Tina Hines, Michael Wacker, Jon Andresen and Marco Brotto

Mighty Mouse to the Rescue

Transgenic super mouse is one of many new mouse models undertaken by a collaborative research group to combat disease

A super mouse soon will be coming to town and it promises to help a new research power team identify signaling pathways/molecules in humans that are linked to obesity, aging-decline in muscle function, diabetes, muscular dystrophies and cardiovascular diseases.

A new animal model for muscle and metabolism research was recently developed by Richard Hanson and colleagues at Case Western Reserve University. These "mighty mice" are transgenic mice – not clones - that were bred to have changes in enzymes that affect skeletal muscles.

Astonishingly fit, these mice can run 30-fold more than control mice, they eat 60 percent more, they are 50 percent thinner, and they survive longer than control mice.

MUBIG Promises Big Payoff

Mighty mouse is one of many new powerful mouse models being developed by the Muscle Biology Research Group (MUBIG), whose members envision important new discoveries of signaling pathways linked to decline in muscle function with aging, fatigue, obesity, diabetes, muscular dystrophies and cardiovascular diseases.

MUBIG is the brain-child of two physiologists in the School of Nursing (SON): Tina Hines, R.N., Ph.D., Thompson Endowed Professor of Research, and Marco Brotto, B.S.N., Ph.D., a new associate professor in the SON with joint appointments in medicine and biological sciences. They are joined by two new physiologists in the School of Medicine: Jon Andresen, Ph.D., an expert in smooth muscle and potassium channels,

and Michael Wacker, Ph.D., a cardiac muscle and arrhythmias expert.

Brotto brings to the group new transgenic mouse models, including the mutsugumin 29 (MG29) knockout that fatigues more and has signs of accelerated aging; the sarcalumenin knockout that is highly resistant to fatigue; and the muscle specific phosphatase (MIP) knockout that recapitulates symptoms of Brody's disease, muscular dystrophies and Charcot-Marie Tooth (CMT) syndromes, devastating diseases that limit millions of people to wheel chairs. Hines is using a unique rat model of eclampsia and cardiovascular consequences of this condition. Her lab is also investigating important metabolic and muscular differences in males and females and along with Brotto have recently received funding from the Kansas City Women's Initiative to expand their studies into these new animal models of research. Wacker investigates arrhythmias in rabbit models and is now extending his efforts to mouse and human models. His laboratory has also developed a novel methodology for identification of genes in humans that require tiny amounts of muscle. Andresen has recently obtained an American Heart Association grant to investigate a novel potassium channel found in cerebrovascular smooth muscle that is thought to regulate vascular tone. His research may have important implications in the areas of hypertension, inflammation and neuroprotection.

MUBIG members are combining forces to develop the basis for research that moves discoveries from the lab bench to the bed side and into the community.

Mighty Mouse

MUBIG members also are excited about mighty mouse, which was bred to display genetic alterations in enzymes that control skeletal and cardiac muscle function.

"Some of the changes observed in these models include astonishing fitness and elite athleticism," said Hines. "They are fatigue resistant and can run six kilometers in a single test. These remarkable mice eat more and weigh less than their controls despite having high blood sugar and fat levels. In addition they continue to reproduce well past their controls."

"These animals are strongly resistant to aging, so one of our major hypotheses is they must have a different mechanism to handle the stress that derives from the production of free radicals," said Brotto. "It may be that these molecules are also markers for other metabolic diseases, such as diabetes and obesity. We are also very interested in possible gender differences in performance and life span in these models."

Through collaborations with CWRU, MUBIG scientists at the schools of Nursing and Medicine hope to understand the molecules responsible for changes in muscle function that lead to the amazing physical abilities in these mice.

"These animals are ***strongly resistant to aging...****"*

"This is a huge opportunity for UMKC and this collaborative group," said Hines, adding that Case Western contacted Brotto because of his connections with their researchers and his national reputation and work in this field.

MUBIG will also pursue other promising collaborative studies, high-profile research grants, seminars, journal articles and collaborations with other UMKC groups and individuals, such as researchers in the School of Pharmacy, leading bone researcher Lynda Bonewald, Ph.D., at the School of Dentistry, and Medicine's Hong-Wen Deng, Ph.D., with his extensive human tissue database that relates to obesity and osteoporosis. The group and individuals will be joining researchers from the University of Kansas and KU Medical Center June 9 for a joint research day to showcase area research and to forge additional partnerships in the life sciences.

In the Mighty Mouse cartoons, the small superhero helped mankind in a matter of minutes. Today, a new group of super heroes is teaming with one another, across disciplines, to find solutions to some of life's most challenging medical problems.

Nursing Research

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