

## **Battles between steroid receptors to regulate fat accumulation**

September 20 2012

The androgen receptor in human cells inhibits fat accumulation, but its activity can be sabotaged by glucocorticoids, steroids that regulate fat deposition and are known drivers of obesity and insulin resistance, said researchers led by those at Baylor College of Medicine in a report in the journal *Chemistry & Biology*.

"The project started with a straightforward search for genes or signals specific to human <u>fat</u> cells," said Dr. Michael A. Mancini, professor of molecular and cellular biology at BCM, and director of its Integrated Microscopy Core. He is senior author of the report and Dr. Sean Hartig, instructor in molecular and cellular biology at BCM, is first author.

"We used a novel approach that combined the gene expression studies with automated microscopy and 'high content' image analysis to identify unique signatures specific to <u>human cells</u> and not the mouse cell line usually used in such studies," said Hartig. The work identified the androgen receptor as a uniquely expressed gene in human fat cells that is both expressed and functional during the early stages of fat cell differentiation.

"Activation of the androgen receptor can inhibit the early stages of human fat maturation," he said. However, he said, another important steroid receptor – the glucocorticoid receptor – tightly regulates how the androgen receptor is expressed.

High levels of glucocorticoids can lead to lipid accumulation in fat cells



and their <u>deposition</u> throughout the body and, in particular, in the abdominal or visceral area. Abdominal fat is associated with higher risks of heart disease and diabetes.

"Using a custom developed image analysis software platform usually found only in large pharmaceutical screening centers, we applied specific algorithms to sensitively detect the glucocorticoid inhibition of androgen receptor activity," said Mancini. "Without the automated, 'high content' image analysis approach, we could not have made these observations."

High content analysis is one of the latest technologies that allow researchers to collect and analyze images quickly, using special computer algorithms that detect signals within the specimens with exquisite sensitivity. Mancini and members of his teams have pioneered these efforts, especially for application to cell models of nuclear receptor function.

The glucocorticoids can affect the expression of the androgen receptor and inhibit its activity, facilitating fat storage.

"This has implications in this era of an <u>obesity</u> epidemic," said Mancini. "If you can reduce glucocorticoids, you might be able to upregulate (or increase) <u>androgen receptor</u> activity and regulate fat storage. This work is another example of the how high throughput approaches can enable research to study basic science problems, with a follow-on paths leading to translational science."

**More information:** Hartig et al.: "Feed-forward Inhibition of Androgen Receptor Activity by Glucocorticoid Action in Human Adipocytes." <u>www.cell.com/chemistry-biology ...</u> <u>ii/S1074552112002785</u>



## Provided by Baylor College of Medicine

Citation: Battles between steroid receptors to regulate fat accumulation (2012, September 20) retrieved 6 May 2024 from https://phys.org/news/2012-09-steroid-receptors-fat-accumulation.html

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