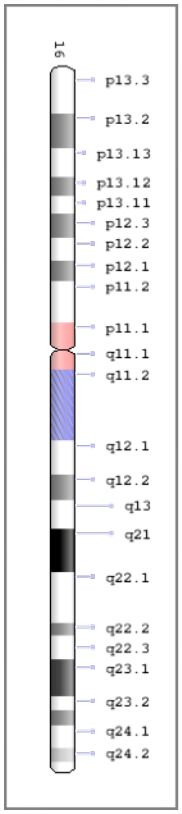
YOU ARE NOT ALONE

CHROMOSOME DISORDER OUTREACH

TOWNES-BROCKS SYNDROME

Townes-Brocks Syndrome



Townes-Brocks Syndrome is a well-known autosomal dominant condition caused by a mutation in the SALL1 gene, which is located on the long arm of chromosome 16 (segment 16q12). Some of these mutations can be de novo, but many have also been seen to be transmitted from parent to child.

SALL1 is a transcription factor known to be required for the proper development of the thumbs, ears, hearing, and anus in humans[1]. Individuals with point mutations in SALL1 have a stronger or more prevalent phenotype. These patients tend to have all three characteristics that are necessary for a diagnosis of Townes-Brocks syndrome[2]. It is hypothesized that these point mutations cause a dominant-negative phenotype due to an early truncation of the protein[3].

A significant proportion of patients with Townes-Brocks syndrome may have deletions in the 16q12 segment affecting either the SALL1 gene itself or its controlling elements. Currently, there are more than 35 known patients with this syndrome caused by interstitial deletions of 16q12. However, patients with deletions, rather than point mutations, tend to have a milder phenotype overall. It appears that a deletion of SALL1 is sufficient to cause a mild form of Townes-Brocks syndrome, but it is not enough to cause a severe form[1]. It does not appear that a larger deletion size contributes to a more severe phenotype[1].

In order to be diagnosed with Townes-Brock Syndrome, individuals must have at least two of the following three characteristics: anorectal malformations, ears malformations, or thumb

malformations. Individuals with these traits can then be screened for any mutations or deletions of the SALL1 gene.

Examples of anorectal malformations include features like an abnormal placement of the anus, imperforate anus, or anal stenosis. Ear malformations can include a wide variety of features. Overfolded superior helices, preauricular tags and microtia, or hearing impairment (both sensorineural and/or conductive) are possibilities in patients. Lastly, thumb and limb malformations can include features like preaxial polydactyly, triphalangeal thumbs, hypoplastic thumbs, clubfoot, syndactyly of the toes, or missing toes[2].

There are several other characteristics that, although seen less frequently, have been identified in patients with Townes-Brocks syndrome. Anomalies in the renal and urologic systems have been identified and include features like renal hypoplasia or dysplasia, multicystid kidneys, and a vesicoureteral reflux[2]. Congenital heart defects are also occasionally seen in patients. Identified defects include tetralogy of Fallot or ventricular septal defects[2]. Typically, severe intellectual disabilities or severe psychomotor delays are not reported among patients[4].

REFERENCES

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