Alpha Synuclein (a-Syn) is one of the most abundant proteins inside the synaptic terminals of the neurons. Even though there is not much information or research about Alpha Synuclein, there is a possibility that Alpha Synuclein can help transmit signals between neurons. However, scientists have recognized that when Alpha Synuclein gene is mutated, it is usually found in a sporadic and familial Parkinson’s disease. With that in mind, Parkinson’s disease is contributed by Lewy bodies and Lewy neurites. Since Lewy bodies and Lewy neurites contains Alpha Synuclein gene, these researchers are trying to understand how impactful Alpha Synuclein gene can be when it is overexpressed. With this experiment, the researchers are going to use Drosophila model to understand how genetic factors can impact the way how a regular Alpha Synuclein gene functions and how overexpressed Alpha Synuclein gene changes normal functions.

First and foremost, researchers use computational resources to analyze the different expressions of Alpha Synuclein gene. In this experiment, the normal expressed amount of Alpha Synuclein gene is the control group while overexpressed Alpha Synuclein gene is the experimental group. When they first started the research, they wanted to understand biological effects on how different genes can respond to Alpha Synuclein overexpression. They screened 806 genes and were able to produce a Linear/Empirical Bayes model, a Clustering analysis, GO and KEGG Enrichment Analysis. The first computational resource, the linear model, was used to fit each of the gene expression and then the Empirical Bayes was used to analyze the residuals to obtain the appropriate t-statistic. Afterwards, they used the clustering analysis to see the expression patterns of the experimental and the control group. Unfortunately, there were not able to find any significant problems with both the experimental and control group since both of them have similar expression patterns. This time, they used Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) to analyze the different expressed genes in each group. The results showed that extracellular matrix signals were significantly enhanced in cellular components, molecular functions, and biological processes after α-Syn overexpression, specifically few signals, such as TNF-Alpha signaling pathway, was enhanced after α-Syn overexpression. Furthermore, the GSEA can help show how too much Alpha Synuclein gene can cause a mutation in a human glioma cell. With GSEA, the results show that Alpha Synuclein overexpression activated nine sub-gene sets and inhibited 18 sub-gene sets within the Hallmark gene set. It also highlighted that the most activated genes are associated with TNF-Alpha signaling.

After they have gotten their results from computational resources, they use Drosophila to confirm the results. With this experiment, they have studied how TNF-Alpha pathway has helped caused Parkinson’s disease due to Alpha Synuclein overexpression. Researchers have decided to use the qRT-PCR detection to examine the expression levels of Drosophila TNF-α homologue eiger and its receptors, Grindelwald (Grnd) and Wengen (Wgn), along with tyrosine hydroxylase (TH) levels. The results showed that one of the Alpha Synuclein gene, A30P, overexpressed in dopamine neurons, it has increased eiger and Grnd levels in the head. This has destroyed the age-dependent loss of specific dopamine neurons. With this experiment, it shows that TNF-Alpha pathway has made an impact to Parkinson’s disease due to the overexpression of Alpha Synuclein gene.

Huang, Y. et al. Gene set enrichment analysis and genetic experiment reveal changes in cell signaling pathways induced by a-synuclein overexpression. Biomedicines; <https://doi.org/10.3390/biomedicines11020263> (2023)