4203-0.5835	0.526	0.551	0.533	0.617	0.961	0.827
C9   P02748   LSPHNLVPVK	58%	51.98%	52.54%	0.087954609	0.36910549	0.270814996	0.4633-0.6967	0.4035-0.6362	0.4438-0.6069	0.639	0.571	0.554	0.362	0.843	0.337
CALM2   P00244   EAFSLFDK	71.45%	64.96%	66.26%	0.000139267	0.005451587	4.39E-05	0.6096-0.8193	0.5373-0.7619	0.5866-0.7387	0.722	0.673	0.636	0.596	0.725	0.745
CD44   P16070   TEARDLC(+57)K	65.74%	48.02%	56.15%	0.003824131	0.36910549	0.068898553	0.5464-0.7685	0.3596-0.6008	0.4806-0.6424	0.649	0.592	0.574	0.468	0.902	0.898
CH13L1   P36222   GNCWGVDDQSEVK	71.40%	75.80%	72.39%	0.000143218	5.55E-06	3.35E-08	0.6121-0.816	0.66-0.8561	0.6526-0.7951	0.68	0.735	0.692	0.511	0.627	0.714
CP   P00450   GEFYIGSK	54.17%	51.69%	50.47%	0.240779186	0.388034514	0.545964324	0.4257-0.6577	0.3974-0.6364	0.4225-0.587	0.557	0.612	0.559	0.638	0.863	0.857
CST3   P01034   VSDNM(+16)YHSR	57.06%	50.73%	51.75%	0.116111384	0.550925694	0.33723835	0.4549-0.6864	0.3883-0.6263	0.4359-0.599	0.588	0.582	0.544	0.553	0.725	0.704
DCN   P07585   VDAASLK	49.02%	52.19%	49.42%	0.567350796	0.646872408	0.55605755	0.3726-0.6078	0.4035-0.6403	0.4125-0.5759	0.577	0.612	0.528	0.255	0.745	0.551
DDAH1   Q94760   EFPVGLSK	69.70%	63.41%	65.72%	0.00042113	0.011224766	7.52E-05	0.5899-0.8041	0.5222-0.7461	0.5803-0.7341	0.68	0.633	0.636	0.681	0.784	0.663
DKS3   Q9UBR4   DODGELLPR	54.47%	48.69%	49.72%	0.22526295	0.412762212	0.5278198	0.4274-0.6619	0.3687-0.605	0.4155-0.5788	0.598	0.571	0.528	0.383	0.745	0.602
EN01   P06733   IEEELGSK	75.96%	78.06%	76.38%	5.42E-06	8.82E-07	9.85E-11	0.6631-0.8561	0.6893-0.8718	0.6977-0.8299	0.732	0.735	0.708	0.532	0.725	0.684
EN02   P09104   IEEELGDEAR	64.98%	67.29%	65.20%	0.005588323	0.001619945	0.000123233	0.5379-0.7617	0.5631-0.7827	0.5748-0.7292	0.66	0.673	0.631	0.596	0.745	0.52
F2   P00734   TATSEYQTFNPR	55.23%	51.23%	51.42%	0.188278068	0.418308379	0.366424179	0.436-0.6687	0.3946-0.63	0.4326-0.5958	0.588	0.561	0.544	0.553	0.804	0.816
GADPH   P04460   AAFNSGK	79.91%	77.14%	78.25%	1.98E-07	1.90E-06	4.79E-12	0.712-0.8863	0.6768-0.866	0.7187-0.8462	0.732	0.724	0.718	0.596	0.745	0.735
GDA   Q9Y273   DHLLGVSDSGK	73.23%	72.38%	69.82%	4.11E-05	6.90E-05	8.76E-07	0.629-0.8357	0.6199-0.8277	0.6244-0.772	0.701	0.724	0.677	0.723	0.784	0.816
GOT1   P12734   VGNLTGVSK	70.34%	65.71%	66.05%	0.00028926	0.00075	5.41E-05	0.595-0.8118	0.5451-0.769	0.5842-0.7368	0.711	0.673	0.641	0.489	0.765	0.765
SSN   P06396   AGALNGAPFLVK	62.13%	51.98%	55.82%	0.020040405	0.36910549	0.080434512	0.5083-0.7343	0.4023-0.6373	0.4773-0.6391	0.619	0.582	0.559	0.745	0.941	0.622
HBA1   P06905   FLASVSTLTSK	54.72%	50.06%	52.71%	0.212540245	0.505673675	0.256719262	0.4305-0.664	0.3836-0.6176	0.4455-0.6088	0.588	0.571	0.549	0.404	1	0.48
HBB   P68871   VNVDEVGEALGR	53.62%	50.06%	52.35%	0.270944614	0.505673675	0.286149571	0.4185-0.6539	0.3837-0.6175	0.4417-0.6052	0.588	0.551	0.549	0.404	0.647	0.561
KNG1   P01042   QDVAGLNFR	51.02%	51.73%	50.04%	0.570187641	0.385312834	0.504555928	0.3927-0.6277	0.3997-0.6349	0.4185-0.5823	0.577	0.571	0.538	0.66	0.902	0.643
LICAM   P32004   GQLSFNLK	52.09%	49.94%	51.30%	0.363133858	0.497163091	0.623983822	0.4036-0.6381	0.3825-0.6163	0.4313-0.5948	0.577	0.541	0.549	0.362	0.51	0.5
LAMP1   P11279   VVVQAFK	62.38%	60.03%	59.57%	0.017998834	0.043941449	0.010494997	0.5107-0.737	0.4857-0.715	0.5162-0.6752	0.629	0.612	0.585	0.532	0.667	0.592
LAMP2   P13473   YLDYFVVK	54.98%	54.03%	46.29%	0.200187322	0.247407982	0.185843017	0.4333-0.6663	0.4228-0.6577	0.3816-0.5443	0.577	0.592	0.518	0.596	0.843	1
LDHB   P07195   FRIPIQVK	75.19%	67.08%	70.85%	9.79E-06	0.001816098	2.47E-07	0.6531-0.8507	0.5608-0.7809	0.636-0.781	0.722	0.684	0.687	0.638	0.745	0.765
LDHC   P07864   VGGSGC(+57)NLDASR	86.72%	73.51%	80.63%	2.39E-10	3.12E-05	7.40E-14	0.7952-0.9393	0.6319-0.8383	0.7445-0.8682	0.814	0.724	0.754	0.851	0.882	0.735
MDH1   P40925   GEFTVTVQQR	77.28%	76.39%	75.37%	1.89E-06	3.49E-06	4.68E-10	0.6777-0.8679	0.6669-0.8608	0.6863-0.8211	0.763	0.714	0.692	0.66	0.686	0.612
NCA1   P13591   GLGEISAASEFK	56.34%	52.23%	51.85%	0.141873696	0.649511282	0.328018842	0.4471-0.6797	0.4045-0.6402	0.437-0.6	0.588	0.582	0.533	0.596	0.804	0.541
NPTX2   P47972   VAELEDEK	63.32%	76.28%	69.73%	0.012042705	3.79E-06	9.69E-07	0.5216-0.7448	0.6657-0.8599	0.6235-0.7712	0.629	0.765	0.672	0.617	0.765	0.531
NPTXR   Q95502   ELDVLGSR	61.62%	68.21%	65.19%	0.04590091	0.000966116	0.000124461	0.5029-0.7295	0.5747-0.7895	0.575-0.7288	0.619	0.663	0.626	0.745	0.863	0.714
NRXN1   P58400   LAIGSFVQVK	53.70%	51.98%	50.55%	0.266183941	0.36910549	0.448006873	0.4197-0.6543	0.4028-0.6369	0.4237-0.5872	0.588	0.571	0.538	0.447	0.784	0.49
QGN   P20774   LSGNPLVLGK	60.38%	53.40%	56.76%	0.039400019	0.282306899	0.051491516	0.491-0.7166	0.4178-0.6502	0.487-0.6483	0.588	0.561	0.574	0.511	0.451	0.449
OMG   P23515   LESLPAHLPR	50.34%	51.81%	50.79%	0.478412474	0.622817883	0.425019432	0.3862-0.6206	0.4005-0.6358	0.4261-0.5897	0.577	0.582	0.549	0.191	0.647	0.684
PARK7   Q94997   ALVIALK	82.09%	69.96%	76.40%	2.68E-08	0.000338011	9.53E-11	0.7359-0.9058	0.5939-0.8054	0.6971-0.831	0.784	0.704	0.708	0.745	0.863	0.847
PEBP1   P30086   VLTPTQVK	69.15%	66.92%	66.03%	0.000587891	0.01988311	5.52E-05	0.5834-0.7996	0.5584-0.7799	0.5841-0.7366	0.711	0.673	0.631	0.553	0.706	0.735
PLG1YR2   Q96P05   TFTLLDPK	57.02%	62.08%	53.65%	0.117528197	0.019933784	0.189602939	0.4546-0.6858	0.5091-0.7325	0.455-0.618	0.608	0.602	0.564	0.66	0.373	0.224
PKM   P14618   QNVNPAVQLPAVSEK	75.49%	73.34%	72.24%	7.79E-06	3.52E-05	4.08E-08	0.6547-0.8551	0.6319-0.835	0.6515-0.7933	0.753	0.714	0.667	0.532	0.843	0.694
PKMisoform [NA]   LFEELVR	74.21%	72.38%	71.94%	2.03E-05	6.90E-05	6.03E-08	0.6386-0.8456	0.6206-0.827	0.6477-0.7912	0.732	0.714	0.677	0.702	0.941	0.755
PON1   P27169   LUIGTVFK	51.66%	54.23%	51.48%	0.612227182	0.236309352	0.361183389	0.3997-0.6335	0.4251-0.6596	0.4331-0.5965	0.546	0.592	0.549	0.681	0.667	0.847
PP1A   P62937   VSEFLADK	76.89%	72.92%	74.94%	2.58E-06	4.73E-05	8.94E-10	0.6707-0.8672	0.6275-0.831	0.6809-0.818	0.773	0.724	0.713	0.617	0.725	0.704
PROX2   P32119   QITVNDPLVGR	59.70%	47.02%	55.14%	0.05027467	0.695675132	0.107537037	0.4813-0.7128	0.3528-0.5875	0.4701-0.6328	0.639	0.571	0.574	0.404	0.922	0.857
PTPRZ1   P23471   AIIDGVESVSR	57.53%	56.74%	44.83%	0.101321865	0.12612675	0.106600997	0.4599-0.6908	0.4503-0.6845	0.3672-0.5295	0.598	0.633	0.513	0.532	0.843	0.49
SCG2   P13521   IESQTEQVK	63.06%	71.71%	67.82%	0.013467676	0.000108742	8.62E-06	0.5171-0.7442	0.6155-0.8188	0.6029-0.7535	0.67	0.684	0.656	0.447	0.843	0.541
SMOIC1   Q9H4F8   AQALAEQSK	82.55%	76.18%	77.60%	1.71E-08	4.12E-06	1.39E-11	0.7421-0.909	0.666-0.8576	0.7113-0.8408	0.773	0.724	0.733	0.83	0.686	0.694
SOD1   P23471   ALCV(+57)VLK	53.53%	54.19%	52.46%	0.275747948	0.238506009	0.2767295	0.4179-0.6527	0.4244-0.6595	0.4431-0.6062	0.588	0.602	0.559	0.553	0.608	0.429
SPPI1   P10451   YPDAAVTWLNPDQSQK	77.49%	81.10%	79.29%	1.58E-06	5.86E-08	8.08E-13	0.6825-0.8673	0.7243-0.8978	0.7307-0.855	0.732	0.745	0.738	0.681	0.627	0.643
THY1   P04216   HVLFGTGVGPEHTYR	45.02%	62.62%	59.28%	0.200188296	0.015874236	0.012639801	0.3339-0.5666	0.5145-0.7379	0.513-0.6725	0.546	0.643	0.579	0.064	0.882	1
TPH1   P60174   IAAVAGNC(+57)YK	72%	61.03%	65.82%	9.64E-05	0.030235754	6.79E-05	0.6165-0.8235	0.4984-0.7223	0.5816-0.7348	0.711	0.592	0.641	0.745	0.412	0.622
VGF   Q15240   EPVAGDAVPGPK	60.30%	75.93%	68.43%	0.040644587	5.03E-06	4.39E-06	0.4887-0.7173	0.6634-0.8552	0.6093-0.7593	0.629	0.714	0.662	0.404	0.745	0.541
YTN   P04004   DWNVEGPDIAFTR	51.91%	55.94%	52.38%	0.638710215	0.156300024	0.283565408	0.4022-0.6361	0.4439-0.675	0.4421-0.6055	0.557	0.592	0.564	0.702	0.765	0.765
YWHA8   P31946   NLSVAYK	89.32%	86.56%	87.82%	1.31E-11	2.14E-10	3.68E-20	0.8308-0.9556	0.7912-0.9418	0.8304-0.926	0.825	0.827	0.821	0.66	0.824	0.837
YWHA8   P61026   YLAEATGEEK	88.38%</														