Additional File 1 for

Integrative genomics approach identifies conserved transcriptomic networks in Alzheimer’s disease

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**Fig. S1: Comparison of modules from cWGCNA to other methods**

(a-d) Heatmaps showing the overlap between gene modules from cWGCNA and gene modules from (a) DICER, (b) DiffCoEx, (c) MEGENA, and (d) Self-organizing map (SOM), colored by -log(p-value) from a hypergeometric overlap test. (e-g) SOM computed using samples from the Mayo cohort, colored by bi-weighted mid correlation with (e) AD Diagnosis, (f) age at death, (g) and sex.
Fig. S2. Single-cell cluster marker gene expression

(a) Marker gene enrichment in cell-type clusters visualized with same t-SNE plot as in Figure3a.
(b) Violin plots of differentially expressed cell-type markers in each cell-type cluster identified by snRNA-seq. (c) RNA ISH of a subset of the differentially expressed cell-type markers in human cortical tissue. Images from the Allen Human Brain Atlas. (d) Dot plot showing differentially expressed inhibitory neuronal markers in cell-type clusters. Color denotes average gene expression, while size denotes percent of nuclei expressing the gene.
Supplemental Figure 3

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A. up-regulated in female samples
B. up-regulated in male
Fig. S3: Differentially expressed genes between sex in snRNA-seq

(a-b) Gene expression heatmaps summarizing differentially expressed genes (DEGs) between cells originating from female and male samples within each cluster. The top 10 genes sorted by average log fold change in female (a) and in (b) male samples for each cluster are displayed.
Fig. S4. Cell-type proportion changes in Mayo and ROSMAP datasets

(a-b) Boxplots depicting estimated cell-type abundance with pathological state by cell-type cluster in RNA-seq dataset from Mayo TC (a) and ROSMAP PFC (b).
Fig. S5. Cell-type proportion changes in MSSM PHG and STG datasets (a-b) Boxplots depicting estimated cell-type abundance with diagnosis by cell-type cluster from RNA-seq dataset from MSSM PHG (a) and STG (b).
Fig. S6. Cell-type proportion changes in MSSM FP and IFG datasets

(a-b) Boxplots depicting estimated cell-type abundance with diagnosis by cell-type cluster from RNA-seq dataset from MSSM FP (a) and IFG (b).
Fig. S7: Trajectory of AD modules projected onto proteomic data

(a-b) Boxplots depicting proteomic module eigenprotein values for modules positively correlated with AD diagnosis (a) and for modules negatively correlated with diagnosis (b).
Fig. S8. Consensus WGCNA analysis in ROSMAP and MSSM datasets
(a) Module eigengene trajectories with CERAD score in ROSMAP PFC dataset. (b-e) Boxplot showing module eigengene trajectory with pathological state for neuronal and non-neuronal consensus modules in MSSM PHG (b), STG (c), IFG (d), and FP (e) RNA-seq datasets.
Fig. S9. ME trajectory, pathway analysis and module plots of CM12, CM23 and CM16 modules

(a-b) Co-expression plot (a) and gene ontology term enrichment (b) for neuronal consensus module CM12. (c-d) Module eigengene trajectory with pathological state (c) and with Braak stage (d) for CM12 in Mayo TC dataset. (e-g) Module eigengene trajectory with pathological state (e), Braak stage (f), and MMSE score (g) for CM12 in ROSMAP PFC dataset. (h) Module eigengene trajectory with age for CM12 in NABEC dataset. (i-j) Co-expression plot (i) and gene ontology term enrichment (j) for non-neuronal consensus module CM23. (k-l) Module eigengene trajectory with pathological state (k) and with Braak stage (l) for CM23 in Mayo TC dataset. (m-o) Module eigengene trajectory with pathological state (m), Braak stage (n), and MMSE score (o) for CM23 in ROSMAP PFC dataset. (p) Module eigengene trajectory with age for CM23 in NABEC dataset. (q-r) Co-expression plot (q) and gene ontology term enrichment (r) for non-neuronal consensus module CM16. (s-t) Module eigengene trajectory with pathological state (s) and with Braak stage (t) for CM16 in Mayo TC dataset. (u-w) Module eigengene trajectory with pathological state (u), Braak stage (v), and MMSE score (w) for CM16 in ROSMAP PFC dataset. (x) Module eigengene trajectory with age for CM16 in NABEC dataset.
Fig. S10. Enrichment of GWAS hits of other neurodegenerative and neurological disorders

Heatmap of consensus module enrichment of GWAS hits from more than 35 different studies
Fig. S11: Potential drug targets for AD consensus modules

(a-b) Bar plots depicting potential drug targets from querying the LINCS database for each module positively correlated with AD diagnosis (a) and for each module negatively correlated with AD diagnosis (b).
Fig. S12. ME trajectory in published AD datasets

(a-e) Boxplots illustrating module eigengene trajectory with diagnosis from RNA-seq dataset from Zhang et al. PFC (61) (a), Berchtold et al. SFG (b) and PCG (77) (c), and Webster et al. FC (78) (d) and TC (e).