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Analysis of MEN1 Variants in Angiofibroma

Elaine Vanterpool
Oakwood University, evanterpool@oakwood.edu

Wendolyn Johnson
Oakwood University

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Wendolyn Johnson and Elaine Vanterpool, PhD

Oakwood University

Department of Biological Sciences Huntsville AL, 35896

ABSTRACT

Angiofibroma, an inherently aggressive neoplasm predominantly localized within the nasopharynx, typically afflicts adolescent males within the age bracket of 10 to 20, although it may manifest in older males. Clinical presentation often encompasses nasal obstruction, recurrent epistaxis, facial neuralgia, and edema. Therapeutic modalities primarily entail surgical excision, supplemented by adjuvant radiotherapy and, in select classes, hormonal manipulation. Despite its benign histological classification, unmitigated or inadequately controlled angiofibroma poses significant morbidity risks. Interrogation of angiofibroma genetics elucidates tumorigenic mechanisms and informs therapeutic stratification, prognostication, genetic counseling, and precision medicine optimization. The MEN1 gene encodes the Menin protein, a critical tumor suppressor. The Menin domain (a conserved motif within the *MEN1* gene) exerts direct regulatory influence over Menin protein conformation and activity. Mutational perturbations within this domain manifest consequential effects across diverse tissue compartments, including the parathyroid glands, pancreatic islet cells, and anterior pituitary gland, precipitating alterations in MEN1 gene expression profiles. Here, Simple ClinVar was used to research angiofibroma, and findings implicated *MEN1* and its variants. *MEN1* variants were then analyzed using Polyphen-2 and SWISS modeling, unraveling their molecular architecture. Polyphen-2 analysis demonstrated potentially pathogenic mutations of Leu22Arg, Met1Val, and Ser38Phe with scores of 0.998, 0.656, and 0.999, respectively. This research unveils the *MEN1* gene's etiological pertinence to angiofibroma pathogenesis and its broader implications within the panorama of human physiology and disease pathophysiology.

Introduction

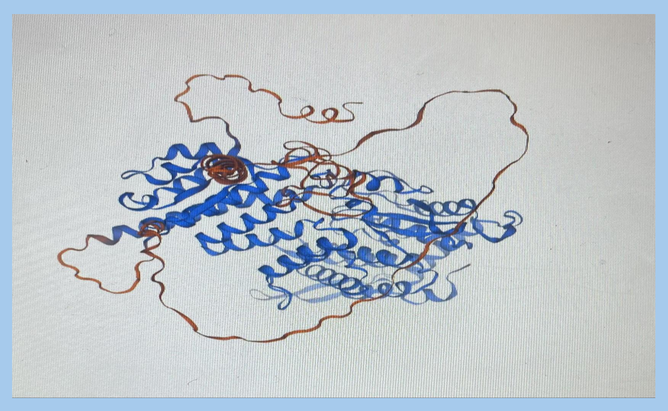
Angiofibroma is a rare autosomal dominant genetic disorder that is associated with a condition called juvenile nasopharyngeal angiofibroma (JNA). The exact cause of JNA is not fully understood, but it is believed to be related to hormonal changes during puberty, as it predominantly affects adolescent males. Juvenile nasopharyngeal angiofibroma affects the body by causing nasal obstruction, nosebleeds, facial deformity, sinus infections, hearing problems, and potential neurological symptoms. Angiofibroma contains four phenotypes, two variants, and two genes (MEN1 and TSC1). In this research, I focused on variants of the MEN1 gene due to its interesting links to the development of various tumors.

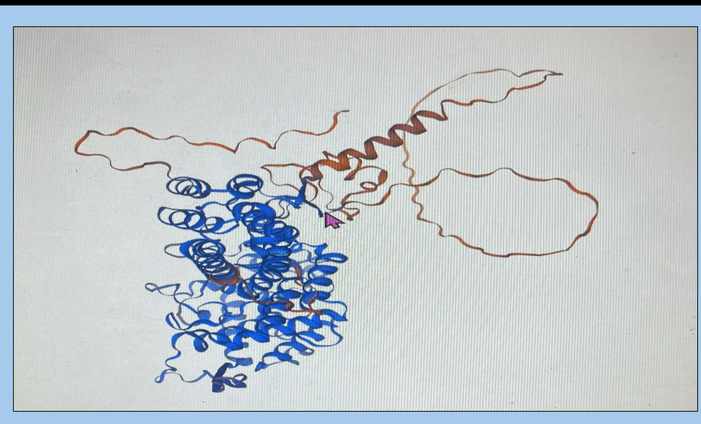
Methods

- Simple ClinVar was used to analyze the connection between angiofibroma and MEN1. It facilitates comprehension by explaining how mutations in the MEN1 gene can predispose individuals to the development of angiofibroma.
- PolyPhen-2 was utilized to predict the potential pathogenicity of mutations identified in the gene.
- The Swiss Model was used to predict the three-dimensional structure (3D) of the MEN protein.
- NCBI was used to identify the conserved domain of MEN1

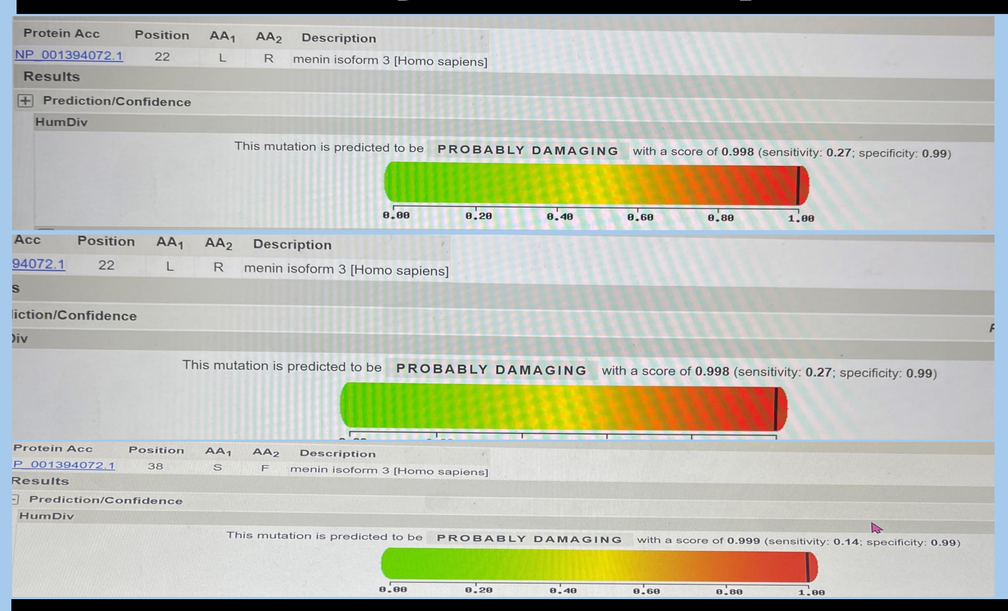
Results

Swiss Model



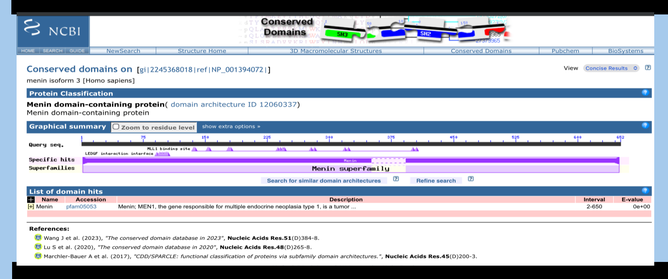


PolyPhen-2 predictions



Each variant, leu22arg, met1val, and ser38phe with high scores of 0.998, 0.656, and 0.999 were predicted to be probably damaging.

Conserved domain



The MEN1 gene contains conserved domains, including the MEN1 homology domain, vital for tumor suppression.

Discussion and Conclusion

In conclusion, Angiofibroma is a type of tumor characterized by a proliferation of blood vessels and fibrous tissue. More specifically, Juvenile nasopharyngeal angiofibroma is commonly found in males between the ages of ten and twenty-five. Symptoms of this disease are often characterized by nasal congestion and obstruction, facial deformity, and hearing loss. MEN1 is one of the two genes (MEN1 and TSC1) associated with Angiofibroma. The MEN1 gene makes the protein Menin, which plays in regulating cell growth and division. Mutation in the MEN1 gene was found to be highly influential in the progression of Angiofibroma,.

References

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CODE

Characterizing Our DNA Exceptions