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Research provides insights into cell division and metabolism

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Cells are the building blocks of the human body. They are a focus of scientific study, because when things go wrong at the cellular and molecular level the consequences for human health are often significant.

A new finding based on multiple collaborations between UNC and Duke scientists over several years points to new avenues for investigation of cell metabolism that may provide insights into diseases ranging from neurodegenerative disorders like Parkinson's and Alzheimer's disease to certain types of cancers.

The finding, published today in the journal Nature Cell Biology, builds on a discovery that co-author Donita Brady, PhD, made when she was a graduate student in pharmacology at UNC, working in the lab of Adrienne Cox, PhD, associate professor in the departments of pharmacology and radiation oncology and a member of UNC Lineberger Comprehensive Cancer Center. A similar observation was made at the same time by Kian-Huat Lim, MD/PhD, then working in the lab of Christopher Counter, PhD, associate professor in Duke University's departments of pharmacology and cancer biology and radiation oncology.

Both scientists observed that a protein related to a gene called Ras, which is known to be associated with several different types of cancer, was concentrated in a part of the cell called the mitochondria. Mitochondria are known as the cell's "power plant" because they produce adenosine triphosphate (ATP), a source of chemical energy for

cells. Brady and Lim noticed that the interaction of two proteins called RalA and Aurora-A, when present in the cell's mitochondria, caused those "power plants" to behave oddly during cell division.

For cellular reproduction and division to remain on a healthy track, the mitochondria have to redistribute themselves proportionately into the 'daughter' cells during mitosis – the process of cell division. So the team knew that this process was important.

Meanwhile, the scientific team was also redistributing itself, with Brady moving on to a postdoctoral fellowship at Duke and beginning to work with David Kashatus, PhD, a UNC-trained biochemist also working in Dr. Counter's lab. There, the team started to look into the 'odd' mitochondria, and found that the RalA protein is at the beginning of a chain of protein signals that regulate how the mitochondria distribute themselves in cell division. If these proteins are disrupted, the mitochondria don't divide properly during mitosis through a process called fission and don't distribute themselves proportionately within the 'daughter' cells. One result is a decrease in the level of the cellular 'fuel', ATP.

"This suggests a number of future avenues for inquiry," says Dr. Cox. "We know that cellular metabolism is regulated through this process. Now that we know more about its disruption, the team will examine cellular metabolism in normal cells compared to cells where mitochondrial fission and re-fusion have been disrupted. There are implications for a number of diseases including cancer and neurodegenerative disorders, where we suspect that underlying cellular metabolism may play a role."

She adds, "As scientists and educators, one of our roles is to teach graduate students the principles of successful collaboration. The close proximity of strong universities like UNC and Duke promotes the

exchange of ideas between labs and investigators, resulting in discoveries with high potential, like this one."

Provided by University of North Carolina School of Medicine