CALIFORNIA STATE SCIENCE FAIR
2017 PROJECT SUMMARY

Name(s)
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Project Number
S0511

Project Title
Identification of Mutations in a Novel Gene Responsible for Blindness

Abstract

Objectives/Goals
The objective of this project is to identify genetic mutations leading to blindness in a family and to study their functional effects using cell culture models.

Methods/Materials
The whole genome sequence of patients and their normal relatives were analyzed using genome analysis software. Selected variants were tested for their segregation with disease by PCR and sequencing. Mutations found in a novel gene were expressed in miMCD3 cells by designing plasmids for over expression and also by gene editing using CRISPR Cas9 method. Expression of the novel gene in the retina was tested by immunostaining. Immunostaining was then conducted on the cell line to see the effects of the mutations on the cells.

Results
Compound heterozygous mutations were found in patients in a novel gene, an intraflagger transport protein 88 (IFT88) found in the cilia of photoreceptor cells. One is a nonsense mutation on exon 13 p.Arg266* (c.796C>T) and the second a missense mutation on exon 20 p.Ala568Thr (c.1702G>A). The IFT88 protein was observed in photoreceptor cells in the retina. Immunostaining showed the cilia were significantly abnormal in cells transfected with both of the mutant plasmids. In addition the IFT88 protein in the cells expressing both mutations was found to be mislocalized away from the cilia as opposed to the cells expressing wild type protein. This mislocalization likely leads to abnormal clila formation and cell death of the photoreceptors which inturn results in the blindess of the affected individuals

Conclusions/Discussion
Based on this study it can be concluded that the mutations in IFT88 gene are the probable cause of the vision loss in the study family. This result is important as this is the first time that a mutation in the IFT88 gene has been found in patients with retinal degeneration. This gives researchers a location to look for when trying to identify the cause of blindness in similarly affected individuals. In addition, while this is the first time that IFT88 has been associated with retinal disease, the family of IFT genes has been associated with other types of blindness, kidney disease, obesity, and diabetes. Therefore, a potential treatment for this gene mutations can affect a much broader range of individuals.

Summary Statement
I identified compound heterozygous mutations that cause blindness in a family and developed a tissue culture model to study the funtional effects of these mutations

Help Received
My mentor Dr. Radha Ayyagari provided space, equipment, and guidance. Along with her Pooja, John, Angel, Rachel, and Anil all helped me in the lab to learn the procedures and also supervised me. I conducted my research at UCSD. My teacher Mrs. Newman helped to review my project and forms.