**Table S3**. **Burden test for APOE ε4 carriers from KALN and ADSP unrelated datasets**. Collapsing and combine (CMC) test of rare variants by Fisher's exact test for (i) variants with a MAF≤1% and categorized to have a high or moderated effect (MAF≤1% HM) and (ii) singleton variants categorized to have a high or moderated effect (AC1 HM), for the individuals carrying one or two copies of the APOE4 allele within the datasets analyzed in this study (unrelated KANL and Sporadic ADSP). Odds ratio (OR) and two sided pvalue (*P*) are given. Enriched genes with nominally significant pvalues are bold highlighted.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | | | | | | | |
|  |  | MAF≤1% HM | | | | | |  | AC1 HM | | | | | |
|  |  | Unrelated KANL (N=705) | | | Sporadic ADSP (N=3049) | | |  | Unrelated KANL (N=705) | | | Sporadic ADSP (N=3049) | | |
| Disease | Gene |  | OR | pval |  | OR | pval |  |  | OR | pval |  | OR | pval |
| AD | *APP* |  | **NA** | **0.006** |  | 1.662 | 0.356 |  |  | **NA** | **0.035** |  | - | - |
| AD | *PSEN1* |  | NA | 0.085 |  | 1.998 | 0.521 |  |  | NA | 0.180 |  | 1.452 | 0.738 |
| AD | *PSEN2* |  | 1.003 | 0.916 |  | 0.563 | 0.058 |  |  | **6.892** | **0.046** |  | 1.272 | 0.766 |
| AD | *PRNP* |  | NA | 0.138 |  | 1.337 | 0.499 |  |  | NA | 1.000 |  | 1.155 | 0.758 |
| FTD | *CHMP2B* |  | **6.386** | **0.040** |  | 0.225 | 0.015 |  |  | NA | 0.180 |  | 0.234 | 0.072 |
| FTD | *FUS* |  | 0.667 | 0.360 |  | 1.367 | 0.630 |  |  | 0.238 | 0.247 |  | 2.962 | 0.305 |
| FTD | *GRN* |  | 0.494 | 0.055 |  | 0.882 | 0.686 |  |  | 0.959 | 1.000 |  | 0.756 | 0.615 |
| FTD | *MAPT* |  | 1.069 | 0.888 |  | 0.887 | 0.621 |  |  | 0.764 | 0.766 |  | 0.401 | 0.073 |
| FTD | *TARDBP* |  | 0.317 | 0.182 |  | 0.096 | 0.106 |  |  | 0.000 | 0.324 |  | - | - |
| FTD | *TBK1* |  | 0.959 | 0.740 |  | 1.446 | 0.504 |  |  | 1.935 | 0.513 |  | 3.755 | 0.203 |
| FTD | *VCP* |  | 0.764 | 0.873 |  | 0.605 | 0.684 |  |  | 0.718 | 0.661 |  | - | - |
| PD | *LRRK2* |  | 0.983 | 0.893 |  | 0.852 | 0.500 |  |  | 0.613 | 0.231 |  | 0.618 | 0.170 |
| PD | *PARK2* |  | 1.387 | 0.567 |  | 0.681 | 0.131 |  |  | 3.394 | 0.448 |  | 0.535 | 0.327 |
| PD | *PARK7* |  | 2.414 | 0.515 |  | 0.363 | 0.109 |  |  | 1.442 | 1.000 |  | 0.242 | 0.070 |
| PD | *PINK1* |  | 0.877 | 0.691 |  | 0.708 | 0.250 |  |  | 1.081 | 1.000 |  | 0.579 | 0.198 |
| PD | *SNCA* |  | 0.959 | 0.942 |  | - | - |  |  | - | 1.000 |  | - | - |
| PD | *UCHL1* |  | 1.442 | 0.816 |  | 1.076 | 0.911 |  |  | - | 1.000 |  | - | - |
| PD | *ATP13A2* |  | 0.738 | 0.256 |  | 0.869 | 0.564 |  |  | 0.732 | 0.417 |  | 0.830 | 0.679 |
| PD | *GIGYF2* |  | 1.083 | 0.850 |  | 1.204 | 0.497 |  |  | 0.472 | 0.161 |  | 1.089 | 0.836 |
| PD | *HTRA2* |  | 1.123 | 0.809 |  | 1.369 | 0.457 |  |  | 0.238 | 0.247 |  | 0.675 | 0.751 |
| PD | *PLA2G6* |  | 0.926 | 0.664 |  | 0.833 | 0.551 |  |  | 0.835 | 0.652 |  | 0.324 | 0.013 |
| PD | *FBXO7* |  | 0.818 | 0.617 |  | 0.888 | 0.807 |  |  | 0.595 | 0.481 |  | 0.510 | 0.231 |
| PD | *VPS35* |  | - | 0.242 |  | 0.469 | 0.320 |  |  | - | 0.310 |  | 0.304 | 0.161 |
| PD | *EIF4G1* |  | 1.718 | 0.064 |  | 0.796 | 0.139 |  |  | 1.029 | 1.000 |  | 0.706 | 0.048 |
| PD | *DNAJC16* |  | 1.315 | 0.471 |  | 0.613 | 0.243 |  |  | 2.110 | 0.290 |  | 0.721 | 0.555 |
| ALS | *SOD1* |  | 0.000 | 0.175 |  | - | - |  |  | 0.000 | 0.324 |  | - | - |
| ALS | *OPTN* |  | 0.837 | 0.825 |  | 1.558 | 0.484 |  |  | 0.959 | 1.000 |  | 1.325 | 0.718 |
| ALS | *UBQLN2* |  | 0.479 | 0.668 |  | - | - |  |  | NA | NA |  | - | - |
| ALS | *PFN1* |  | - | - |  | - | - |  |  | NA | NA |  | - | - |
| ALS | *SQSTM1* |  | 0.755 | 0.463 |  | 0.716 | 0.270 |  |  | 0.553 | 0.369 |  | 1.234 | 0.796 |
| TOTAL AD | |  | **2.116** | **0.033** |  | 0.822 | 0.438 |  |  | **14.764** | **1.83E-04** |  | 2.298 | 0.184 |
| TOTAL FTD | |  | 0.739 | 0.149 |  | 0.915 | 0.370 |  |  | 0.923 | 0.868 |  | 0.912 | 0.367 |
| TOTAL PD | |  | 0.977 | 0.820 |  | 0.748 | 0.058 |  |  | 0.796 | 0.240 |  | 0.587 | 0.027 |
| TOTAL ALS | |  | 0.700 | 0.264 |  | 1.136 | 0.575 |  |  | 0.576 | 0.232 |  | 1.234 | 0.560 |