NFX1

NFX1 (Nuclear Transcription Factor, X-Box Binding 1) is a Protein Coding gene. Among its related pathways are PI3K-Akt signaling pathway and Apoptosis and survival Caspase cascade. Gene Ontology (GO) annotations related to this gene include nucleic acid binding and DNA-binding transcription factor activity. An important paralog of this gene is NFXL1.

Exome sequencing (ES) was performed in a dominant likely family with intracranial aneurysms (IAs). Variants were analyzed by an in-house developed pipeline and prioritized using various filtering strategies, including population frequency, variant type, and predicted variant pathogenicity. Sanger sequencing was also performed to evaluate the segregation of the variants with the phenotype.

Based on the ES data obtained from five individuals from a family with 7/21 living members affected with IAs, a total of 14 variants were prioritized as candidate variants. Familial segregation analysis revealed that NFX1 c.2519T>C (p.Leu840Pro) segregated in accordance with Mendelian expectations with the phenotype within the family-that is, present in all IA-affected cases and absent from all unaffected members of the second generation. This missense variant is absent from public databases (1000genome, ExAC, gnomAD, ESP5400), and has damaging predictions by bioinformatics tools (Gerp ++ score = 5.88, CADD score = 16.43, MutationTaster score = 1, LRT score = 0). In addition, 840Leu in NFX1 is robustly conserved in mammals and maps in a region before the RING-type zinc finger domain.

NFX1 c.2519T>C (p.Leu840Pro) may contribute to the pathogenetics of a subset of FIAs [1)]

1)
Ding X, Zhao S, Zhang Q, Yan Z, Wang Y, Wu Y, Li X, Liu J, Niu Y, Zhang Y, Zhang M, Wang H, Zhang Y, Chen W, Yang XZ, Liu P, Posey JE, Lupski JR, Wu Z, Yang X, Wu N, Wang K. Exome sequencing reveals a novel variant in NFX1 causing intracranial aneurysm in a Chinese family. J Neurointerv Surg. 2019 Aug 10. pii: neurintsurg-2019-014900. doi: 10.1136/neurintsurg-2019-014900. [Epub ahead of print] PubMed PMID: 31401562.