Researchers uncover new role for mitochondria during RNA processing

March 16 2011

Michael Frohman, M.D., Ph.D., Chair of the Department of Pharmacological Sciences at Stony Brook University School of Medicine, and colleagues, have discovered a new role for mitochondria during ribonucleic acid (RNA) processing. This latest finding, reported in *Developmental Cell*, may hold clues to some causes of male infertility.

Long-recognized by scientists as the powerhouse of the cell involved in the role of energy production, mitochondria help regulate numerous cell biological processes. These processes involve communication between the mitochondria and the rest of the cell via signaling pathways on the mitochondrial surface that mediate interactions with cytoplasmic proteins. Some of the pathways involve lipids.

The research team studied a specific aspect of this mitochondria activity – the machinery that generates and senses protein and lipid signals. They focused their investigation of activities that occur on and around the mitochondrial surface.

“Our experimentation uncovered a new role for mitochondria in a specialized form of RNA-processing that appears to take place at the interface between the mitochondrial surface and adjacent granules of RNA and RNA-associated proteins,” says Dr. Frohman, summarizing the research results. “More specifically, we linked a signaling enzyme on the mitochondrial surface, called MitoPLD, to the production of piRNAs, which are produced from RNA copies early in spermatogenesis during meiosis.”

Dr. Frohman explained that the significance of the finding is that piRNAs are known for suppressing cellular transcription (copying of RNA) and thus mobilization of genetic elements known as transposons, which make up almost half of the human genome. Many types of piRNAs also target non-transposon genes. But without piRNAs, transposons replicate, leading to widespread DNA damage and subsequent death of differentiating sperm cells.

Furthering the research, the team genetically engineered mice to lack the gene MitoPLD. They found the mice to be normal, except that the males were infertile. No effect has been seen on female fertility.

“The long-term potential significance of our laboratory findings is the possibility that some cases of male infertility may be caused by inherited mutations in MitoPLD, the signaling enzyme, especially since at least one inactivating mutation is found in the database of sequenced human DNA,” says Dr. Frohman. “Conversely, pharmacological inhibitors of MitoPLD could have potential utility as male contraceptives.”

In their study, titled “piRNA-Associated Germline Nuage Formation and Spermatogenesis Require MitoPLD Profusogenic Mitochondrial-Surface Lipid Signaling,” the authors point out that despite their findings, the piRNA generation pathway is complex and the mechanism underlying MitoPLD effects on mitochondrial morphology and fusion are unknown. However, they believe the biological significance of their work has pharmacological potential.

“Because inhibitors have been developed for other members of the same enzyme family, MitoPLD is likely a feasible target,” theorizes Dr. Frohman.

Provided by Stony Brook University