Sculpting a cell's backside: New protein found to help cells move from behind

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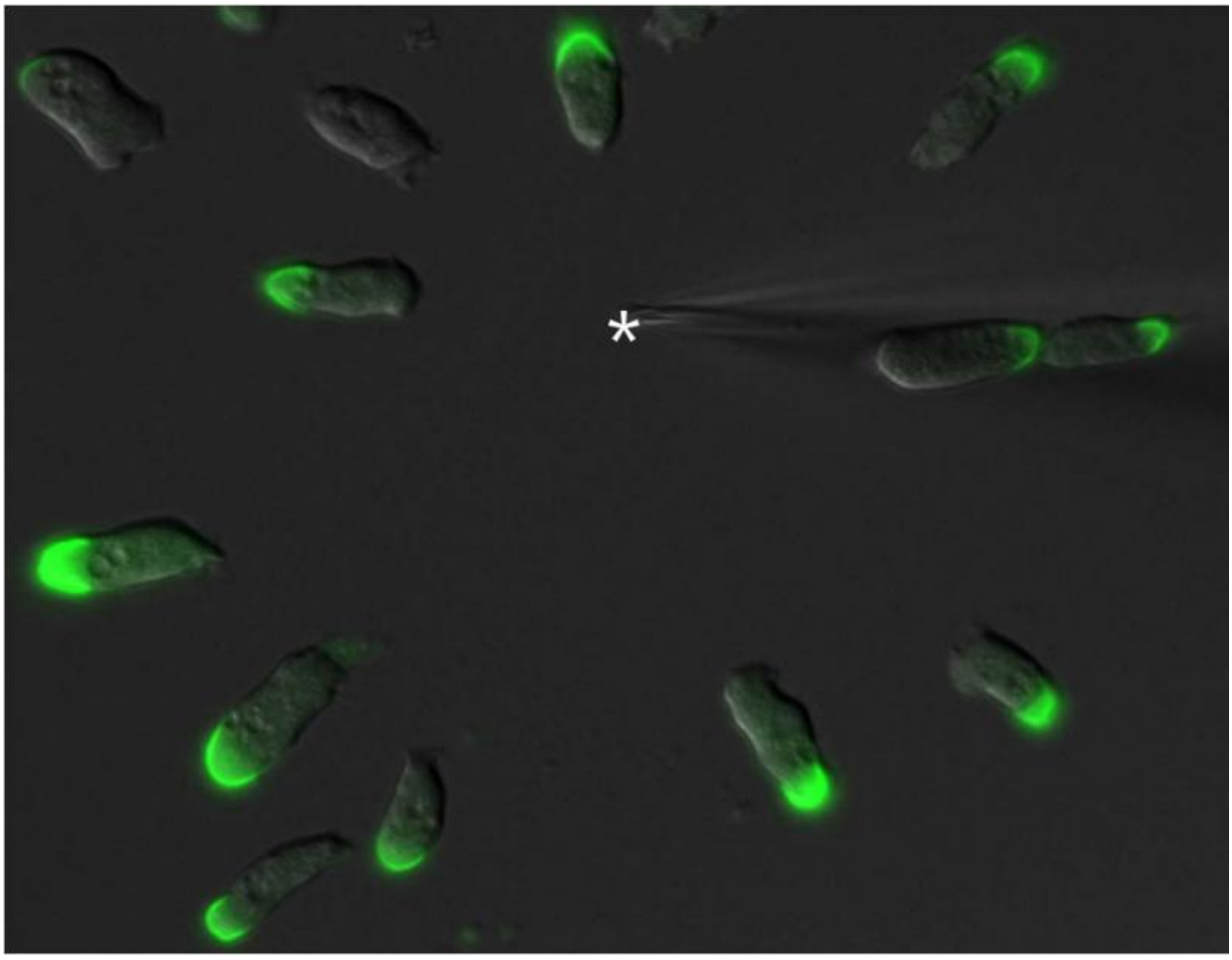

Cells migrate toward a glass needle (*) releasing a chemical attractant. Callipygian (green) is at the back of the cells. Credit: Kristen Swaney, Johns Hopkins Medicine

When Greek mythology and cell biology meet, you get the protein Callipygian, recently discovered and named by researchers at The Johns Hopkins University for its role in determining which area of a cell becomes the back as it begins to move.

The findings, made in the amoeba Dictyostelium discoideum, shed light on how symmetrical, round cells become "polarized," or asymmetrical and directional. A summary of the findings was published online June 30 in the *Proceedings of the National Academy of Sciences*.

"Cells have to have a front and a back to migrate," says Peter Devreotes, Ph.D., professor and director of the Department of Cell Biology at the Johns Hopkins University School of Medicine. "Callipygian shuts off proteins that work at the front edge of cells. By doing so, it helps create the back of a cell, so we named it after the statue Venus Callipyge."

During cell migration, the front and back of the cell have to coordinate with each other, almost like dance partners. When a chemical "move-this-way" signal reaches a cell, a single protrusion, or pseudopod, begins to form in that direction due to rodlike actin filaments that grow and push the cell's membrane out. The back of the cell is then pulled forward, and the process repeats itself. Both extension of the front and retraction of the back require specific sets of proteins that must localize to the correct sites within the cell for proper migration.

To find more proteins involved in cell movement, Kristen Swaney, Ph.D., then a graduate student in Devreotes' laboratory, decided to mark proteins by genetically attaching a fluorescent tag to them. Based on their sequences, two dozen of these were predicted to interact with the well-known front molecule PIP3, suggesting that they too would move to the front of the cell after a migration signal was received. Most of them did, but Callipygian went to the back, says Swaney. It didn't bind to PIP3, either.

"We already knew a lot about front proteins and how pseudopods are generated, but the formation of the back of the cell is more of a mystery, so we decided to follow Callipygian's lead," says Devreotes.

One challenge migrating cells face is preventing pseudopods from forming anywhere other than the front of the cell. The researchers found that Callipygian assists in this by accumulating at the back of the cell and preventing actin rods from growing to form a pseudopod. "Callipygian essentially turns off the back of the cell," says Swaney.

The team found that Callipygian uses a positive feedback mechanism to help polarize the cell. "It responds to cell polarity by moving to the back of the cell where it makes changes that create more polarity, which causes more Callipygian to move to the back of the cell," says Devreotes.

The team then studied its structure and figured out which part of the protein makes it move to the back of the cell. They found that adding a key segment from Callipygian to any other protein will make it move to the back of the cell too. According to Swaney, this ability to steer proteins to the "wrong" place in the cell will be a useful tool for studying many other proteins involved in cell polarity.

The researchers are continuing to work on understanding the dynamics of "front-and-back proteins" and how they contribute to cell polarity and migration, hoping to shed light on processes such as wound healing and cancer cell metastasis.

More information: Novel protein Callipygian defines the back of migrating cells, Kristen F. Swaney, DOI: 10.1073/pnas.1509098112

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