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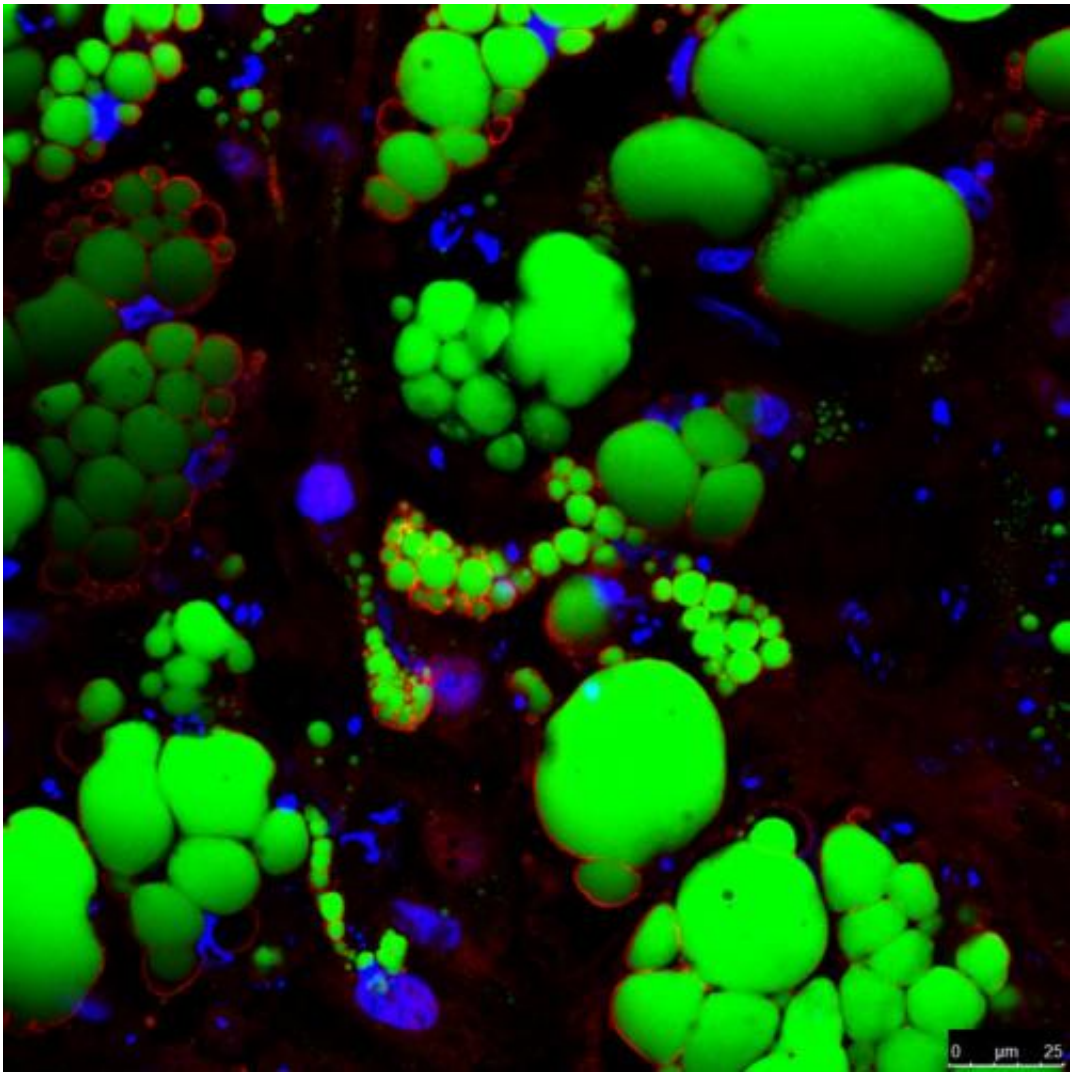
Brief: A pill for obesity? Stem cell scientists convert white fat to brown fat

December 8 2014



Human pluripotent stem cell-derived fat cells. Credit: Tim Ahfeldt/Harvard University

Harvard Stem Cell Institute researchers at Harvard and Massachusetts General Hospital have taken what they are describing as "the first step toward a pill that can replace the treadmill" for the control of obesity - though it of course would not provide all the additional benefits of exercise.

Chad Cowan, an HSCI Principal Faculty Member and his HSCI team report that they have created a system using human stem cells to screen for compounds that have the potential to turn white, or 'bad', fat cells into brown, or 'good' fat cells.

The research team have already identified two compounds that can accomplish that in human cells.

The study is published in *Nature Cell Biology* today.

More information: White-to-brown metabolic conversion of human adipocytes by JAK inhibition, *Nature Cell Biology*, DOI: 10.1038/ncb3075

Abstract
The rising incidence of obesity and related disorders such as diabetes and heart disease has focused considerable attention on the discovery of new therapeutics. One promising approach has been to increase the number or activity of brown-like adipocytes in white adipose depots, as this has been shown to prevent diet-induced obesity and reduce the incidence and severity of type 2 diabetes. Thus, the conversion of fat-storing cells into metabolically active thermogenic cells has become an appealing therapeutic strategy to combat obesity. Here, we report a screening platform for the identification of small molecules capable of promoting a white-to-brown metabolic conversion in human adipocytes. We identified two inhibitors of Janus kinase (JAK) activity with no precedent in adipose tissue biology that stably confer brown-like

metabolic activity to white adipocytes. Importantly, these metabolically converted adipocytes exhibit elevated UCP1 expression and increased mitochondrial activity. We further found that repression of interferon signalling and activation of hedgehog signalling in JAK-inactivated adipocytes contributes to the metabolic conversion observed in these cells. Our findings highlight a previously unknown role for the JAK–STAT pathway in the control of adipocyte function and establish a platform to identify compounds for the treatment of obesity.

Provided by Harvard University