Link found between insulin sensitivity, cells' powerhouses

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Deepa Sathyaseelan, Ph.D., is research assistant professor of cellular and structural biology in the School of Medicine at The University of Texas Health Science Center San Antonio. She conducts research in the university's Barshop Institute for Longevity and Aging Studies. She and her colleagues found, quite unexpectedly, that diminished activity of a protein complex involved in mitochondrial function did not have a damaging effect, but rather was associated with an increase in life span and beneficial metabolic effects. Credit: The University of Texas Health Science Center San Antonio

If findings of a new study in mice are any indication, it might be possible

to fine-tune cellular powerhouses called mitochondria, tweaking one aspect to increase insulin sensitivity, reduce body and fat mass, and even extend life. Exploiting this target could one day lead to novel treatments for type 2 diabetes—an endocrine system disease that affects 8 percent of the U.S. population. The research also points to promising new avenues of investigation in the biology of aging.

The study, reported in *The* FASEB Journal by authors from the School of Medicine at the UT Health Science Center San Antonio and the university's Barshop Institute for Longevity and Aging Studies, found that diminished activity of a protein complex involved in mitochondrial function was associated with healthy changes in the mice. The median life span of this strain of mice is 20 percent longer.

Paradoxical

"This is an unexpected finding because you would think that something that decreases mitochondrial function would have a damaging effect, but instead we saw an increase in life span and beneficial metabolic effects," said lead author Deepa Sathyaseelan, Ph.D., research assistant professor of cellular and structural biology in the School of Medicine.

"The most important thing we noticed is reduced body weight and decreased fat mass in the mice," Dr. Sathyaseelan said. "We found that this decreased fat mass is due to increased fat utilization."

Fat utilization

Mitochondria produce an energy source called ATP that is necessary for the functions of life, everything from breathing to thinking. Additionally the cellular powerhouses are a major site of fat utilization, said study senior author Holly Van Remmen, Ph.D., professor of cellular and

structural biology. Fat is an endocrine organ that performs many functions, and having it in the correct proportions is important for the body. Too much or too little fat is harmful.

The scientists also observed that mice with the mutation, in contrast to control animals, make greater numbers of new mitochondria. This is important because cells are constantly remodeling themselves, including mitochondrial overhaul.

Age-related

Mitochondrial dysfunction occurs with age and is associated with many age-related diseases such as type 2 diabetes, heart disease and cancer. Dr. Sathyaseelan said the study "opens the door to new clues about how mitochondrial function might modulate insulin sensitivity," representing an important step for diabetes research.

Type 2 diabetes involves abnormalities with insulin, a hormone secreted by beta cells in the pancreas. Insulin helps the body store and use sugar from food, but in type 2 diabetes the body is insulin resistant, that is, it inefficiently responds to the hormone. With time the beta cells in diabetic patients start to die, resulting in less insulin to handle the demands. Levels of the hormone become progressively lower and sugar levels are increased progressively, damaging blood vessels and organs.

Understanding longevity

"I would also like to point out that these mice live longer," Dr. Van Remmen said. "For us they are very important from an aging standpoint. We want to understand how these animals can have added longevity, yet have a 60 percent reduction in a protein complex involved in mitochondrial function."

Dr. Sathyaseelan noted that life extension in association with decrease of the complex's activity is seen across species, including roundworms and flies. Shane Rea, Ph.D., assistant professor of physiology at the Barshop Institute, is one of the first to make this discovery in the worms.

The Barshop Institute team obtained the study mice from an Italian institute where studies are ongoing. Dr. Sathyaseelan recently received a two-year, $140,000 grant from the American Heart Association to understand how mitochondrial dysfunction is related to insulin sensitivity.

Provided by University of Texas Health Science Center at San Antonio