THE FRONT ROW at Scripps Research | 100 YEARS | A Century of Science Changing Life

Peering into the mitochondria to reveal cellular stress and disease

Danielle Grotjahn, PhD

Assistant Professor
Department of Integrative Structural and Computational Biology
Scripps Research

ABOUT THE LECTURE

Mitochondria are known colloquially as the "powerhouses" of cells because of their unique ability to generate the energy needed for biochemical reactions. However, emerging research now shows that these organelles—down to their shapes and sizes—are responsible for much more than energy generation. In her Front Row lecture, Scripps Research professor Danielle Grotjahn, PhD, discussed how her lab is harnessing advanced imaging technology to explore the once-mysterious shapes of mitochondria and determine how they may even be predictors of cell health and disease progression.

TOP TAKEAWAY POINTS

- Although mitochondria are known for generating cellular energy, they also serve as crucial "stress sensors." The organelles change their shapes in response to cellular stress, which may signify resilience or deterioration within cells. Grotjahn's research challenges the traditional view of mitochondria purely as energy producers, emphasizing their broader role in cellular homeostasis and disease response. There's now a growing body of evidence demonstrating that mitochondria are critical regulators of cellular health, with their structures and functions closely tied to cells' adaptive capacities.

- The shapes of mitochondria don't always resemble the ovals often seen in textbooks. Mitochondria exhibit diverse forms, which correlate with different cellular states. Grotjahn found that elongated "linguini-like" mitochondria generally indicate healthier, functional cells that promote cellular survival, whereas fragmented "risotto-like" shapes are linked to cellular damage and stress, often signaling a cell's move toward self-destruction

- Using a microscopy technique known as cryo-electron tomography, Grotjahn's lab captures high-resolution 3D images of mitochondria in precise detail. Such advanced technology permits tracking subtle mitochondrial changes, offering new ways to study stress responses and previously undetectable cellular processes. This also provides key insights into mitochondrial structure and function, offering valuable clues for understanding diseases ranging from cancer to Parkinson's. Although mitochondrial dysfunction plays a role in both illnesses, cancer stems from uncontrolled cellular overgrowth, whereas Parkinson's is a result of excessive cellular death.

- By mapping out the inner membranes—or cristae—within mitochondria, Grotjahn has identified structural patterns of membrane folds associated with different functional states of cells. For example: Healthy, elongated mitochondria have organized, ladder-like cristae, whereas unhealthy, fragmented mitochondria have balloon-like cristae that appear swollen. These varying shapes may affect cellular processes like energy production, cellular survival and apoptosis—the natural process where a cell dies after being damaged beyond repair. By observing mitochondrial adaptations in diseased cells, Grotjahn suggests that changes in structural patterns could serve as early indicators of disease onset, potentially guiding preventive measures or treatments.

- Although still in its early stages, research from Grotjahn's lab has singled out molecules that can potentially reverse mitochondrial fragmentation, turning "risotto" structures back into healthier "linguini" forms. While not yet at the therapeutic stage, these findings may lead to tools that increase our understanding of—and eventually treat—mitochondrial dysfunction in various diseases.

Learn more and view all past lectures at frontrow.scripps.edu.

SUPPORT SCRIPPS RESEARCH