Researchers have immune cells running in circles

November 2 2009

(PhysOrg.com) -- University of Illinois at Chicago College of Medicine researchers have identified the important role a protein plays in the body's first line of defense in directing immune cells called neutrophils toward the site of infection or injury.

Their results are described online in the Proceedings of the National Academy of Sciences.

Neutrophils are white blood cells that are activated by chemical cues to move quickly to the site of injury or infection, where they ingest bacteria. When alerted to infection, neutrophils move by changing shape, developing a distinct front and back, sending a "foot" out in front of them, and "crawling" toward the site of infection.

Hoping to better understand the role of a protein called p55 or MPPI that they had previously identified as highly expressed in neutrophils, the UIC researchers bred the first mice that completely lacked this protein.

The "knockout" mice had marked difficulty fighting infection and were slow to heal, according to Athar Chishti, professor of pharmacology and principal investigator in the study.

Instead of forming a single large pseudopod, or foot-like extension, in the direction of the infection, neutrophils from the knockout mice formed a number of small extensions all around the cell, said Chishti.

Neutrophils lacking p55 would follow a meandering path, wandering in circles. "It was as though the neutrophils had lost their sense of direction," said Brendan Quinn, graduate assistant researcher in pharmacology and first author of the study.

Neutrophils are part of the body's innate immunity and its first line of defense, so the speed of the response is key to healing. "The neutrophils eventually get to the infection site, but they would get there late," Quinn said.

The researchers also established how p55 wields its effect on neutrophils, demonstrating that although the cell's ability to reorganize its actin skeleton to produce pseudopods was undisturbed, a signaling lipid known to be important in establishing polarity, called PIP3, failed to localize on the leading edge of the p55-null neutrophils, instead diffusing throughout the cell.

Further, the p55-null neutrophils had a marked reduced activation of another important signaling protein, Akt, which is believed to play an important role in many cancers.

"This study offers clues to an important cell signaling pathway that is critical to cellular polarization processes in neutrophils and many other cells," said Chishti.

Source: University of Illinois at Chicago (news : web)