Researchers investigate why a limited number of white blood cells are attracted to injured tissue

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As any weekend warrior knows, an errant elbow or a missed ball can put a crimp in an afternoon of fun. The bruising and swelling are painfully obvious, but the processes occurring under the skin remain full of mystery.

What is known is that leukocytes, or white blood cells, mobilize to protect injured body tissue from infection. What is not understood is why some leukocytes —but not others—are attracted to damaged tissue.

The response begins when leukocytes travel through blood vessels near the site of the injury and stop. Eight out of ten white blood cells will eventually continue traveling through the blood vessel, while the other two cells will actually enter the tissue to begin fighting against infection. Thanks to a $9.2 million grant from the National Institutes of Health, a research team led by Richard Waugh, chairman of the Biomedical Engineering Department at the University of Rochester, is trying to find the reasons.

As Waugh points out, it's not necessarily bad for leukocytes to pass by the site of an injury. Inflammation occurs when there's injury to the tissue, combined with an influx of white blood cells to fight off potential infection. But the presence of too many white blood cells can damage the very tissue they're designed to protect. Chronic inflammation is responsible for many health problems, including arthritis, heart disease,

and stroke. While most research into leukocytes has been from a biochemical point of view, Waugh and his team bring a different perspective—one that accounts for the role of mechanics and fluid dynamics in the process. Waugh expects a better understanding of leukocyte behavior will result in pharmaceutical treatments that modulate the response of white blood cells.

The project team includes: Minsoo Kim and Ingrid Sarelius of the University of Rochester; Michael King and Moonsoo Jin of Cornell University; Daniel Hammer of the University of Pennsylvania; and Micah Dembo of Boston University.

For the last 10 years the research project has focused on a specific type of leukocyte called neutrophils, which are the first of the white blood cells to show up at the site of an injury or infection. The project team discovered that while many neutrophils attracted to the injured tissue roll along the surface of the blood vessel, only some are "captured" while flowing by, and fewer still actually enter the tissue. Adhesion molecules are expressed in high concentrations at the site of the injury, which makes the surface of the blood vessel stickier and causes many neutrophils to slow down or stop for a few minutes. Waugh likens the situation to fuzz balls rolling along a Velcro surface. The fuzz balls may or may not come to a stop, but they will certainly move more slowly as they remain in contact with the surface. Ultimately, most of the neutrophils will resume their flow through the blood vessel, while others will enter the tissue through specific locations that Waugh refers to as "hot spots."

The neutrophil does more than simply sit there after it comes to a stop. The cell, which has a wrinkled surface, flattens out, allowing more of its receptors to come in contact with the lining of the blood vessel, thereby increasing the level of communication between the neutrophil and the blood vessel wall. If the cell does not flatten out, it won't get enough

information and will simply move on.

"We know there are preferred sites for egress and that the cells use some kind of tactile cues to find their way into the tissue space," said Waugh. "But we don't quite know what determines the existence of hot spots. That's one thing we're working to understand."

Provided by University of Rochester