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Analysis of SLX4 Gene in Breast Cancer

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ABSTRACT

Breast cancer is a type of cancer that begins in the cells of the breast. It can occur in both men and women, although it is much more common in women. Breast cancer can develop in various parts of the breast, including the ducts that carry milk to the nipple (ductal carcinoma), the glands that produce milk (lobular carcinoma), or in other cells within the breast. The objective of this study is to identify the gene variants associated with breast cancer. Simple-ClinVar was used to identify the gene, SLX4. SLX4 is a type of gene that provides instructions for making structure-specific endonucleases and other proteins involved in the repair of DNA interstrand cross-links. Due to its vital role in DNA repair, pathogenic mutations in SLX4 may have detrimental effects, including significant DNA damage, an increased cancer risk, and many other physical abnormalities. The computational prediction tools, SIFT and PolyPhen2, were used to analyze the possible pathogenic mutations in protein function. PolyPhen2 predicted that the mutation is possibly damaging with a score of 1.000. The SWISS MODEL tool was used to acquire information on the protein structure. Understanding more about SLX4 and all of its processes can provide further insights into cancer development and potential treatments in the future.

INTRODUCTION

Breast cancer currently stands as the most prevalent form of cancer, impacting women across all races and ethnicities globally. Within the United States, statistics reveal that 1 in 8 women will face a breast cancer diagnosis during their lifetime, with varying incidence and mortality rates observed among different racial groups.

The analysis of the SLX4 gene is important in order to speculate the error occurring which inhibits SLX4 from properly repairing defective DNA and maintaining genomic stability. Understanding more about SLX4 can provide insights into cancer development and potential treatment options in the future.

METHODS

Simple ClinVar was a program used to make initial observations of the SLX4 genes presence in breast cancer.
PolyPhen2 was used to predict the pathogenicity of the mutations in the SLX4 gene.
SIFT was a program that used the sequence homology to make predictions as to whether an amino acid substitution would affect protein function.
Swiss Modeling produced an animated replica of the protein structure.

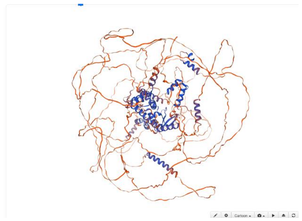
RESULTS

Gene Identification

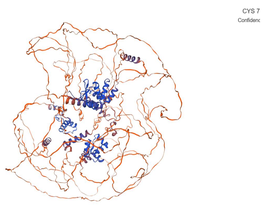
SLX4 is a type of gene that provides instructions for making structure-specific endonucleases and other proteins involved in the repair of DNA interstrand cross-links. The SLX4 protein is part of a complex of proteins that work together to ensure the stability of the genetic material within the cells.

Protein Homology

Normal Protein

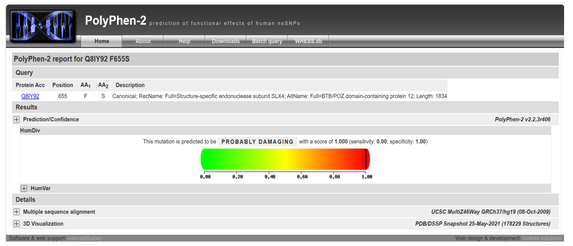


Mutated Protein



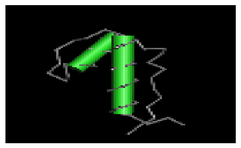
Prediction of Pathogenicity: PolyPhen2 Analysis

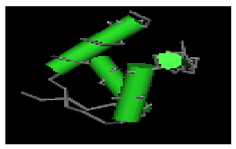
PolyPhen2 predicted that the mutation is possibly damaging with a score of 1.000, a



Conserved Domains

“SLX4, also called BTB/POZ domain-containing protein 12 (BTBD12), is a Holliday junction resolvase subunit that binds multiple DNA repair/recombination endonucleases and is required for DNA repair. Mutations in the SLX4 gene are found in Fanconi anemia. This model corresponds to a conserved region called the SAP domain, which is responsible for the binding of MUS81, which plays a distinct role in interstrand crosslink repair” (National Library of Medicine).
“The Slx4 protein is a heteromeric structure-specific endonuclease found from fungi to mammals. Slx4 with Slx1 acts as a nuclease on branched DNA substrates, particularly simple-Y, 5'-flap, or replication fork structures by cleaving the strand bearing the 5' non-homologous arm at the branch junction and thus generating ligatable nicked products from 5'-flap or replication fork substrates”(National Library of Medicine).





DISCUSSION AND CONCLUSION

- The SLX4 protein plays a critical role in several major DNA repair pathways. These include the repair of DNA crosslinks and the resolution of Holliday junctions. These processes are important for maintaining the integrity of the genome, preventing mutations, and ensuring proper cell division.
- Mutations in the SLX4 gene can lead to numerous types of conditions, including Fanconi anemia, which is a rare inherited disorder characterized by bone marrow failure, increased cancer risk, specifically breast cancer, and many other physical abnormalities. Individuals containing a mutation in the SLX4 gene are more susceptible to DNA damage because their cells are far less efficient at repairing damage. An accumulation of mutations over time is what ultimately causes such an increased risk of cancers and other health problems.

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