Novel functions of platelets discovered

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A new finding could lead to novel treatments to reduce bleeding in trauma and severe infections. The research, from Oklahoma Medical Research Foundation scientists Lijun Xia, M.D., Ph.D., Jianxin Fu, M.D., Ph.D., and Brett Herzog, Ph.D., appears in the most recent issue of the journal *Nature*.

One way the immune system keeps a body healthy is through immune surveillance. Lymphocytes, a type of white blood cell, constantly exit the bloodstream and "check in" at the lymph nodes to learn about possible pathogens or abnormal cell growth. The function prepares the immune system to fight infections and dispose of pre-cancerous cells.

For years, scientists have wondered how lymphocytes exit the bloodstream at a large volume without causing bleeding. Xia and his team of researchers found that platelets, which normally stop blood loss by clumping and forming plugs in blood vessel holes after injuries, activate a screening process. And this process allows lymphocytes to exit into lymph nodes without letting red blood cells leave the blood vessel.

"Platelets are the smallest blood cells that work in clotting to heal cuts because they stick to the site of the injury," said Xia, a member of OMRF's Cardiovascular Biology Research Program. "This novel function requires platelets to dump a specific lipid content, but does not need intact platelets because it's not forming a clot. We never knew they could do this before."

Not only are platelets making it possible for lymphocytes to leave the

blood vessel, they're doing so by going outside the vessel, themselves—another novel finding, he said.

When scientists interrupted the process by removing a protein called podoplanin, the screening process stopped working, allowing both lymphocytes and red blood cells to escape. The new study reveals a novel function of platelets independent of their hemostatic role. The findings could alter the ways in which doctors use platelets to treat traumatic injuries and serious infections.

Intact platelets that can clot usually only last 5 to 7 days in the blood and cannot be frozen, making storage a problem, Xia said. Since these new functions do not rely on intact platelets, it points to different uses for platelets, perhaps even some that have been frozen. If it works out, the discovery could be useful in stopping widespread internal bleeding caused by explosive traumas or severe infections.

"As the research continues, I think there's a possibility this will lead to new therapeutics that could slow or stop hemorrhaging in trauma and sepsis-related illnesses," Xia said.

The breakthrough has opened several avenues for further research, he said. One will be a better understanding of how platelets go outside the vessels to start the process. They will also be looking to see if platelets perform the same role in letting rapid-attack immune cells called neutrophils out of the bloodstream to fight infections.

"This is a prime example of the important research that the Institutional Development Award program makes possible in states that have historically had low levels of funding from the National Institutes of Health," said NIH grant program official María Teresa Canto, D.D.S., M.S., M.P.H. "Dr. Xia's study sheds light on a process that is key to vascular health as well as to the development of inflammation and

associated diseases."

More information: Podoplanin maintains high endothelial venule integrity by interacting with platelet CLEC-2, *Nature*, DOI: 10.1038/nature12501

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