SSBP1

Extreme Clinical Variability Among Carriers of Pathogenic Variant in SSBP1 [1].

Five families with previously unsolved optic atrophy and retinal dystrophy underwent whole genome sequencing as part of the National Institute for Health Research BioResource Rare-Diseases and the UK's 100,000 Genomes Project. In silico analysis and protein modelling was performed on the identified variants. Deep phenotyping including retinal imaging and International Society for Clinical Electrophysiology of Vision standard visual electrophysiology was performed.

Results: Seven individuals from five unrelated families with bilateral optic atrophy and/or retinal dystrophy with extraocular signs and symptoms in some are described. In total, 6 SSBP1 variants were identified including the previously unreported variants: c.151A>G, p.(Lys51Glu), c.335G>A p.(Gly112Glu), and c.380G>A, p.(Arg127Gln). One individual was found to carry biallelic variants (c.380G>A p.(Arg127Gln); c.394A>G p.(Ile132Val)) associated with likely autosomal recessive SSBP1-disease. In silico analysis predicted all variants to be pathogenic and Three-dimensional protein modelling suggested possible disease mechanisms via decreased single-stranded DNA binding affinity or impaired higher structure formation.

SSBP1 is essential for mitochondrial DNA replication and maintenance, with defects leading to a spectrum of disease that includes optic atrophy and/or retinal dystrophy, occurring with or without extraocular features. This study provides evidence of intrafamilial variability and confirms the existence of an autosomal recessive inheritance in SSBP1-disease consequent upon a previously unreported genotype [2].

1)
Melo ES, Paiva ARB, de Amorim AD Jr, Lima de Carvalho JR Jr, Bezerra MER, van der Linden V, Lynch DS, Kok F. Extreme Clinical Variability Among Carriers of Pathogenic Variant in SSBP1. Mov Disord. 2022 Feb 10. doi: 10.1002/mds.28956. Epub ahead of print. PMID: 35142387.
2)
Jurkute N, D'Esposito F, Robson AG, Pitceathly RDS, Cordeiro F, Raymond FL, Moore AT, Michaelides M, Yu-Wai-Man P, Webster AR, Arno G; Genomics England Research Consortium. SSBP1-Disease Update: Expanding the Genetic and Clinical Spectrum, Reporting Variable Penetrance and Confirming Recessive Inheritance. Invest Ophthalmol Vis Sci. 2021 Dec 1;62(15):12. doi: 10.1167/iovs.62.15.12. PMID: 34905022; PMCID: PMC8684315.