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Mutation in PAX3 Gene that leads to Albinism.

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ABSTRACT

Albinism is a genetic disorder characterized by reduced or absent melanin pigment in the skin, hair, and eyes. The PAX3 gene has emerged as a significant player in the development of albinism, owing to its critical involvement in melanocyte development and migration during embryonic stages. The PAX3 gene, part of the PAX3 transcription factor family, holds pivotal importance in fetal development due to its paired box and homeodomain structures. Mutations in PAX3 are linked to Waardenburg syndrome, a condition characterized by hearing loss and pigmentation abnormalities. Our research, however, delves specifically into PAX3 mutations' role in causing albinism in humans. This study focuses on elucidating the impact of PAX3 gene mutations on the manifestation of albinism in humans. Through comprehensive analysis using Simple ClinVar, we identified several phenotypes, genes, and variants associated with albinism, ultimately narrowing our focus to the PAX3 gene. There were 64 missense mutations found. 28 of them were uncertain/conflicting, 5 were likely benign, 14 were likely pathogenic and 17 were pathogenic. Utilizing predictive tools such as Polyphen2 and SIFT, we assessed the pathogenicity of PAX3 gene variants, highlighting mutations such as Pro50Leu, Asn47 Lys. Additionally, we employed the Swiss Model to generate 3D protein structure models, enhancing our understanding of the structural implications of these mutations. Expression analysis revealed that silencing of PAX3 inhibits key genes involved in melanin synthesis, underscoring its pivotal role in pigmentation regulation. Mutations identified in my study were predicted to be pathogenic. Mutations at positions 47 and 50 of the Pax3 gene were shown to affect protein function, with a score of 0.00 in protein function prediction tools. This indicates a potential disruption in normal cellular processes associated with these mutations. This research aims to provide valuable insights into the molecular mechanisms underpinning albinism, particularly in the context of PAX3 gene mutations. By unraveling the intricate interplay between PAX3 and melanin synthesis pathways, we seek to deepen our understanding of albinism pathogenesis and pave the way for targeted therapeutic interventions.

INTRODUCTION

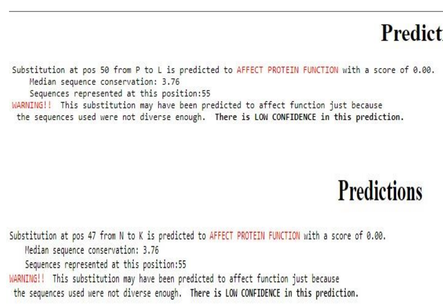
Albinism is a genetic disorder characterized by the absence or reduction of melanin pigment in the skin, hair, and eyes. It poses significant challenges to affected individuals due to their increased susceptibility to sunburns, vision impairment, and social stigma. Understanding the molecular mechanisms underlying albinism is crucial for developing targeted therapies and improving patient outcomes. One of the genes implicated in the development of albinism is Pax3, a transcription factor known for its critical role in melanocyte development and migration during embryonic development. While mutations in Pax3 have been associated with various syndromes and cancers, their specific contributions to albinism remain to be fully elucidated. This research aims to explore the relationship between Pax3 gene mutations and the development of albinism, shedding light on the molecular pathways involved and paving the way for future diagnostic and therapeutic strategies. Through a comprehensive analysis of Pax3 variants and their effects on protein function, this study seeks to deepen our understanding of albinism pathogenesis and offer new insights into potential treatment approaches. By bridging the gap between genetic alterations and clinical manifestations, this research strives to contribute to the growing body of knowledge in the field of medical genetics.

METHODS

- Throughout this study, we first used simple clinvar to get background on Albinism.
- There were many phenotypes, genes, and variants associated with this disease. One gene was focused on called PAX3. This gene was put into Simple Clinvar to get a deeper analysis.
- The FASTA sequence of the gene was obtained. This sequence was used in polyphen, which determined whether the gene is benign or possibly damaging, and SIFT, which determines the prediction of the effect to protein due to the mutation.
- Swiss Model Prot was used to get the model of the gene. NCBI was used to get more information and analysis on the gene.

RESULTS

SIFT PREDICTIONS



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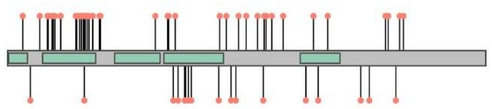
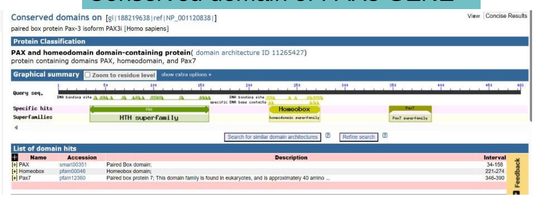
Polyphen2 and SIFT, we assessed the pathogenicity of PAX3 gene variants, highlighting mutations such as Pro50Leu, Asn47 Lys.

PolyPhen2 Predicts

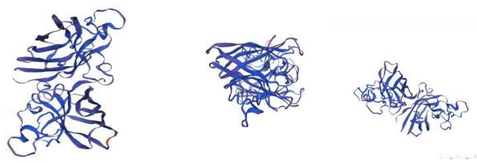
Coding variant mapping and domain for PAX3 GENE



Conserved domain of PAX3 GENE



SWISS MODEL OF PAX3 GENE IN 3D



DISCUSSION AND CONCLUSION

The findings of our study underscore the pivotal role of the PAX3 gene in the pathogenesis of albinism. Through a comprehensive analysis of PAX3 gene mutations, we have elucidated the impact of these mutations on the manifestation of albinism in humans. Our research identified a total of 64 missense mutations in the PAX3 gene, with 17 of them predicted to be pathogenic. Among these, mutations at positions 47 and 50 were particularly noteworthy, as they were shown to significantly affect protein function, potentially disrupting normal cellular processes associated with melanin synthesis. Furthermore, our expression analysis revealed that silencing of the PAX3 gene inhibited key genes involved in melanin synthesis, providing further evidence of its crucial role in pigmentation regulation. These findings suggest that mutations in the PAX3 gene can lead to dysregulation of melanin synthesis pathways, contributing to the development of albinism in affected individuals. In conclusion, our research sheds light on the molecular mechanisms underlying albinism, particularly in the context of PAX3 gene mutations. We have deepened our understanding of albinism pathogenesis and paved the way for targeted therapeutic interventions. Our research aims to improve patient outcomes and enhance the quality of life for individuals affected by this debilitating genetic disorder.

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