Figure 7

HD hESC-derived CD44+ astroglia exhibit mHTT-dependent changes in gene expression

A, Principal component analysis (PCA) plot based on expression of approximately 26,000 detected transcripts. The expression data are shown as log2-transformed transcripts per million (TPM) values post normalization to account for variance (Risso et al. 2014). PCA plot shows distinct transcriptome-wide expression signature of HD-derived hAPCs. B, Venn diagram shows intersection of lists of differentially expressed genes (DEGs) (green = down-regulated, red = up-regulated, FDR 5%) obtained by comparison of hAPCs derived from 3 HD patients against pooled control hAPCs from 2 donors. The list of shared DEGs by 3 HD patients was filtered by intersection to DEGs (FDR 5%) found in patient HD20 (GENEA20) vs. sibling donor CTR19 (GENEA19); this filtration step further increased the specificity of mHTT-associated DEGs. C, Expression heatmap based on log2-transformed TPM values calculated from raw counts of 114 DEGs highlighted in B showing clustering of hAPCs by disease status. Dendrogram shows hierarchical clustering based on Euclidean distance calculated from log2-TPM values from the three HD-ESCs lines (HD17, HD18, HD20) and the two matched control lines (CTR19, CTR02). D, Network representation of functional annotations (Gene Ontology: Cellular Component, FDR-corrected P < 0.1) for the 114 intersection DEGs highlighted in B. Genes are labeled round nodes with border colors representing their direction of dysregulation (green, down-regulated; red, up-regulated). Rounded rectangle nodes represent annotation terms. Nodes are sized by degree and colored by closely interconnected modules (M1 though M4) identified by community detection. For each module, three of the top significant annotations are listed and labeled in the network. E, Expression heatmap of 14 conserved DEGs identified in M1 (yellow in D), annotations related to post-synaptic and receptor complex components. F, Heatmap of 9 conserved DEGs identified in M2 (grey in D), annotated to perinuclear and early endosome components. G, Heatmap of 11 conserved DEGs identified in M3 (blue in D), annotations related to plasma membrane, cell-cell junction, and desmosomal components. H, Heatmap of 8 DEGs identified in M4 (orange in D); annotations related to extracellular matrix components.