ANGPTL6

ANGPTL6 (Angiopoietin Like 6) is a Protein Coding gene. Diseases associated with ANGPTL6 include Gnathomiasis and Enterobiasis. Among its related pathways are p70S6K Signaling and Akt Signaling. An important paralog of this gene is ANGPTL2.

Bourcier et al. identified one rare nonsense variant (c.1378A>T) in the last exon of ANGPTL6 (Angiopoietin-Like 6)-which encodes a circulating pro-angiogenic factor mainly secreted from the liver-shared by the four tested affected members of a large pedigree with multiple IA-affected case subjects. We showed a 50% reduction of ANGPTL6 serum concentration in individuals heterozygous for the c.1378A>T allele (p.Lys460Ter) compared to relatives homozygous for the normal allele, probably due to the non-secretion of the truncated protein produced by the c.1378A>T transcripts. Sequencing ANGPTL6 in a series of 94 additional index case subjects with familial IA identified three other rare coding variants in five case subjects. Overall, we detected a significant enrichment ($p = 0.023$) in rare coding variants within this gene among the 95 index case subjects with familial IA, compared to a reference population of 404 individuals with French ancestry. Among the 6 recruited families, 12 out of 13 (92%) individuals carrying IA also carry such variants in ANGPTL6, versus 15 out of 41 (37%) unaffected ones. We observed a higher rate of individuals with a history of high blood pressure among affected versus healthy individuals carrying ANGPTL6 variants, suggesting that ANGPTL6 could trigger cerebrovascular lesions when combined with other risk factors such as hypertension. Altogether, our results indicate that rare coding variants in ANGPTL6 are causally related to familial forms of IA [1)].

1)
Bourcier R, Le Scouarnec S, Bonnaud S, Karakachoff M, Bourcereau E, Heurtebise-Chrétien S, Menguy C, Dina C, Simonet F, Moles A, Lenoble C, Lindenbaum P, Chatel S, Isidor B, Génin E, Deleuze JF, Schott JJ, Le Marec H; ICAN Study Group, Loirand G, Desal H, Redon R. Rare Coding Variants in ANGPTL6 Are Associated with Familial Forms of Intracranial Aneurysm. Am J Hum Genet. 2018 Jan 4;102(1):133-141. doi: 10.1016/j.ajhg.2017.12.006. PubMed PMID: 29304371.