Biologists Uncover Mechanisms That Shape Cells for Better Or Worse

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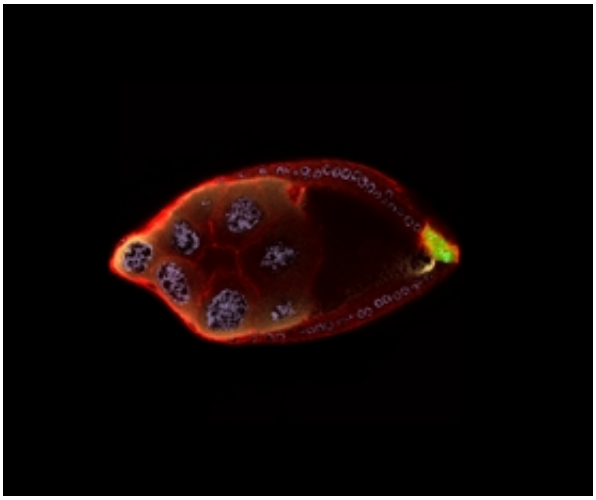

"Cell polarity in the unfertilized egg of the fruit fly requires cell-to-cell signaling to regulate key protein levels and location in the developing egg chamber." Courtesy of Wu-Min Deng and John Poulton

In a landmark study, biologists at Florida State University have uncovered a specific genetic and molecular mechanism that causes cell polarity -- the asymmetric shape or composition critical to a cell's proper functioning. Their findings in fruit fly eggs may help to clarify how muscular dystrophy and some cancers develop in humans.

That's because many of the genes involved in the cell-to-cell communication that triggers the development of cell polarity in Drosophila oocytes (unfertilized fruit fly eggs) also are known players in

the pathogenesis of those diseases.

The research performed by FSU Assistant Professor Wu-Min Deng and doctoral student John S. Poulton in the department of biological science could foster a better overall understanding of polarity and how it develops -- and why it doesn't, sometimes with dire consequences -- in other types of cells and organisms.

Results from the FSU study are described in the Aug. 14 online edition of the journal PNAS (*Proceedings of the National Academy of Sciences*).

“We have identified a novel component in the polarization of the fruit fly egg and the signals that determine the anterior-posterior positioning of its head and abdomen,” said Deng.

“Such a discovery in the biological model provided by Drosophila oocytes has broad implications in humans, where, for example, neurons in the brain are designed, or polarized, to interpret information from the sense organs, and intestinal cells are polarized to take up nutrients and move them into the bloodstream,” he said.

Poulton explained that in order to ensure cell polarity in the Drosophila oocyte, the cells surrounding it activate a classic signaling pathway known as the Epidermal Growth Factor Receptor (EGFR) in a process that is also essential to development in humans and a wide range of other organisms.

“Our study shows that EGFR activation in the cells surrounding the fruit fly oocyte acts to turn off a gene known as Dystroglycan, halting production of its protein. EGFR must shut down Dystroglycan in order for the oocyte to properly polarize,” Poulton said.

“We proved this by observing that mutated forms of genes in the EGFR

pathway of cells surrounding the oocyte led to abnormally high levels of Dystroglycan protein, which in turn disrupted oocyte polarity. However, even with the mutated EGFR pathway gene, we were able to restore normal polarity by turning Dystroglycan off artificially," he said.

"While much remains unknown, our research confirms that EGFR regulation of Dystroglycan plays a key role in the polarization of the oocyte," Deng said. "That knowledge adds a pivotal link to our understanding of precisely how cell-to-cell communication occurs in this model system."

In recognition of groundbreaking work to-date by the FSU scientists -- and to further the understanding of the mechanisms involved in cell-cell communication leading to oocyte polarity -- the National Institutes of Health have awarded Deng a highly competitive "R01" (Research Project Grant) for health-related research and development.

Just after joining the FSU faculty in 2004, Deng led a Drosophila oogenesis study that revealed mechanisms of cell-to-cell signaling along other key pathways. Those findings were published in the 2005 editions of the journal *Development.*

The current study -- "Dystroglycan down-regulation links EGFR signaling and anterior-posterior polarity formation in the Drosophila oocyte" -- relied heavily on the state-of-the-art laser confocal microscope in FSU's Biological Science Imaging Resource facility.

Source: Florida State University

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