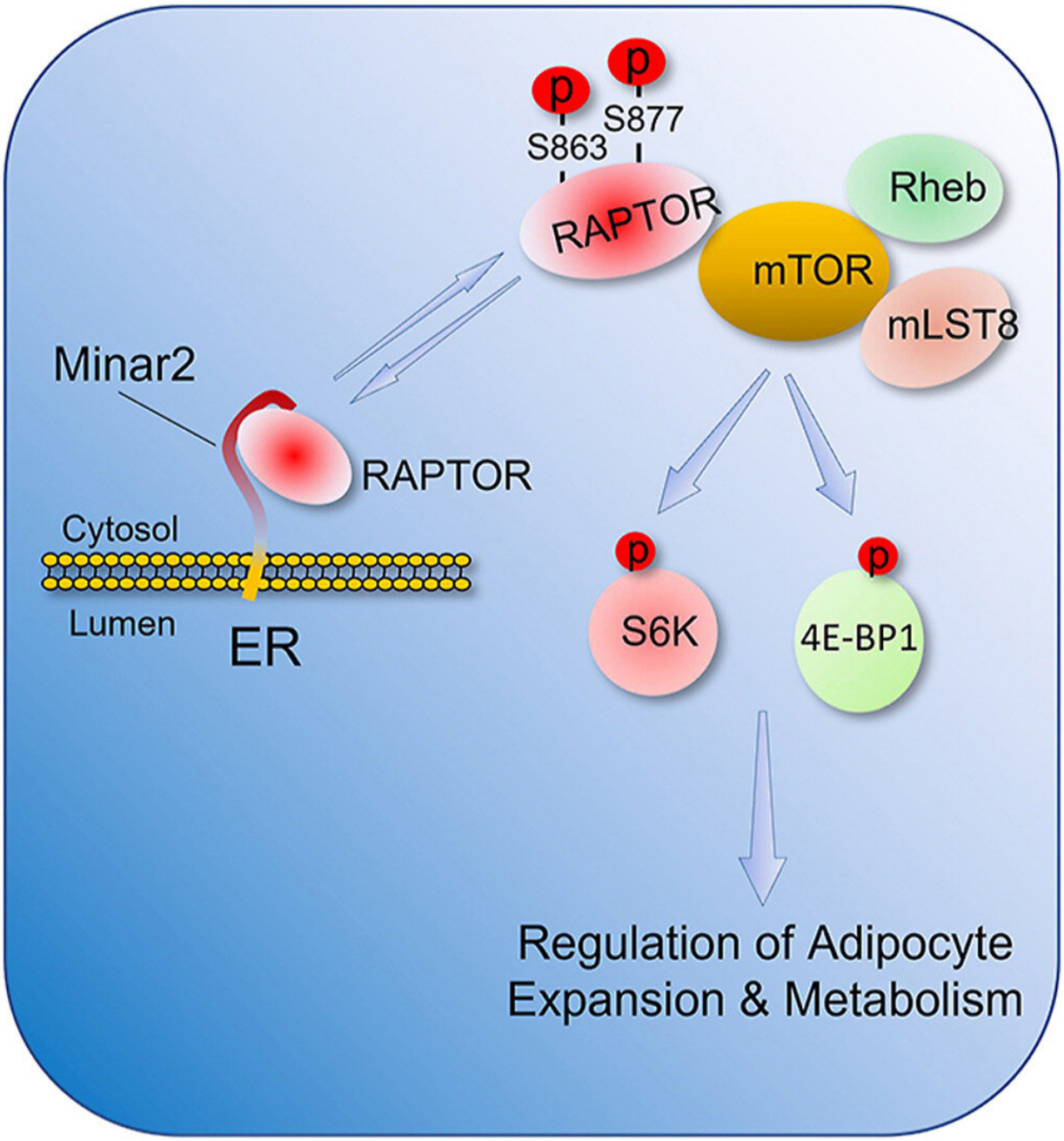
New study uncovers role of previously unknown protein in obesity and diabetes

May 26 2023



Graphical abstract. Credit: *Molecular Metabolism* (2023). DOI: 10.1016/j.molmet.2023.101744

More than 40% of Americans are considered obese, and the trend continues to grow. The treatments or preventive options for obesity and obesity-associated diseases are limited. It is a major national healthcare and public health burden significantly increasing the risk of diseases such as diabetes, hypertension, and cancer and is linked to the severity of COVID-19.

A research team from Boston University Chobanian & Avedisian School of Medicine has identified a novel druggable signaling molecule involved in obesity, a previously unknown protein (MINAR2) discovered in 2020 in the laboratory of Associate Professor of Pathology and Laboratory Medicine Nader Rahimi, Ph.D.

"This finding can help to unravel new aspects in the mechanisms of obesity and diabetes, which could lead to the development of novel therapeutics for the prevention and treatment of obesity and diabetes," said Rahimi, a corresponding author of the paper titled "Inactivation of Minar2 in Mice Hyperactivates mTOR Signaling and Results in Obesity" and published online in *Molecular Metabolism*.

To study the role of MINAR2 in obesity, the research team generated global MINAR2 knockout animal models that eliminated that gene's function. MINAR2-deficient animal models fed on a normal non-high fat diet showed an increased fat mass ratio compared to control sex- and age-matched models. When MINAR2-deficient animal models were fed a high-fat diet (HFD), they gained weight faster than control models and

developed obesity with impaired glucose tolerance, a hallmark of type 2 diabetes.

Researchers found that mammalian target of rapamycin (mTOR) signaling which regulates metabolism and other cellular processes such as cell proliferation, and autophagy is hyperactivated in the fat cells of MINAR2-deficient animal models. MINAR2 interacts with raptor, a specific and essential component mTOR complex 1 and is a physiological negative regulator of mTOR signaling with a significant role in obesity and metabolic disorders.

"Anti-obesity therapy has proven challenging and most of the anti-obesity medications to date have poor or insufficient efficacy with questionable safety. MINAR2 is a druggable molecule and drugs that targets MINAR2 could lead to the development of effective therapeutics," said Rahimi. "Control of excess body fat is one of the greatest scientific and medical challenges of our time. Further basic and translational research on MINAR2 could lead to a promising therapeutic target for diet-induced obesity."

More information: Saran Lotfollahzadeh et al, Inactivation of Minar2 in Mice Hyperactivates mTOR Signaling and Results in Obesity, *Molecular Metabolism* (2023). DOI: 10.1016/j.molmet.2023.101744

Provided by Boston University School of Medicine