New animal model for hemophilia A developed

September 3 2010

(PhysOrg.com) -- Researchers at Yale School of Medicine have developed a new animal model for studying hemophilia A, with the goal of eventually treating people with the disorder. Hemophilia A, a hereditary defect that prevents blood from clotting normally, is caused by a variety of mutations in the factor VIII gene.

Published online in the *Journal of Thrombosis and Haemostasis*, the study aimed to provide a better understanding of hemophilia A, according to first author and veterinarian Carmen Jane Booth, assistant professor of comparative medicine, and co-director of Mouse Research Pathology at Yale School of Medicine.

Booth and her team studied an inbred colony of rats that lived healthily for many years before spontaneously exhibiting symptoms similar to those of humans with hemophilia A, including hemorrhage, spontaneous bruising, swollen joints, prolonged bleeding from minor wounds and unexplained deaths among pregnant and postpartum rats. The team ruled out environmental factors as being responsible for the bleeding disorder in these rats, showed that it was inherited, and conducted diagnostic tests to identify the specific coagulation factor and underlying genetic defect responsible for the disorder.

The team found that the affected animals had a decreased amount of factor VIII. They sequenced the rat factor VIII cDNA and identified a mutation in this gene that was similar to mutations in some people with severe hemophilia. The factor VIII gene is located on chromosome 18 in

rats, in contrast to its location on the X chromosome in mice and humans. "The larger size of the rat and the gene location difference makes the rat a unique model, well suited to developing novel therapies for acquired and hereditary factor VIII deficiencies," said Booth.

When we get a minor cut, bleeding should stop in about 20 to 30 seconds, but in hemophiliacs, the bleeding is prolonged because the blood cannot form or maintain a proper blood clot. This can lead to bruises, injured joints and even life-threatening bleeding from everyday activities. The research team found that treating the affected rats with human recombinant factor VIII corrected their coagulation abnormality and stopped the prolonged bleeding.

"This is the only spontaneous rat model of hemophilia A," said Booth. "Rats bruise and bleed similarly to humans with hemophilia A. Ultimately, we plan to translate this model for use in developing gene therapies and evaluating novel therapeutics for treating people with hemophilia A."

More information: *Journal of Thrombosis and Haemostatis* doi: 10.1111/j.1538-7836.2010.03978

Provided by Yale University