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Control of blood clotting by platelets described; provides medical promise

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Cell fragments called platelets are essential to promote blood clotting. Virginia Tech faculty members and students have discovered novel molecular interactions at the surface of platelets that control blood clotting.

The Virginia Tech researchers describe how platelets perform this life-saving magic in the November 24 online issue of the journal *PLoS ONE* (Public Library of Science) in the article "Sulfatides Partition Disabled-2 in Response to Platelet Activation," by Karen E. Drahos, biological sciences Master's degree student from Roanoke, Va.; John D. Welsh, a biological sciences undergraduate student from Pennington, N.J.; and biological sciences Assistant Professors Carla V. Finkielstein and Daniel G. S. Capelluto.

Capelluto and Finkielstein study how proteins signal from biological membranes. One such membrane protein is the integrin receptor that resides on the surface of platelets. A protein that strongly promotes platelet activation through the integrin receptor is thrombin. When there is tissue injury, thrombin converts fibrinogen into fibrin to form a network that traps red blood cells and platelets, creating a clot.

However, the platelets may not remain trapped. They can break their bonds with the network and thin or remove a clot - a good thing if the clot is blocking an artery, as in thrombosis or stroke.

One part of the process is well known. When a platelet is stimulated,

such as by thrombin, the protein Disabled-2 (Dab2) moves from where it is stored inside of the platelet to the surface, where it interacts with the integrin receptor. If this is the case, Dab2 inhibits blood clotting.

Experimentation and measurements by the Virginia Tech researchers revealed that Dab2 also binds to sulfatides, a lipid that also resides on the surface of platelets. Sulfatides sequester Dab2 proteins, preventing them from binding to the integrin receptor.

"That is, sulfatides partition Dab2 into two pools - one pool that is part of the clotting process and one pool that prevents coagulation," said Capelluto.

When no longer on high alert to regulate clotting, the Dab2 proteins return to the interior of the platelet. "They are likely recycled for the next time they are needed," said Capelluto.

The study was Drahos' Master's thesis research, conducted in both Capelluto's and Finkielstein's labs. The thesis received the 2009 William Preston Society Thesis Award in Life Sciences for the best original research with potential to benefit all people. Co-author John Welsh is now a graduate student in Finkielstein's lab.

The PLoS ONE article stops with the definition of the chemistry of platelets' two responses to thrombin. But research by Finkielstein and Capelluto is looking at the platelet aggregation inhibitor process as a target for intervention to control bleeding and clotting. "This promises a high impact at the clinical level," said Capelluto. "The goal is a tool that could be used in surgery and could help people with bleeding or blood clotting disorders without drugs and side effects."

Source: Virginia Tech (news : web)