Specific variants in HESX1

- Dattani et al [1998] found a homozygous missense HESX1 variant (p.Arg160Cys) in a brother and sister with septooptic dysplasia, agenesis of the corpus callosum, and CPHD (OMIM 182230).

- Individuals homozygous for the recessive variant p.Arg160Cys had septo-optic dysplasia (SOD/Morsier syndrome) with agenesis of the corpus callosum and CPHD [Brickman et al 2001].

- Individuals with a monoallelic variant had milder phenotypes suggesting that they result from haploinsufficiency of the HESX1 protein [Tajima et al 2003].

- In 2011, Vivenza et al describe a novel mutation (c.357+3G>A), identified at the heterozygous state in an IGHD patient. This mutation prevents the generation of one of the alternative isoforms normally produced by the wild-type allele, predicting a truncated HESX1 protein. The mutation is likely to cause IGHD in the heterozygous patient by interfering with the downregulation of HESX1 expression mediated by alternative splicing and nonsense-mediated decay.

- In 2011, Durmaz et al found a novel homozygous mutation (R160H) within the homeodomain of HESX1, which, is the first to be described in humans. Neuroimaging studies revealed anterior pituitary aplasia, a normal posterior pituitary gland, and a thin pituitary stalk but no midline abnormalities. Optic nerve studies showed no pathology. HESX1 mutation causing an R160H substitution can result in panhypopituitarism without midline defects.

- Also in 2011, Reynaud et al studied 83 patients with pituitary stalk interruption syndrome and found one novel HESX1 homozygous nonsense mutation generating a truncated protein, resulting in total loss of homeodomain and co-repressor binding. This HESX1 p.Arg109X mutation leads to a severely truncated protein including the homeodomain that is involved in DNA binding and required to recruit components of N-CoR-associated co-repressors.

- In 2013, a novel heterozygous sequence variant (c.142A>T, p.T48S) was found in HESX1 in one PSIS patient by Yan Yang et al.
References


