Functional annotation reveals HD-associated impairment in transcription of glial differentiation, myelination, and synaptic transmission-related genes

Gene Ontology (GO) functional annotation was performed for the 429 differentially expressed genes (DEGs) in the 3 lines of mHTT hGPCs relative to pooled control hGPCs (see Figure 1B-C). 50 significantly associated GO annotation terms (Biological Process and Cellular Component, Bonferroni-corrected p<0.01) were identified by the ToppCluster annotation tool (Kaimal et al., 2010). By network analysis, these GO terms together with their associated DEGs were grouped into three functionally related modules (M1 through M3, see Figure 1D). For each GO term, the expected value assumes a constant ratio, given the number of annotated DEGs and the total number of human protein-coding genes found in the term. The fold enrichment is the ratio of the number of observed DEGs found in the term, to the expected number. Within each functional module, the GO terms were ranked first by p value, then by fold-enrichment. Three GO terms, GO:0007268 (chemical synaptic transmission), GO:0098916 (anterograde trans-synaptic signaling), and GO:0099537 (trans-synaptic signaling), were respectively ranked 3 through 5 within module M3. They contained an identical set of 37 associated DEGs, which were contained within the 38 DEGs associated to GO:0099536 (synaptic signaling) ranked at number 2 in M3. To reduce redundancy, these three GO terms were thus omitted from the figure. A, The bar graph shows the top 5 GO terms for each functional module. B, The table lists the calculated values and the associated DEGs for each of the top-ranked terms. Associated DEGs are color-coded according to their direction of dysregulation in HD- vs. control-derived hGPCs (green, down-regulated; red, up-regulated).