ZEB1, Oscar for leading role in fat storage

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A team from Ecole polytechnique fédérale de Lausanne in Switzerland, in collaboration with ETH Zurich, has managed to decode the process of adipogenesis by identifying the precise proteins that play the leading roles in fat absorption. Their findings have been published in the open-access scientific journal eLife.

And the winner is ... ZEB1! There are many actors involved in the process of adipogenesis, used by the body to store the fat that it absorbs from food. Up to now there had been some uncertainty as to how it was regulated. Yet, understanding this mechanism is of crucial importance to prevent the diseases related to fat accumulation in adipose tissue.

A research team led by Carine Gubelmann and Petra Schwalie at EPFL's Laboratory of Systems Biology and Genetics, directed by Bart

Deplancke, joined forces with Christian Wolfrum's researchers from ETH Zurich, to decode the process of adipogenesis. They performed a large scale study of the action of no less than 734 "transcription factors", the proteins that specifically regulate gene expression.

To do this, the researchers "over-expressed" each factor to see which one had an impact on adipogenesis. Their observations, performed in vitro, allowed to identify 26 transcription factors involved in the differentiation of fat cells and to "rank" their importance in the process. The first place went to the ZEB1 factor, which left no doubt about being the undisputed champion. "We found that it clearly dominated the action of other important proteins known in adipogenesis," said Petra Schwalie.

Using this information, the researchers studied the in vivo effects of an intervention on the ZEB1 factor – only to find that, once again, its role was crucial. Its level of expression accurately corresponds to the human body's fat storage potential as well as its tendency to obesity, calculated through the waist/hip ratio.

Is the development of a miracle drug against weight gain in the horizon? "The problem is that this protein plays an important role in at least nine vital physiological processes," said the researcher. "If turned off completely, the body does not survive. Thus, a therapeutic molecule acting on ZEB1's expression should specifically target a precise type of tissue, which is a big challenge."

Nevertheless, these findings, published in the new open-access journal *eLife*, contribute information that is essential to understanding a key physiological process.

More information: *eLife*, elifesciences.org/content/3/e03346

Provided by Ecole Polytechnique Federale de Lausanne