Microcephaly capillary malformation syndrome

Microcephaly-capillary malformation syndrome is a congenital and neurodevelopmental disorder caused by biallelic mutations in the STAMBP gene.

Hori et al., identify a novel homozygous mutation located in the SH3 binding motif of STAMBP (NM_006463.4) (c.707C>T: p.Ser236Phe) through whole exome sequencing. The case patient was a 2-year-old boy showing severe global developmental delay, progressive microcephaly, refractory seizures, dysmorphic facial features, and multiple capillary malformations. Immunoblot analysis of patient-derived lymphoblastoid cell lines (LCLs) revealed a severe reduction in STAMBP expression, indicating that Ser236Phe induces protein instability. STAMBP interacts with the SH3 domain of STAM and transduces downstream signals from the Jaks-STAM complex. The substitution of Ser236Phe found in the case patient was located in the SH3-binding motif, and we propose the mutation may block STAM binding and subsequently induce STAMBP degradation. Contrary to previously reported STAMBP mutations, the Ser236Phe mutation did not lead to constitutive activation of the PI3K-AKT-mTOR pathway in patient-derived LCLs, as indicated by the expression of phosphorylated S6 ribosomal protein, suggesting that it is not the major pathomechanism underlying the disorder in this patient [1].

1)
Hori I, Miya F, Negishi Y, Hattori A, Ando N, Boroevich KA, Okamoto N, Kato M, Tsunoda T, Yamasaki M, Kanemura Y, Kosaki K, Saitoh S. A novel homozygous missense mutation in the SH3-binding motif of STAMBP causing microcephaly-capillary malformation syndrome. J Hum Genet. 2018 Jun 15. doi: 10.1038/s10038-018-0482-3. [Epub ahead of print] PubMed PMID: 29907875.