Identification of Co-Expressed Genes to BDNF and trk-B as Major Depressive Disorder Related Biomarkers Using Microarray Data

**Background**
Neuropasticity Hypothesis for Depression
Neuropsychiatric disorders are thought to arise from adverse neurodevelopmental events that manifest as early as the fetal stage. The hypothesis is supported by research that shows that depressed patients do have changes such as reduced hippocampal volume in comparison to controls (Dwivedi, 2003).

**Research Question**
Are there novel neuroplasticity biomarkers related to major depressive disorder that are significantly co-expressed with BDNF and/or trk-B genes?

**Variables/Goals**
BDNF/trk-B: Gene expression map of one BDNF/trk-B probe with log2 intensity values from 3702 samples in the brain
New Biomarker: Gene co-expressed with BDNF/trk-B with an above +0.5 Pearson's correlation coefficient (r-score) to indicate a significant correlation
To determine gene co-expression correlations between variables
To research potential biomarkers found for relevance to neuroplasticity and depression research

**Methodology for Data Analysis**
- **Data Collection and Download**
  - Downloaded 3055 probes including BDNF/trk-B with gene symbol, ID, and chromosome information into Excel spreadsheets
  - Utilized raw probe data with 3702 log2 intensity values measuring gene expression in different brain structures instead of calculated z-scores
- **Calculate Average Expression Level**
  - Wrote a Java program to automatically find average expression level for all probes
  - Java file "numbers" holds probe data and Scanner reads the file and assigns values in a 2D array, one row for each probe
  - Calculates average of each row and prints in console
  - Manually went through data to identify the probe with the highest average per gene
  - Left with 1228 gene probes for next analysis
- **Screen Data for One Probe Per Gene**
  - Identified co-expressed genes above +0.5 r-score and researched them for involvement in neuroplasticity
  - Identified important trends
- **Calculate r-score with BDNF/trk-B**
  - Trend r-score

**Table of 72 Co-Expressed Genes Involved in Identified Trends**

**Results**
Identified 93 significantly co-expressed genes with BDNF (r-score: 0.82 < x < 0.50)
Identified 27 significantly co-expressed genes with BDNF (r-score: 0.68 < x < 0.50)
Determined 72 genes to be especially important to depression research
- Trends of cell adhesion, neurogenesis, and involvement in MAPK pathways were found in 72 of 120 identified genes
- Found through research into gene function as well as connection to existing articles involving depression, neuroplasticity, or stress response

**Future Applications**
Future research
Further research can be done to confirm that the identified genes are biomarkers for major depressive disorder by determining changes in gene expression level between depressed patients and healthy controls. Finding whether increased or reduced expression causes reduced neuroplasticity and vulnerability to depression is needed for developing drugs that can target these genes.

**Conclusion**
Meeting Project Goals
Project goals were met by finding potential neuroplasticity biomarkers through significant gene to gene correlations with BDNF/trk-B r-score > 0.5. A total of 93 and 27 co-expressed genes were identified for trk-B and BDNF respectively, and 72 genes were further determined to be important potential biomarkers based on gene functions relevant to neuroplasticity or BDNF/trk-B pathway research.

**Limitations**
The data used in the Allen Human Brain Atlas are from healthy controls and need comparison to depressed patient brains before the genes identified can be considered major depressive disorder biomarkers. Furthermore, only 6 donor brains were included, and more trials should be done to confirm results. Lastly, while human error and experimenter bias were reduced through the use of computational programs, these are still a factor that may affect results.

**References**