Researchers discover new mechanism behind cellular energy conversion

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Researchers from Mount Sinai School of Medicine have enhanced our understanding of the mechanism by which cells achieve energy conversion, the process in which food is converted into the energy required by cells. This groundbreaking research helps scientists gain atomic-level insight into how organisms synthesize their major form of chemical energy. The researchers' findings were published in the August issue of *PLoS Biology*.

Cells use the enzyme ATP synthase to generate a chemical called ATP, the form of energy cells use to function. Structurally, ATP synthase is a nano-machine, a cellular "motor" that consists of proton turbines, or rotor rings, with the output being ATP. The investigators wanted to find out more about how these ATP synthase rotors work.

David Hicks, PhD, Assistant Professor of Pharmacology & Systems Therapeutics and Terry Krulwich, PhD, Sharon & Frederick A. Klingenstein-Nathan G. Kase, MD Professor of Pharmacology & Systems Therapeutics, led the Mount Sinai-based part of the effort. They and their co-investigators, Thomas Meier, PhD, and two members of his research team at the Max Planck Institute of Biophysics in Germany, grew three-dimensional protein crystals of an unusually stable rotor found in bacteria called Bacillus pseudofirmus and evaluated them using X-ray technology.

The researchers were surprised to find that these ATP synthase rotor rings use a water molecule as part of the rotary mechanism of ATP synthesis, providing a clearer understanding of how these nano-machines function. Previous studies of a rotor from a blue-green alga, the only other proton-moving rotor observed at this atomic level, showed that it did not use a water molecule.

With this new insight, they were able to infer how ATP synthase captures the protons that drive the rotation of the "motor" and visualize how those protons remain bound to the rotor. This discovery has added interest because the rotor structure of these bacteria is similar in some ways to the motors driving ATP synthesis in human cells and pathogens like the tuberculosis bacteria.

"We are excited about the broad implications of these data in helping us move toward a more detailed model of the mechanisms of action behind cellular energy conversion," said Dr. Krulwich. "These findings provide a launching pad for better understanding a basic life process in organisms ranging from bacteria to humans. We look forward to studying this development further."

Drs. Hicks and Krulwich and the Meier team will continue studying this finding and plan to further evaluate these cellular nano-machines. Working with this discovery, they will next evaluate mutations or malfunctions in the ATP synthase rotor.

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