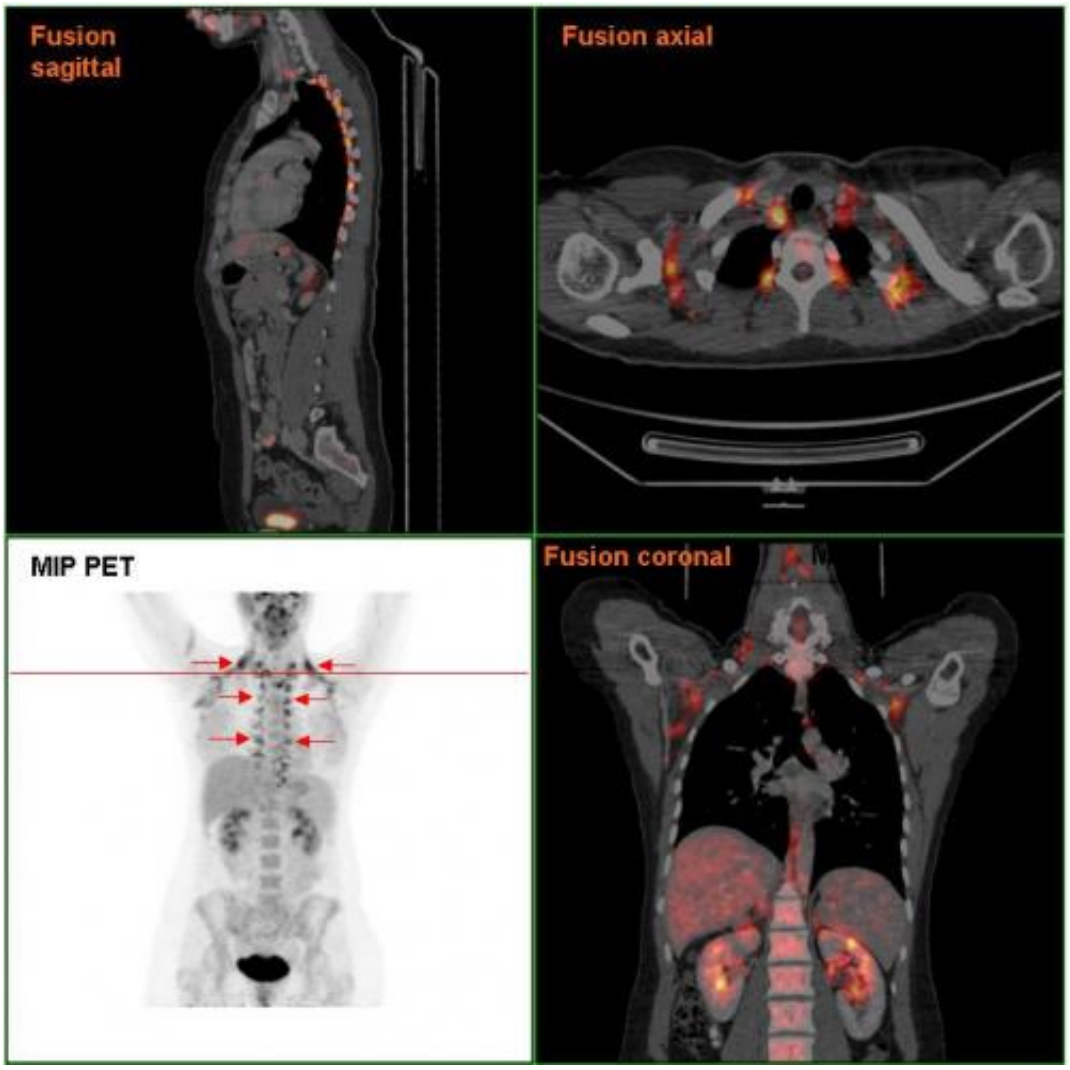
Can a new drug brown the fat and trim the obese person?

May 28 2015, by Melissa Healy, Los Angeles Times



Brown adipose tissue in a woman shown in a PET/CT exam. Credit: Public Domain

New research has found that a variant of a drug used to treat pulmonary arterial hypertension prompts weight loss in obese mice. Among mice fed a high-fat diet, those who did not get the medication became obese while medicated mice did not, the same study showed.

The experimental drug used, a stimulator of soluble guanylyl cyclase, or sGC, is a member of the same class of novel drugs as the drug riociguat, which was approved by the Food and Drug Administration in 2013 as a treatment for high blood pressure in the blood vessels that lead to the heart from the lungs. The drug, produced by Bayer HealthCare Pharmaceuticals, is marketed as Adempas.

In mice, the sCG stimulator drug prompted a shift in fat tissue, turning some stored white fat in the mice to a form of fat that burns up more energy and improves metabolic function.

That beneficial fat is called beige or brown fat because it is richly populated with cellular furnaces known as mitochondria, which appear brown under a microscope. Unlike white adipose tissue, which issues hormonal signals that prompt the storage of still more white fat, brown fat burns up fat and appears to protect against weight gain, even when caloric intake is high.

The new research, published Tuesday in the journal *Nature Communications*, showed that in mice made obese by a high-fat, high-calorie diet, the sCG stimulator not only promoted weight loss, it also improved glucose tolerance, reduced insulin levels and drove down signs of fatty liver - a damaging consequence of established obesity. It even shrunk white fat cells.

In plump mice on the sCG stimulator, circulating dietary fatty acids were increasingly drawn into the brown fat, which, during physical activity, burned it up at high rates. Even muscle and white fat in those mice

increased their use of the circulating fatty acids. The result: those mice burned up more calories, and their abnormal metabolic function improved.

The new research, led by researchers at the University Hospital in Bonn, Germany, also shed light on a key "pathway" - a sequence of molecular events that takes place in the normal generation of brown fat. In doing so, they highlight a number of targets, or links in that chain of molecular events, at which experimental therapies might intervene to prompt the shift of white fat to brown.

Some of those have already been explored and found impractical, while others may result in new experimental drugs for obesity and its health consequences. Among those under investigation are drugs that mimic the action of natriuretic peptides, hormones that play key roles in rescuing the heart and its blood vessels from failure.

In the meantime, the sCG stimulator used here, the authors concluded, "might be used to enhance weight loss induced by physical activity."

If a drug related to riociguat is to enter broad use for obesity, however, it will have to be cheaper than its close chemical relative. At doses taken by those with pulmonary arterial hypertension, a typical month's prescription of Adempas costs close to $2,800, or about $90,000 a year.

As a treatment for the nation's more than 72 million obese adults, that cost could prove prohibitive, especially as obesity and its consequences are increasingly understood to be chronic conditions that will need long-term management.

More information: *Nature Communications*, DOI: 10.1038/ncomms8235