

New weight loss discovery moves us closer to 'the Pill' for obesity

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An important discovery in mice may make a big difference in people's waistlines thanks to a team of Harvard scientists who found that reducing the function of a transmembrane protein, called Klotho, in obese mice with high blood sugar levels produced lean mice with reduced blood sugar levels. This protein also exists in humans, suggesting that selectively targeting Klotho could lead to a new class of drugs to reduce obesity and possibly Type 2 diabetes for people. This finding was recently published online in The *FASEB Journal*.

"Our study is a small step toward reducing the sufferings of obese and diabetic individuals to bring back the joy of healthy life," said M. Shawkat Razzaque, M.D., Ph.D., a researcher involved in the work from the Department of Oral Medicine, Infection and Immunity at Harvard School of Dental Medicine in Boston. "In the dark horizon of obesity and diabetes, Klotho brings a ray of hope."

To make this discovery, Razzaque and colleagues fed increased amounts of food to leptin-deficient mice with the Klotho protein which caused obesity with high blood sugar levels. A second set of mice was bred that was both leptin- and Klotho-deficient, and was fed the same diet as the first set. The second set of mice was lean and had low blood sugar levels, suggesting that reduced Klotho function may not only diminish obesity, but also decrease blood sugar levels. Furthermore, mice without Klotho function gained no body weight after eating a high-fat diet, while mice with functioning Klotho proteins gained body weight following a high-fat diet.



"In Greek mythology, Klotho was the youngest of three fates, the one responsible for spinning the thread of life; since then we have learned that <u>obesity</u> cuts the thread short," said Gerald Weissmann, M.D., Editorin-Chief of The <u>FASEB Journal</u>. "It's good to know that the new molecular biology of Klotho points to agents that will keep us fit and well-spun."

More information: Mutsuko Ohnishi, Shigeko Kato, Junko Akiyoshi, Azeddine Atfi, and M. Shawkat Razzaque. Dietary and genetic evidence for enhancing glucose metabolism and reducing obesity by inhibiting klotho functions. *FASEB J fj*.10-167056; doi:10.1096/fj.10-167056

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