Medical Xpress

Insights into cell movement likely to aid immune study, cancer research

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Scientists at Washington University School of Medicine in St. Louis have used yeast cells to better understand a collection of proteins associated with the formation of actin networks, which are essential to cell movement.

The cell's ability to move is important to a broad range of biomedical concerns, including understanding how immune system cells pursue disease-causing invaders and how metastasizing cancer cells migrate from a tumor.

"One of the bad things that cancer cells do is to walk away from where they're supposed to be," says senior author John Cooper, M.D., Ph.D., professor of cell biology and physiology. "If they didn't walk away, cancer would be something that you could just cut out, and that would be the end of it. So one hope is that if we learn more about how cancer cells are moving, we can someday try to block that process."

The study appears this month in *Public Library of Science Biology*.

In yeast, the proteins Cooper's lab studied regulate actin networks' contributions to a process called endocytosis. Yeast cells use this process to take in materials from their surface by forming pits on their cell membrane. Actin networks provide the push that forms these pits and drives them into the cell.

In more complex cells like those found in humans, the proteins have

additional responsibilities that include helping regulate a process that cells use to thrust themselves forward. That process assembles many thin branching filaments of a polymer, actin, on the cell's surface. As these growing filaments reach nearby structures, they exert force that propels the cell in the desired direction.

Scientists know all the ingredients of actin networks, but they don't fully understand how the cell regulates their construction.

"One of the critical steps in generating an actin network is generating the seed of a new filament," says first author Brian Galletta, Ph.D., a postdoctoral scholar in Cooper's lab. "Scientists have identified a protein complex that can do this called Arp2/3."

Cooper's lab and others also had found several proteins that regulate Arp2/3 activity. In yeast, whose complete genetic code has been sequenced and can be searched, there appears to be a total of six proteins that activate or deactivate Arp2/3. These proteins are regularly found in actin patches on the surfaces of yeast cells, which are areas where endocytosis is about to take place.

"We wanted to know why there needed to be six of these proteins, if any one could either turn Arp2/3 on or off," says Galletta.

To learn more, Galletta mutated each of the six proteins alone and in various combinations. Researchers also attached two different fluorescent labels to other proteins involved in the early and late stages of endocytosis. The labels let them use a light microscope to make movies of hundreds of actin patches in the various yeast lines, recording the patches' movement across cell membranes and into cells.

With the help of a computerized tracking program from Anders Carlsson, Ph.D., professor of physics at Washington University, they

quantitatively analyzed the results, uncovering both dramatic and subtle variations in actin patch activity caused by the mutations.

"We found that sometimes the Arp2/3 regulatory proteins had a unique function of their own, and sometimes they cooperated," Galletta says. "That was surprising, because in the test tube, all of these proteins have very similar functions."

In addition to actin networks' use by immune cells chasing invading microorganisms, those same microorganisms sometimes hijack the actin networks in host cells, effectively seizing the cells' steering wheels and driving them around. The networks also play important roles in the developing embryo, enabling cells to assume specialized shapes or migrate to where they need to be in the body.

Cooper notes that a powerful regulator of Arp2/3 is mutated in a rare human disorder, Wiskott-Aldrich syndrome(WAS). Mutations in the protein, known as WAS protein, lead to autoimmune problems, eczema, increased risk of cancer and a variety of other symptoms. Humans have multiple versions of this protein, but yeast only has one, allowing Cooper's research to potentially provide guidance for scientists working to develop treatments for WAS.

Cooper plans further study of how yeast cells regulate and use actin networks. His lab is also looking at how Arp2/3 regulatory proteins contribute to function in mammalian immune system cells and cancer cells.

Source: Washington University

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