Genes may predict vascular malformation

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A pair of studies, led by Medical College of Wisconsin scientists at Children's Research Institute in Milwaukee, may translate into rapid molecular tests to distinguish between hemangiomas and congenital blood or lymph vessel malformations in infants. Hemangiomas are common birthmarks consisting of benign tumors of blood vessels. The studies appear in the January 29, 2009 issue of the journal *Blood*.

"Our findings may lead to earlier diagnosis, precise classification and ultimately, targeted therapy for infants with hidden congenital vascular malformations," says study author Ramani Ramchandran, Ph.D., associate professor of pediatrics in the division of developmental biology.

In the first paper, the team used genetic manipulations to study blood vessel formation in the fast-developing and conveniently transparent zebra fish embryo. They identified sucrose non-fermenting receptor kinase-1 (Snrk-1), as a gene that plays a role in the creation, migration and differentiation into arteries and veins of angioblasts, the parent cell of all blood vessels.

In the second paper, similar zebra fish embryo studies revealed that Dusp-5, a vascular-specific gene that is expressed in these parent cells and in the established blood vessels, counteracts the function of Snrk-1 to control the population of parent cells. Most importantly, the team then identified mutations in Dusp-5 and Snrk-1 genes in the affected tissues of humans with vascular malformations, thus linking the Snrk-1/Dusp-5 signaling pathway to human disease.

While the pathway these genes target in humans is novel, and remains undiscovered, it may provide the breakthrough needed to identify potential causes of vascular malformation, according to Dr. Ramchandran. He noted that these and other issues are under active investigation in his laboratory.

"We believe that specific mutations in Dusp-5 and Snrk-1 may provide keys to distinguish between hemangiomas and vascular malformations. Vascular malformations fall into different classes based on the affected vessel type. For example, venous malformations affect veins and arterial malformations affect arteries. Mutations in Snrk-1 may actually help classify vascular malformations as venous or lymphatic malformations and thus distinguish them from other malformations," he says.

"Ultimately, we plan to expand the mutation study to include more patients to determine the predictability, severity and correlation of disease to mutations, and identify the cell type that harbors the mutation. Then, we can model the structure of the mutated protein to generate drugs that selectively target the diseased tissue.

Source: Medical College of Wisconsin