New discovery could change the face of cell-biology research

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Rewrite the textbooks and revisit old experiments, because there's a new cog in our cellular machinery that has been discovered by researchers from the University of Alberta and the University of Cambridge Institute for Medical Research.

Inside every cell that isn't bacterial, there is a "membrane trafficking system." It has long been known to have four protein complexes, called adaptins, which are all involved in moving things in, out and around the cell. Joel Dacks, in the Department of Cell biology in the U of A Faculty of Medicine & Dentistry, along with Cambridge colleague Margaret Robinson, have discovered there is a fifth adaptin. According to their research it has been around for billions of years, but no one has been able to spot it.

"What this does for cell biology is open up a whole new avenue of research," said Dacks. "We thought there were four big players in the processes of how things got moved around in the back half of the cell. There's a fifth player on the field; we just couldn't see it."

Understanding how trafficking works in cells is vital because when something goes wrong in this system, oftentimes this is when you get disease. Mutations in genes involved in trafficking are implicated in a number of neurodegenerative disorders including Alzheimer's, Huntington's disease and ALS, also known as Lou Gehrig's disease.

"We already have one disease where we know where this complex is

involved," said Dacks. It is called hereditary spastic paraplegia which causes increasing leg spasms and eventually loss of mobility.

"More importantly it goes back to that idea that to understand the diseased cell, we have to know what a healthy one really looks like. You need to understand the basic map of the cell to be able to identify how it has gone wrong. We have discovered a previously unrecognized major feature on that map."

Dacks says that this machinery is widespread, not only in human cells but in plants, parasites and algae, meaning it is not only a general feature of our types of cells but it is also ancient. The more they learn about this fifth adaptin, the more insight they'll be able to gain about the earliest events – the building of cells.

Dacks thinks this discovery, published Oct. 11 in *Public Library of Science Biology*, could help many scientists answer questions they may have been left with following their research projects.

"Scientists have to build explanations using the pieces that they know exist. This may help to incorporate some observations that didn't fit, because now you can explain things with five guys, not four," said Dacks.

Dacks found this extra adaptin protein in a harmless soil amoeba. Realizing that the same protein is also found in human cells, he contacted Robinson, his colleague. Her lab at Cambridge analyzed the biology of the newfound adaptin for three years. They passed it back to Dacks and his lab at the U of A to study the evolutionary genomics.

"It was a really nice example of collaboration," said Dacks. "The Robinson lab is a leader in this area and together we can ask questions that neither group could tackle on their own."

While this will likely change a lot of cell biologists' research, for Dacks the next step is to integrate his lab's theories and create a better idea of how the cell evolved.

"It gives us some new evolutionary hypotheses to test with other proteins that also act at these cellular steps, and see if the data are consistent with our models."

His research is funded by the Natural Sciences and Engineering Research Council and he is an Alberta Innovates Technology Futures new investigator.

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