

## *Supplementary Material*

**Supplementary Table 1.** Four panels of proteins of sizes 11, 2, 29, and 7 respectively resulted in the best performance in NN classification of high vs. low A $\beta$ , p-tau, t-tau, and AT(N) burden when combined with age and *APOE*  $\epsilon$ 4 status. These four panels were listed below. In each panel, the proteins were sorted by corrected *p* values from the regression analysis.

| <b>UniProt</b>             | <b>Protein Name</b>                    |
|----------------------------|----------------------------------------|
| <b>A<math>\beta</math></b> |                                        |
| O75437                     | Tubulin-specific chaperone A           |
| Q6UXK5                     | Leucine-rich repeat neuronal protein 1 |
| P0C0L4/P0C0L5              | Complement C4-A/B                      |
| O00391                     | Sulfhydryl oxidase 1                   |
| Q13113                     | PDZK1-interacting protein 1            |
| P02775                     | Platelet basic protein                 |
| Q92765                     | Secreted frizzled-related protein 3    |
| P02751                     | Fibronectin                            |
| P63098                     | Calcineurin subunit B type 1           |
| Q9H2E6                     | Semaphorin-6A                          |
| P04004                     | Vitronectin                            |
| <b>P-tau</b>               |                                        |
| O75347                     | Tubulin-specific chaperone A           |
| P14635                     | G2/mitotic-specific cyclin-B1          |
| <b>T-tau</b>               |                                        |
| P0C0L4/P0C0L5              | Complement C4-A/B                      |
| P08294                     | Extracellular superoxide dismutase     |
| O75347                     | Tubulin-specific chaperone A           |
| P02775                     | Platelet basic protein                 |

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|--------|----------------------------------------------------------------------------------------|
| Q9H2E6 | Semaphorin-6A                                                                          |
| Q96PQ1 | Sialic acid-binding Ig-like lectin 12                                                  |
| Q07817 | Bcl-2-like protein 1                                                                   |
| Q9P109 | Beta-1,3-galactosyl-O-glycosyl-glycoprotein beta-1,6-N-acetylglucosaminyltransferase 4 |
| Q96KP4 | Cytosolic non-specific dipeptidase                                                     |
| Q96A84 | EMI domain-containing protein 1                                                        |
| P48736 | Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit gamma isoform         |
| Q9NRN5 | Olfactomedin-like protein 3                                                            |
| P07202 | Thyroid peroxidase                                                                     |
| Q6UX15 | Layilin                                                                                |
| P30101 | Protein disulfide-isomerase A3                                                         |
| Q9BY41 | Histone deacetylase 8                                                                  |
| Q14982 | Opioid-binding protein/cell adhesion molecule                                          |
| O60869 | Endothelial differentiation-related factor 1                                           |
| P63098 | Calcineurin subunit B type 1                                                           |
| Q9P0G3 | Kallikrein-14                                                                          |
| Q92765 | Secreted frizzled-related protein 3                                                    |
| O75351 | Vacuolar protein sorting-associated protein 4B                                         |
| Q8NCW0 | Kremen protein 2                                                                       |
| P05019 | Insulin-like growth factor I                                                           |
| O00391 | Sulfhydryl oxidase 1                                                                   |
| P07951 | Tropomyosin beta chain                                                                 |
| P46734 | Dual specificity mitogen-activated protein kinase kinase 3                             |
| Q08431 | Lactadherin                                                                            |
| P36888 | Receptor-type tyrosine-protein kinase FLT3                                             |

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**AT(N)**

|               |                                        |
|---------------|----------------------------------------|
| O75347        | Tubulin-specific chaperone A           |
| Q6UXK5        | Leucine-rich repeat neuronal protein 1 |
| P02775        | Platelet basic protein                 |
| Q9H2E6        | Semaphorin-6A                          |
| P0C0L4/P0C0L5 | Complement C4-A/B                      |
| Q96A84        | EMI domain-containing protein 1        |
| O00391        | Sulfhydryl oxidase 1                   |

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**Supplementary Table 2.** Spearman's rank correlation coefficients between protein  $p$  values obtained from logistic regression with each AD-related outcome.

|                            | <b>AT(N)</b> | <b>T-tau</b> | <b>P-tau</b> |
|----------------------------|--------------|--------------|--------------|
| <b>A<math>\beta</math></b> | 0.887        | 0.736        | 0.587        |
| <b>P-tau</b>               | 0.776        | 0.712        |              |
| <b>T-tau</b>               | 0.892        |              |              |

**Supplementary Figure 1.** We implemented NNs to predict high vs. low (A) A $\beta$ , (B) p-tau, (C) t-tau, and (D) AT(N) burden from proteins, age, and *APOE*  $\epsilon 4$  status. From 1 to 100 top proteins, sorted by their significance of linear association with the AD-related outcome, were used as input features. For each combination of input and output, NNs were trained and tested 10 times to obtain the average AUC ROC scores.

