The heart 'talks' to fat cells, scientists discover

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Walter J. Koch, PhD, W.W. Smith Endowed Chair in Cardiovascular Medicine, Professor and Chair of the Department of Pharmacology, and Director of the Center for Translational Medicine at the Lewis Katz School of Medicine at Temple University. Credit: Lewis Katz School of Medicine at Temple University

Like sending a letter through the mail or a text over a cellular network, the heart can generate messages that travel long distances through the body. Those messages ultimately reach fat cells, new research by scientists at the Lewis Katz School of Medicine at Temple University (LKSOM) shows.

"The ability of the heart to communicate directly with fat had been suspected, but our study is the first to provide evidence of crosstalk between heart and fat tissue that is regulated by the enzyme, G protein-coupled receptor kinase 2 (GRK2)," said senior investigator Walter J. Koch, Ph.D., W.W. Smith Endowed Chair in Cardiovascular Medicine, Professor and Chair of the Department of Pharmacology, and Director of the Center for Translational Medicine at LKSOM.

The findings could have implications for modulating weight gain in patients with heart failure, a condition that arises when the heart can no longer effectively pump blood through the body.

In the breakthrough paper, published online in the journal *JCI Insight*, Dr. Koch and colleagues show that the heart relies on a cardiac-specific messenger, the signaling enzyme, GRK2, to relay information about metabolism to fat cells.

"GRK2 signaling in the heart effectively regulates fat accumulation in the body," said Dr. Koch. "Through this pathway, the heart 'talks' to fat and alters how fat responds to certain conditions." In previous work, Dr. Koch's laboratory showed that GRK2 serves essential roles in both normal heart function and heart failure.

The researchers carried out their investigation in mice with GRK2 activity inhibited in the heart. When fed a high fat diet, GRK2-inhibited mice accumulated significantly more fat than their littermates with normal GRK2 expression. The experiment was repeated in mice with GRK2 overexpressed in the heart, mimicking the increase in GRK2 that occurs in heart failure in humans. When given a high fat diet, these mice gained less body weight compared to their normal littermates.

Using complex metabolomics, a way of investigating metabolites associated with cellular processes, Dr. Koch's team found that GRK2 signaling specifically altered branched chain amino acid (BCAA) and endocannabinoid metabolism in the heart. GRK2-overexpressing mice on high fat diets had metabolite profiles that were distinct from those of GRK2-inhibited mice and normal animals.

"We also took the work a step further and identified one BCAA metabolite that enhanced fat cell differentiation in vitro," Dr. Koch said. His team plans next to look for other metabolites and protein factors that are involved in crosstalk between the

heart and fat tissue.

More information: Benjamin P. Woodall et al, Alteration of myocardial GRK2 produces a global metabolic phenotype, *JCI Insight* (2019). DOI: 10.1172/jci.insight.123848

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