

The SIM Laboratory

Our lab focuses on understanding the genetic basis of intracranial aneurysms. An intracranial aneurysm is an abnormal out-pouching or dilation of an intracranial blood vessel and affects up to 10% of the general population. Excluding trauma, intracranial aneurysm rupture is the most common cause of subarachnoid hemorrhage, and often leads to severe disability or death. Ten to twenty percent of intracranial aneurysm patients have a positive family history for aneurysms or aneurysmal rupture and there is up to five-fold increased risk of aneurysm incidence among first-degree relatives compared to the general population. Although many genetic loci have been linked to familial intracranial aneurysms, no single disease-causing gene variant has been identified.

Our goal is to identify genetic determinants that may provide not only a deeper understanding of aneurysm pathobiology, but also diagnostic tools for identifying individuals at increased risk for aneurysm formation or rupture. In our lab, we employ genetic approaches such as a genome-wide linkage approach to search for genetic mutations in single, large affected families. An example of a family that is being studied in our lab and for which a novel disease susceptibility locus has been identified is shown below.

We also use a candidate gene approach to characterize genes that might be important for aneurysm development based on their known function, for instance, in vascular wall formation, extracellular matrix remodeling; or based on their role in other familial diseases that have been associated with intracranial aneurysms such as aortic aneurysms (transforming growth factor genes) or autosomal dominant polycystic kidney disease (polycystin genes).

Publications

Santiago-Sim T, DePalma SR, Ju KL, McDonough B, Seidman CE, Seidman JG, Kim DH. Genomewide Linkage in a Large Caucasian Family Maps a New Locus for Intracranial Aneurysms to Chromosome 13q. *Stroke*. 2009 (in press).

Santiago-Sim T, Mathew-Joseph S, Pannu H, Milewicz DM, Seidman CE, Seidman JG, Kim DH. Sequencing of TGF- β pathway genes in familial cases of intracranial aneurysm. *Stroke*. 2009 (in press).

Santiago-Sim T, Kim DH: Pathobiology of Intracranial Aneurysms. In Winn HR (ed): Youmans Neurological Surgery 6e. Philadelphia, WB Saunders (in press).

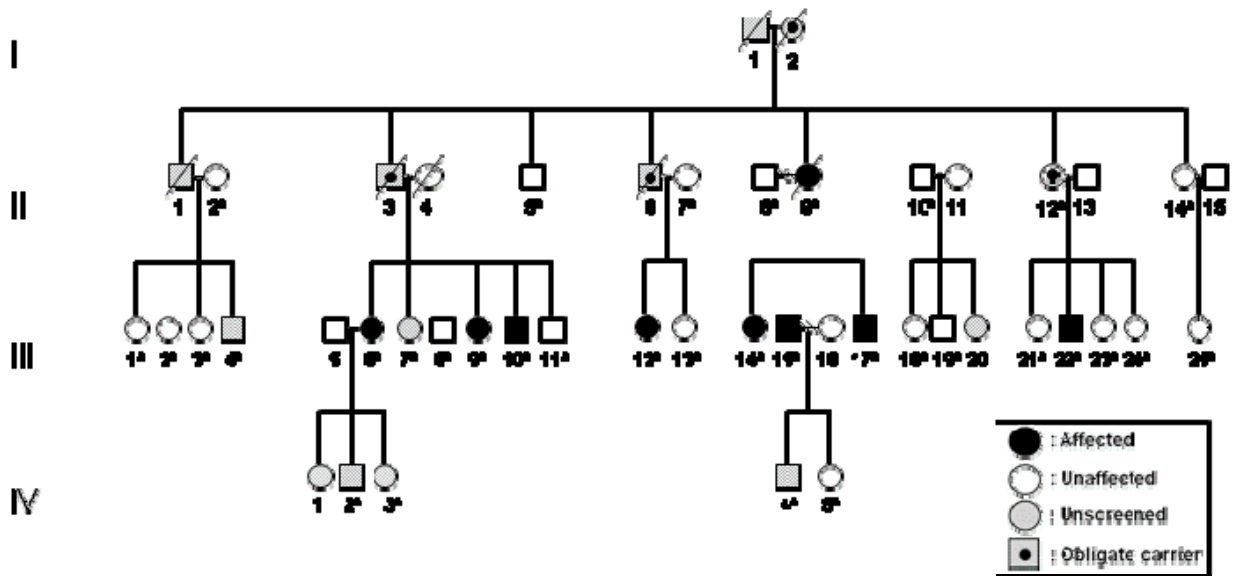
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Intracranial Aneurysm



CVM family pedigree



Linkage analysis results for the CVM family

