Thesis\_Summary

## Objectives

Provide a short summary of the 4 project objectives

## Method

Design a flow chart showing the four steps 1. Select target proteins 2. Protein PRS -> AD status 3. AD PRS -> protein 4. Bidirectional MR significant proteins -> AD AD -> significant proteins

## Results

## Exec Sum / TLDR

2-3 key summary findings Table with summary results for each protein at each step of analysis

## Step 1 - Select target proteins

71 candidate proteins were identified from a literature review of 33 papers.  
Proteins were marked as candidates if significantly associated with an AD related phenotype in an independent discovery study (univariate or multivariate) or if previously replicated in 3 or more studies in Kiddle et al’s comprehensive 2014 review.

25 proteins with GWAS data from Sun et al were selected for further analysis (see Table 1 below).

### Table 1: Target proteins for further analysis

Table continues below

|  |  |
| --- | --- |
| Protein | SomaLogic Assay Target ID |
| Alpha-2-HS-glycoprotein | a2-HS-Glycoprotein |
| Amyloid beta A4 protein | amyloid precursor protein |
| Amyloid-beta A4 precursor protein-binding family B member 3 | APBB3 |
| Apolipoprotein E | Apo E3 |
| Brain-derived neurotrophic factor | BDNF |
| Clusterin | Clusterin |
| Complement C3 | C3adesArg |
| Complement C4 A/B | C4 |
| Complement component C6 | C6 |
| Complement factor H | Factor H |
| Fibrinogen gamma chain | D-dimer |
| Fibronectin | FN1.4 |
| Fibulin-1 | fibulin 1 |
| Granulocyte colony-stimulating factor | G-CSF |
| Haptoglobin | Haptoglobin, Mixed Type |
| Insulin-like growth factor-binding protein 2 | IGFBP-2 |
| Inter-alpha-trypsin inhibitor heavy chain H1 | ITI heavy chain H1 |
| Interleukin-10 | IL-10 |
| Interleukin-3 | IL-3 |
| Pancreatic prohormone | PH |
| Plasma protease C1 inhibitor | C1-Esterase Inhibitor |
| Prostate-specific antigen | PSA |
| Receptor tyrosine-protein kinase erbB-2 | ERBB2 |
| Serum amyloid P component | SAP |
| Vitronectin | Vitronectin |

Table continues below

|  |  |
| --- | --- |
| UniProtID | Number of studies in which blood plasma protein was significantly associated with an AD-related phenotype (exc. studies in Kiddle et al 2014 review) |
| P02765 | 1 |
| P05067 | 1 |
| O95704 | 1 |
| P02649 | 1 |
| P23560 | 1 |
| P10909 | 3 |
| P01024 | 1 |
| P0C0L4,P0C0L5 | 2 |
| P13671 | 1 |
| P08603 | 1 |
| P02671,P02675,P02679 | 1 |
| P02751 | 2 |
| P23142 | 1 |
| P09919 | 1 |
| P00738 | 1 |
| P18065 | 2 |
| P19827 | 1 |
| P22301 | 1 |
| P08700 | 1 |
| P01298 | 2 |
| P05155 | 1 |
| P07288 | 1 |
| P04626 | 1 |
| P02743 | 1 |
| P04004 | 1 |

|  |  |
| --- | --- |
| Number of studies in which blood plasma protein was significantly associated with an AD-related phenotype (Kiddle et al 2014 review) | In\_Final\_Shortlist |
| NA | Y |
| NA | Y |
| NA | Y |
| 6 | Y |
| NA | Y |
| 2 | Y |
| 5 | Y |
| NA | Y |
| 1 | Y |
| 5 | Y |
| NA | Y |
| 1 | Y |
| NA | Y |
| 2 | Y |
| 2 | Y |
| 2 | Y |
| NA | Y |
| 3 | Y |
| 3 | Y |
| 5 | Y |
| 4 | Y |
| NA | Y |
| NA | Y |
| 4 | Y |
| 3 | Y |

## Step 2 - Protein PRS -> AD status

Summarise QC for base and target data e.g. variants removed - display final sample sizes in a table [programmatically reference sample sizes?]

Estimate statistical power

Display protein heritability results - show example python code with ldsc - chart comparing heritability for all proteins (scatter with variance) [load in summary results] - correlation matrix for all proteins [load in summary results] - short commentary

Display PRS results - include snippet of PRSice command - bar chart (No APOE) comparing all proteins (individual samples and meta-analysis) [load in summary results] - commentary on results - (appendix) detailed supplementary table [load in summary results] - (bonus) select drop down tables for individual charts on each protein -> distribution of PRS scores in sample -> bar charts of threshold significance

## Step 3 - AD PRS -> protein

Summarise QC for base and target data e.g. variants removed, proteins with ANM data available - display final sample sizes in a table [programmatically reference sample sizes?]

Estimate statistical power

Display PRS results - include snippet of PRSice command - bar chart (No APOE) comparing all proteins (individual samples and meta-analysis) [load in summary results] - commentary on results - (appendix) detailed supplementary table [load in summary results] - (bonus) select drop down tables for individual charts on each protein -> distribution of PRS scores in sample -> bar charts of threshold significance

## Step 4 - Bidirectional MR

Summarise preparation - Table of proteins analysed - Table of SNPs selected for each protein - Table of SNPs selected for AD

(Optional) Estimate statistical power

Display MR Results - Include MR base code - summary chart of effect size and p-value for each protein (Protein -> AD, AD -> Protein) - summary table of results for each protein - comm - (bonus) select drop down tables for individual charts on each protein