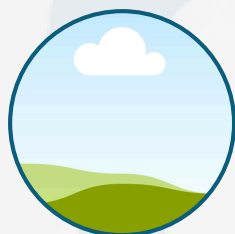


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A homozygous SP7/OSX mutation causes osteogenesis and dentinogenesis imperfecta with craniofacial anomalies

Abstract

Osteogenesis imperfecta (OI) is a heterogeneous spectrum of hereditary genetic disorders that cause bone fragility, through various quantitative and qualitative defects of type 1 collagen, a triple helix composed of two $\alpha 1$ and one $\alpha 2$ chains encoded by COL1A1 and COL1A2, respectively. The main extra-skeletal manifestations of OI include blue sclerae, opalescent teeth, and hearing impairment. Moreover, multiple genes involved in osteoblast maturation and type 1 collagen biosynthesis are now known to cause recessive forms of OI. In this study a multiplex consanguineous family of two affected males with OI was recruited for genetic screening. To determine the causative, pathogenic variant(s), genomic DNA from two affected family members were analyzed using whole exome sequencing, autozygosity mapping, and then validated with Sanger sequencing. The analysis led to the mapping of a homozygous variant previously reported in SP7/OSX, a gene encoding for Osterix, a transcription factor that activates a repertoire of genes involved in osteoblast and osteocyte differentiation and function. The identified variant (c.946C > T; p.Arg316Cys) in exon 2 of SP7/OSX results in a pathogenic amino acid change in two affected male siblings and develops OI, dentinogenesis imperfecta, and craniofacial anomaly. On the basis of the findings of the present study, SP7/OSX:c. 946C > T is a rare homozygous variant causing OI with extra-skeletal features in inbred Arab populations (Al-Mutairi et al., 2024).

Reference

Al-Mutairi, D.A., Jarragh, A.A., Alsabah, B.H., Wein, M.N., Mohammed, W. & Alkharafi, L. (2024) A homozygous SP7/OSX mutation causes osteogenesis and dentinogenesis imperfecta with craniofacial anomalies. JBMR Plus, 8, ziae026.