Immune cells use tethered slings to avoid being swept away

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Neutrophils, critical components of the immune system's response to bacteria and other pathogens, throw out tube-like tethers that act as anchor points, controlling their speed as they roll along the walls of blood vessels during extremely fast blood flow en route to an infection site, according to research presented on Dec. 17 at the American Society for Cell Biology Annual Meeting in San Francisco.

To attack a bacterial infection in tissue, neutrophils have to leave the blood stream and approach the infection site through tiny venules that are part of the microcirculation system, according to Prithu Sundd, PhD, who is in the laboratory of Klaus Ley, PhD, at the La Jolla Institute for Allergy and Immunology, La Jolla, CA.

Extensions of the cell membrane, the slings turned out to be vital aids in the navigation because if neutrophils lose control while attempting to enter infected tissue, they can be swept away in the blood flow, which could delay the immune defense mechanism. Flow in these narrow venules is measured as wall shear stress. A shear stress exceeding 2 dyn/cm2 can sweep away other leukocytes, but neutrophils have a special ability to move under control at shear stress 10 times higher.

Shear-resistance in neutrophils was known to be aided by cell flattening and by these mysterious membrane extensions but the details were poorly understood. To determine the exact mechanism behind neutrophils' rolling, Dr. Sundd working with physicist Alex Groisman, PhD, of the University of California, San Diego, to shoot a high-speed

video, using total internal reflection fluorescence microscopy to track labeled neutrophils from mouse bone marrow rolling along an artificial venule, all driven by a microfluidic device at a shear stress of 6 to 10 dyn/cm2.

In the 15-second video, the red-dyed neutrophil used its long membrane tether like a sling to anchor itself without being swept away by the high shear force of blood. Instead of a single anchor point, the sling tether is coated by patches of cell adhesion molecules that latched onto the passage walls but peeled loose, patch by patch, as the neutrophil gently rolled forward. At the tether's end, the neutrophil swung it ahead like a lasso to gain new leverage.

The researchers say their dramatic video underscores the complexity of the body's immune system. The slings are not only unique structures, says Dr. Sundd, but may help explain how rolling neutrophils are able to present their antigen-sensing ligands at the blood vessel wall before entering the site of infection.

More information: "Slings enable leukocyte rolling during inflammation," Monday, Dec. 17, 2012, 12:30 pm, Session: Intermediate Filaments, presentation:1290, poster: B575, Exhibit Halls A-C

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