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Specific AIMs

The gene POG1(POLGa) has been identified as a major contributor to serious genetic diseases. One of which is Alpers-Huttenlocher Syndrome which is a neurological disorder as well as affecting some other parts of the body. The POLG1 gene provides the instructions for the development of the alpha subunit of the protein polymerase gamma. This protein is necessary for the mitochondria to replicate mitochondrial DNA (mtDNA), and allow for the cell to survive. The mutations in the POLG1 gene cause issues with the alpha subunit and this leads to issues during replication of mtDNA which causes a drop in the amount of energy the cell receives. Although we know the outcome of what happens from the mutation, we do not know what happens to the alpha subunit that makes the polymerase gamma so inefficient at replication and insight into this could lead to treatments of the disease.

My goal is to obtain a better and more complete understanding of the effects of the POLG1 gene on the mitochondria and the human body overall. We will test our hypothesis that the alpha subunit is important in correct replication in the mitochondria. The hypothesis is based off of preliminary research on the protein polymerase gamma.

1. Identify all of the subunits of the polymerase gamma using **CLEM**(correlative light and electron microscopy) which is one of the more powerful techniques to elucidate the localization and structure of the polymerase gamma. It is important to realize understand all of the subunits of the polymerase gamma in order to better understand the alpha subunit.

2. Identifying mutations on the POLG gene is critical to understanding how the cell is effectedWe will use **PFAM** and **SMART** programs to identify proteins that are homologous to the POLG domains found in other model organisms in order to further research on POLG mutations.

3. We will study the protein interactions within the protein polymerase gamma. Specifically we will look at the alpha subunit by using **Pull-Down assays**, Pull-down assays are useful for confirming the existence of a protein-protein interactions.

This project will help us better understand the Alpers-Huttenlocher syndrome and possibly lead us to more effective treatments and a better understand of the mitochondria as a whole. Along with this disease we will also be able to better understand other disorders associated with the POLG1 gene.

References

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- *"Pull-Down Assays." Pull-Down Assays. N.p., n.d. Web. 26 Feb. 2015.*