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Potential target for reducing obesity-related inflammation found

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Scientists at the National Institutes of Health have identified a potential molecular target for reducing obesity-related inflammation. Researchers have known that overeating (that is, excess calorie consumption) by individuals with obesity often triggers inflammation, which has been linked to such diseases as asthma and Type 2 diabetes. In their study, published recently in The *Journal of Clinical Investigation*, the investigators found that a protein called SIRT3 provides resistance to this inflammatory response and could potentially prevent or reverse obesity-associated diseases of inflammation.

Lead researcher Michael N. Sack, M.D., Ph.D., a senior investigator at NIH's National Heart, Lung, and Blood Institute, explained that he and his team identified the role of SIRT3 through an investigation involving 19 healthy volunteers who fasted for a 24-hour period.

"Previous research has shown that intermittent fasting or intermittent calorie restriction—by way of eating fewer calories for a few days a month—reduces inflammation," said Dr. Sack. "We found through our study that this effect is mediated, in part, on a molecular level when SIRT3 blocks the activity of another molecule known as the NLRP3 inflammasome." He explained that NLRP3 inflammasomes are components of an intracelluar immune response triggered when mitochondria undergo stress, such as from excess calorie intake.

By using cultured cells from a group of eight volunteers who did not fast, Dr. Sack and his team found evidence suggesting that SIRT3 can be

activated not only through fasting, but also through the use of nicotinamide riboside, a vitamin B derivative. "Taken together, these early results point to a potential mechanism for addressing obesity-related inflammation, and thus diseases linked to this type of inflammation, such as asthma, Type 2 diabetes, rheumatoid arthritis, and atherosclerosis—conditions associated with a reduced quality of life and/or premature death," Dr. Sack said.

Obesity remains a substantial health problem for the nation, affecting more than a third of adults and 17 percent of children, according to the Centers for Disease Control and Prevention. Efforts to manage weight, however, can be hindered by the effects of obesity-related diseases. "It is a vicious cycle," said Dr. Sack. "Take asthma for example. An increase in obesity incidence has been associated with an increase in asthma incidence, but asthma makes it difficult for some to be physically active enough to lose weight."

Dr. Sack and colleagues—who include researchers from the National Institute of Arthritis and Musculoskeletal and Skin Diseases and Weill Cornell Medical College—are conducting a follow-up study at the NIH Clinical Center to determine whether the vitamin B derivative nicotinamide riboside can specifically reduce bronchial inflammation in individuals with asthma. If the results of the study are promising, Dr. Sack and colleagues will aim to conduct larger clinical trials to validate the findings and potentially inform treatment of obesity-related inflammation in asthma.

More information: The paper is available online: www.jci.org/articles/view/83260

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