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New mouse models generated for MYH9 genetic disorders

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Researchers have created the first mouse models of human MYH9 genetic disorders, which cause several problems -- including enlarged platelets and sometimes fatal kidney disease.

The MYH9 gene makes non-muscle myosin II-A protein. This protein plays a critical role in helping cells move to their correct home during embryonic development. Later in life, the protein continues its involvement in cell migration, cell-cell adhesion and also in maintaining cell shape, says Yingfan Zhang, Ph.D., a postdoctoral fellow at the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health.

Zhang, with the NHLBI's Laboratory of Molecular Cardiology, has focused on three of the more than forty MYH9 mutations identified in humans. One of the mutations impaired myosin's motor activity, while the other two affected the protein's ability to form filaments.

In work she will present today at the 55th Annual Biophysical Society Annual Meeting in Baltimore, MD, Zhang generated specific mutations in the MYH9 gene, then bred mice with one or two copies of the impaired gene. While mice with two copies of the gene causing motor impairment died as embryos, those with one mutated gene showed symptoms similar to humans. The filament forming impaired mice showed symptoms with both one and two mutant genes.

Inactivation of the MYH9 gene in humans causes a disorder called the

May-Hegglin anomaly (MHA), a rare genetic disorder of the blood platelets that causes them to be abnormally large and also causes abnormalities known as Dohle bodies in leukocytes. Mutations of the MYH9 are also associated with kidney disease in humans.

"The mice had very, very large platelets, exactly like humans, and those platelets didn't work very well," says senior author Robert Adelstein,M.D. also with the NHLBI's Laboratory of Molecular Cardiology. "The mice also developed kidney disease."

The mouse models will help scientists better understand MYH9 disorders in humans, Adelstein says. "Now we can study the development of the disease in real-time, and try to figure out what has gone wrong and why the gene product has led to these defects."

More information: The presentation, "Mouse Models of Human MYH9-Related Diseases" by Yingfan Zhang et al is at 10:30 AM on Wednesday, March 9, 2011 in the Baltimore Convention Center, Hall C. Abstract: tinyurl.com/4f8a6zb

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