CALIFORNIA STATE SCIENCE FAIR
2005 PROJECT SUMMARY

Name(s)
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Project Number
S1002

Project Title
Nail-Patella Syndrome Phenotype Expression and Inheritance of LMX1B Gene Mutation

Abstract

Objectives/Goals
Nail-Patella Syndrome (NPS) is a rare genetic disorder involving the bones, joints, and connective tissue (loss of patterning across the dorso-ventral axis of the limb). NPS is caused by mutations in the transcription factor LMX1B gene on chromosome 9q34. This project examines the gene mutation inheritance pattern, and the variability and severity of the NPS phenotype in my family compared to national incidence.

Methods/Materials
NPS phenotype expression in 102 family members was evaluated by observation of nails, knees, elbows, feet, back, and glaucoma eye exam records. Buccal cell samples from 15 individuals were collected with Omni Swabs, and DNA extracted with QIAamp spin columns per manufacturer's instruction. PCR was performed with primers based on genomic sequence of LMX1B gene. The products were sequenced to identify the mutation. A pedigree chart was prepared to trace mutation inheritance.

Results
Twenty-two individuals in my family were found to express the NPS phenotype. Fingernail dysplasia was present in all affected subjects. Triangular moons were observed in 79%. Toenail dysplasia was identified in 80%. Kneecap dysplasia was detected in 56%. Reduced elbow extension was found in 55%; lumbar lordosis in 57%; glaucoma in 14%; hip/pelvis involvement in 38%; talipes in 9%; and nephropathy in 6%. The specific mutation in the LMX1B gene was detected by PCR amplification and sequencing of extracted DNA from an affected individual with NPS. A mutation of C>T at nucleotide 175 in exon 2 was identified.

Conclusions/Discussion
The study supported the hypothesis that NPS is a pleiotropic disorder exhibiting autosomal dominant inheritance of a LMX1B gene mutation in my family. On the average, 50% of the offspring from affected individuals were affected (with no skips in generations). The range and severity of symptoms varied within my family. The subject's phenotype manifestations presented in nails, knees, and elbows compared with national incidence expression. The mutation was located in the LIM-A domain causing a nonsense mutation at amino acid residue 59 (glutamine to a premature stop codon). For further study, it would be important to learn what other transcription factors regulate and cooperate with LMX1B function since potentially this understanding could lead to strategies for treating conditions such as neurological disorders.

Summary Statement
The LMX1B gene mutation producing the rare genetic disorder, Nail-Patella Syndrome in my family follows an autosomal dominant inheritance pattern with complete penetrance and wide variation in phenotype expression.

Help Received
Used laboratory equipment at BioSource; Dr. Geoffrey Routh provided training and guidance in performing PCR testing.