New molecular pathway could reveal how cells stick together

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Researchers at Rensselaer Polytechnic Institute have found a new pathway by which cells change their adhesive properties. With a $1.4 million grant from the National Institutes of Health, they plan to fill in the details behind how cells decide to stick to a surface, which could lead to a better understanding of the importance of this pathway to the physiology and development of organisms.

Cells must interact with each other to produce system responses, like the remodeling of a tissue during development or for orchestration of an integrated immune response. One way they do this is by physically attaching to one another and to surfaces. Andrea Page-McCaw, assistant professor of biology at Rensselaer and principal investigator for the project, has focused on matrix metalloproteinases (MMPs) -- proteins that play a role in development and immunity.

"MMPs have gotten a lot of attention primarily because of their regulation in a lot of disease states, most notably cancer and other inflammatory conditions," Page-McCaw said. Yet the normal function of these proteins is not well understood.

The job of MMPs is to cleave other proteins that reside in the space in between cells. Page-McCaw has previously identified a specific protein, called ninjurin, that gets cut by MMP. Now she is working out the interplay between MMPs and ninjurin, with the goal of characterizing this previously unknown pathway by which cells signal to each other.

Ninjurin is anchored to the surface of cells, but after being cut by MMP, a ninjurin segment travels to adjacent cells and signals them to alter their adhesive state. Page-McCaw published these findings earlier this year and was recently awarded an individual investigator research grant to extend her work from cells in a Petri dish to an organism. The grant, from the National Institute of General Medical Sciences, is for $ 1.4 million over five years.

"We're trying to figure out how it works in whole flies," Page-McCaw said. "When you take a cell out of the organism it behaves a little bit differently. So while you can work out cell mechanisms in cell culture, then you want to go back and demonstrate their relevance to the animal."

To study the role of ninjurin in development and immunity, Page-McCaw uses a strategy to exclude the protein from the animal. By developing a mutant fly lacking the gene that codes for the protein, she can examine what goes wrong without the protein and then infer the normal function of that protein.

She has previously done similar work knocking out MMP in flies. "One of the defects in MMP mutants is in their ability to control cell adhesion," she said. Many tissues undergo remodeling as the flies grow and develop, but at least one, the breathing tubes, do not develop properly in the mutant flies. Page-McCaw calls it a "cellular adhesion defect that causes problems for the animal at the tissue level."

Now she plans to find how ninjurin affects breathing tube development, as well as the role it plays in immunity. "The immune system is all about immune cells circulating around and being able to attach to tissues that need their attention," she said.

A new signaling pathway holds promise of new therapeutic targets. "We're talking about an entirely new signaling pathway that hasn't been

identified previously," Page-McCaw said. But it's too soon to know how her findings will be used in terms of human health.

"There are lots of examples of times where the ability of cells to communicate goes awry in disease and ninjurin could be playing a role in any of those," she said. "The goals of my research are contributions of new ideas and mechanisms that can then be realized by the broader biomedical community."

Source: Rensselaer Polytechnic Institute