

# Down-regulation of calcium and MAPK signaling in R6/2 mice

## Abstract

Huntington's disease (HD) is characterized by a genetic mutation that leads to progressive movement, emotional, and cognitive deficits. Recently, research into the genetic mechanism of this disease has begun to provide new insights. In this study, transgenic R6/2 mice carrying the HD mutation were compared to wild type in an effort to determine the changes in gene expression caused by this mutation. R6/2 mice display aberrant gene expression, and this is thought to contribute to their cognitive deterioration. Samples from R6/2 and normal mice were examined using the Affymetrix® GeneChip® U74A. Statistical analysis was performed with GeneSifter (VizX Labs, Seattle, WA). This microarray data analysis system was also used to map differentially expressed genes to candidate biological terms and pathways. Several clear patterns of gene expression were discovered which correlated with genes involved in neural signal transduction.

## Analysis Methodology

The raw data is available from the NCBI Gene Expression Omnibus (GEO) (<http://www.ncbi.nlm.nih.gov/projects/geo/>), GDS717. Data was normalized to the global median of gene expression, and  $\log_2$ -transformed. Initial analysis focused on removing genes that did not meet our criteria for differential expression. This process was carried out by applying a t-test (student's, two-tailed), followed by the Benjamini-Hochberg method for estimating the false discovery rate (FDR). Genes changed by less than 1.5 fold, or with adjusted  $p > 0.05$  were also removed from subsequent analysis. A quality control criteria was selected to view only those genes flagged as "P" by the Affymetrix

MAS5 algorithm. These filtering steps reduced the dataset to 439 genes that were subjected to subsequent scatter plot analysis. This subset was further mined for biological information using the Ontology Report and KEGG Report in GeneSifter.

Normalization	Global median
Transformation	$\log_2$
Statistical test	Student's t-test (two-tailed, unpaired) $p < 0.05$
Fold change (minimum)	1.5
Quality	1 (all Present calls)
Multiple testing correction	Benjamini-Hochberg (FDR)

Figure 1. Analysis methodology. A summary of the analysis parameters used to filter the raw data. Application of these methods resulted in a filtered gene list of 439 genes, which were analyzed further for biological information.

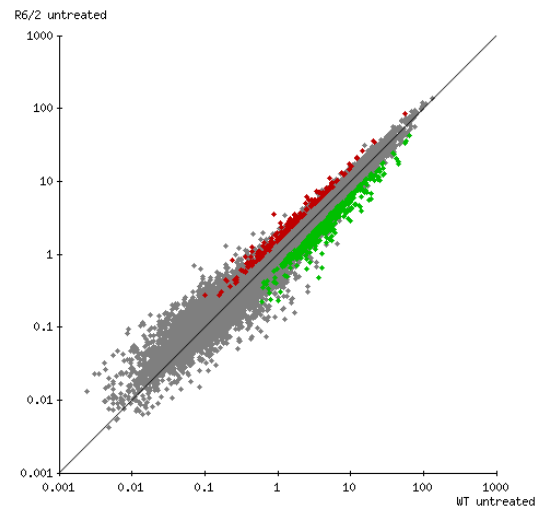


Figure 2. Scatter plot of all data points. We initially filtered the dataset from ~12,500 genes of raw data to 439 differentially expressed genes. Genes that did not pass the filtering criteria are displayed in gray, upregulated genes are shown in red, while downregulated genes are shown in green.

