CALIFORNIA STATE SCIENCE FAIR
2016 PROJECT SUMMARY

Name(s)

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Project Number

S0513

Project Title

Discovery of a Novel Mutation Causing Retinal Degeneration through Genomic Analysis

Abstract

Objectives/Goals

To determine the underlying cause of retinal degeneration (RD) in a five generation consanguineous pedigree.

Methods/Materials

A family with four affected males and two consanguineous marriages was recruited for the study. The family history was collected by interviewing the available members, while the clinical phenotype was established through fundus examination, electroretinography (ERG) and measurement of visual acuity. The exomes were captured using agilentV5+UTR probes and subsequently sequenced on HiSeq2000 genome analyzer. The reads were mapped to human reference sequence hg19 and variants were called using GATK. ExomeSuite was used to filter and prioritize the variants for further analysis. Segregation of candidate variants with the clinical phenotype was tested by Sanger sequencing.

Results

Five unaffected relatives and three affected members of a family were recruited for the study. The exomes of two affected males were sequenced that identified 61,932 single nucleotide variants (SNV), and 4,344 indels (insertion/deletions) in the first, and 61,717 SNVs and 4509 indels in the second affected individual, respectively. Filtering the variants with exomeSuite identified 12 novel or rare variants as the possible candidate sequence alterations. Additional filtering based on the predicted impact of the variants identified a two base pair (TA) deletion in exon 14 of the CHM (Choroideremia) on the X- chromosome. The two base pair deletion causes a frame-shift mutation that is likely to result in the formation of a truncated protein lacking 89 C-terminal amino acids. However, as this mutation resides in the penultimate exon of CMH, the mutant transcript may undergo nonsense mediated (NMD) decay. This deletion is observed to segregate with the RD phenotype in this family.

Conclusions/Discussion

A novel two base pair deletion in exon 14 of CHM segregates with an X- linked retinal degeneration in this family. Two female members of this family were identified as carriers of the causative mutation. To the best of my knowledge, this is the first report identifying this mutation in the CHM gene.

Summary Statement

I identified a new mutation that is causing a retinal disease in multiple members of a family through genome analysis

Help Received

Biswas, Pooja; Suk, John; Ayyagari, Radha: They helped me in the lab to understand the genetics and genome analysis. Riazuddin, S Amer; Hejtmancik, James F.: They preformed clinical analysis on the patients. UCSD: This is where I did all the genome analysis and the lab work.