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White blood cells move like millipedes, scientists show

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How do white blood cells - immune system 'soldiers' - get to the site of infection or injury? To do so, they must crawl swiftly along the lining of the blood vessel - gripping it tightly to avoid being swept away in the blood flow - all the while searching for temporary 'road signs' made of special adhesion molecules that let them know where to cross the blood vessel barrier so they can get to the damaged tissue.

In research recently published in the journal *Immunity*, Prof. Ronen Alon and his research student Ziv Shulman of the Weizmann Institute's Immunology Department show how white blood cells advance along the length of the endothelial cells lining the blood vessels.

Current opinion maintains that immune cells advance like inchworms, but Alon's new findings show that the rapid movement of the white blood cells is more like that of millipedes. Rather than sticking front and back, folding and extending to push itself forward, the cell creates numerous tiny 'legs' no more than a micron in length - adhesion points, rich in adhesion molecules (named LFA-1) that bind to partner adhesion molecules present on the surface of the blood vessels. Tens of these legs attach and detach in sequence within seconds - allowing them to move rapidly while keeping a good grip on the vessels' sides.

Next, the scientists turned to the Institute's Electron Microscopy Unit. Images produced by scanning and transmission electron microscopes, taken by Drs. Eugenia Klein and Vera Shinder, showed that upon attaching to the blood vessel wall, the white blood cell legs 'dig'

themselves into the endothelium, pressing down on its surface. The fact that these legs - which had been thought to appear only when the cells leave the blood vessels - are used in crawling the vessel lining suggests that they may serve as probes to sense exit signals.

The researchers found that the shear force created by the blood flow was necessary for the legs to embed themselves. Without the thrust of the rushing blood, the white blood cells couldn't sense the exit signals or get to the site of the injury. These results explain Alon's previous findings that the blood's shear force is essential for the white blood cells to exit the blood vessel wall. The present study suggests that shear forces cause their adhesion molecules to enter highly active states. The scientists believe that the tiny legs are trifunctional: Used for gripping, moving and sensing distress signals from the damaged tissue.

In future studies, the scientists plan to check whether it is possible to regulate aggressive immune reactions (such as in autoimmune diseases) by interrupting the 'digging' of immune cell legs into the endothelium. They also plan to investigate whether cancerous blood cells metastasize through the blood stream using similar mechanisms in order to exit the blood vessels and enter different tissues.

Source: Weizmann Institute of Science (news : web)