# Gene expression analysis of ND non-NFT neurons identifies significant alterations that occur prior to NFT formation

**“ The differentially expressed genes that are identified in comparisons of AD NFT neurons and AD non-NFT neurons were anticipated to fall into two broad classes, those that may cause NFT formation and those that may result from NFT formation. Additionally, thioflavin-S identifies only late stage NFTs. Thus there may be important pre-NFT molecular changes present in our AD non-NFT neuronal population that contribute to NFT formation. To facilitate the identification of these pre-NFT changes, we have compared expression profiles of 14 control non-NFT neuronal (ND non-NFT) samples to nine age-matched mid-stage AD NFT and AD non-NFT neuronal samples using the whole genome Affymetrix U133 plus 2.0 array. Genes that are the most likely early contributors to NFT formation would be anticipated to show dysregulation prior to NFT formation. These genes should have consistently increasing or decreasing expression when comparing ND non-NFT neurons to AD non-NFT neurons and then to AD NFT neurons. Using a one way ANOVA and post hoc permutational *t*-tests ($p < 0.05$), we have identified 225 genes that satisfy these criteria of consistently increasing or decreasing alterations across all three data sets (see Supplemental Data for complete list). The top 100 genes from this analysis are shown in Fig. 4. These genes were found to include IRAK1, APOJ, CD44, PAK7, and CAPN7. Clearly genes that are induced or repressed in AD non-NFT neurons compared to ND non-NFT neurons are also of interest and we present for public download the entire data set to enable these types of independent analyses and testing of multiple additional hypotheses (http://www.tgen.org/neurogenomics/data).”**