Novel ATPase/ubiquitin ligase Mysterin is responsible for familial Moyamoya disease and is involved in proper angiogenesis

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Moyamoya disease is an idiopathic disorder characterized by occlusive lesions that resemble “puffs of smoke” (moyamoya vessels;). Its susceptibility locus has been mapped to 17q25.3. Here, we report on the cloning of *mysterin* as a susceptible gene for moyamoya disease. This gene encodes a huge cytosolic protein that possesses two functional domains, an ATPase motif and an ubiquitin ligase motif. We found one missense SNP in East Asian patients, which elevated the susceptibility to moyamoya disease by 111.8 ($p=10^{-119.2}$), and a mutation in a Caucasian family. Mysterin knock-down zebrafish showed the unique anomaly of angiogenesis. Aberrant function of mysterin may underlie the characteristic vascular phenotype observed in moyamoya disease.