Mitosis mystery solved as role of key protein is confirmed

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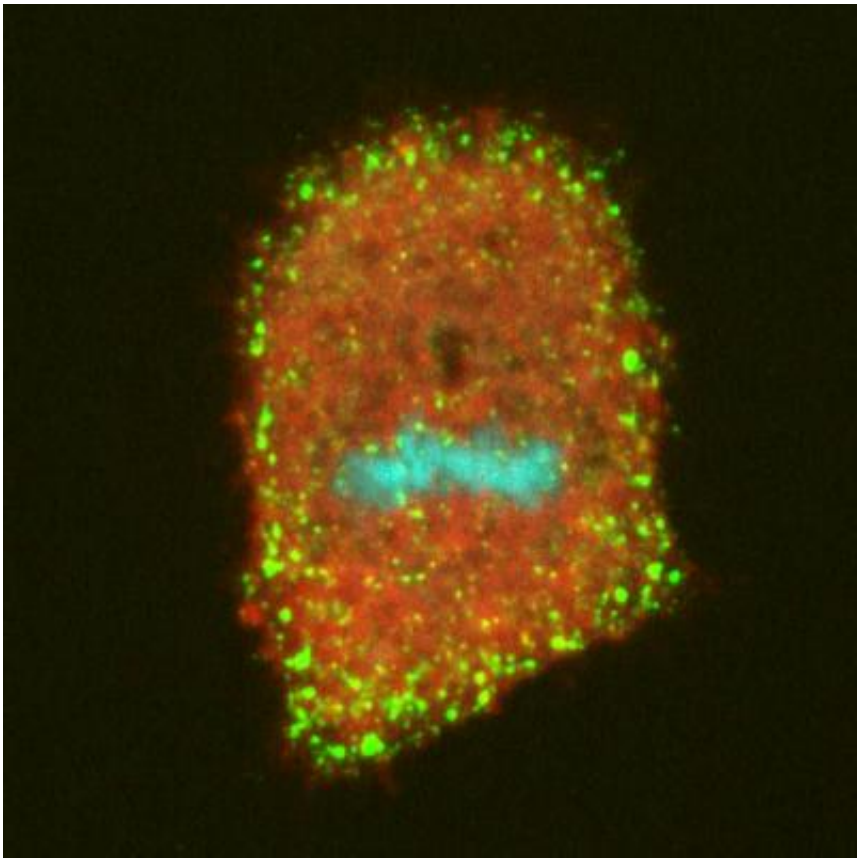

This shows restarted endocytosis in a mitotic cell. Credit: Royle/University of Warwick

Researchers from Warwick Medical School have discovered the key role of a protein in shutting down endocytosis during mitosis, answering a question that has evaded scientists for half a century.

The study, published today in the journal *eLife*, is the first to outline the role of actin, a protein, in shutting down clathrin-dependent endocytosis during mitosis.

Endocytosis is the process by which cells absorb molecules that are too large to pass through the plasma membrane, such as proteins. Clathrin-dependent endocytosis is the most common route for this. Clathrin, a protein, forms a pit on the inner surface of the membrane which allows the cell to engulf and bring in a small volume of fluid from outside the cell.

The team, led by Dr Steve Royle, were able to answer a question that was first asked in 1965 by American cell biologist, Don Fawcett. Fawcett became aware that clathrin-dependent endocytosis shuts down during mitosis, but the understanding of why it happens has eluded researchers until now.

In the latter part of the 20th Century, two competing theories emerged. One theory suggested that the tension of the plasma membrane is too high for endocytosis to occur. The other theory stated that the cell actually switches off the proteins involved by a process of mitotic phosphorylation, the addition of a phosphate group to the cell proteins.

More recently, scientists found that in non-dividing cells, when membrane tension is high, endocytosis can still occur because actin can be recruited to help clathrin to overcome the high tension in the membrane.

The Warwick team measured membrane tension in mitotic cells and found it to be much higher than in non-dividing cells, thus sparking the investigation into why actin is not recruited to help out in this case. They found that during mitosis, actin is busy forming a stiff cortex in the cells and so cannot be used to help out endocytosis. In other words, actin is

needed, but is unavailable for use.

By tricking the cell into making actin available during mitosis, the researchers were able to restart endocytosis in mitotic cells. The paper also describes how mitotic phosphorylation does not inhibit the process, arguing against the alternative theory.

The newfound appreciation for the role played by actin opens the door for further developments, both for researchers and for possible clinical applications.

Dr Royle explained, "The implications for human health are truly fascinating; by knowing the role played by actin we can look to use it to restart endocytosis during cell division. That could mean that we're able to make dividing cells receptive to pharmaceuticals or other medical treatments in a way that we haven't before."

"It also opens up other strands of research and questions for our field. For instance, how does the cell know that the membrane tension is too high for normal endocytosis? When and how does it call in actin? There is plenty we are yet to discover."

More information: www.elife.elifesciences.org/lo … /10.7554/elife.00829

Provided by University of Warwick