



# Gerald Shadel

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## The Problem

Life cannot exist without energy. For us to move, think, and withstand stress and infections, the cells in our body must generate energy from the food we eat. This occurs in dynamic “powerhouses” inside cells called mitochondria. Mitochondria are also involved in cellular signaling and immunity via pathways that are only starting to be identified. However, harboring mitochondria comes at a cost—they wear out with age, produce damaging metabolites, and contain their own DNA (mtDNA) that can cause inherited diseases. A greater understanding of these complex organelles is essential to unravel their role in human disease and aging.

## The Approach

Gerald Shadel studies the basic biology of mitochondria and mtDNA, and, in doing so, has identified novel ways that mitochondria contribute to disease, aging and the immune system. He is also interested in understanding how mitochondria are involved in cellular signaling processes. He seeks to identify what the signals are, what pathways they trigger and how they play a part in aging, cancer, and metabolic and degenerative diseases. His group takes a multidisciplinary view, exploring mitochondrial function—and dysfunction—via cultured cells, model organisms, and other genetic and biochemical approaches.

## The Innovations and Discoveries

- Shadel has elucidated context-specific ways that mitochondria and the reactive oxygen species (ROS) they produce are involved in the neurodegenerative disease ataxia-telangiectasia (A-T), maternally inherited deafness, and cancer.
- He also discovered that mtDNA, which is derived from an ancient bacterium, can trigger the immune system if exposed to the rest of the cell, causing antiviral and other defensive responses.
- He is currently studying adaptive responses to mitochondrial stress in mammals based on his discovery in yeast that mitochondrial ROS signals induce changes in gene expression in the cell nucleus that extend this organism’s lifespan.

**For more information, please visit:**  
[www.salk.edu/scientist/gerald-shadel](http://www.salk.edu/scientist/gerald-shadel)

## Mitochondria, Aging, Genetics