Press information 15.11.2016

Embargo: 17.11.2016, 9:00 GMT

Reduced mobilization of fat contributes to metabolic health

Obesity and unhealthy diets trigger a variety of health problems, including type 2 Diabetes with more than 60,000,000 Europeans suffering from it. Since many people do not change their unhealthy life styles, pharmaceutical companies have long been seeking for therapeutic interventions to protect from the health problems associated with the metabolic syndrome. A team led by Richard Moriggl from the Ludwig Boltzmann Institute for Cancer Research has now discovered a molecular mechanism that might be suitable as target for such a therapy. The results have been published in Diabetologia, the journal of the European Association for the Study of Diabetes (EASD).

Excess energy is stored in form of fat deposits all over the mammalian body, which are not only affecting dress sizes but also general health. Aberrant fat mobilization can contribute to the development of metabolic diseases such as insulin resistance and type 2 diabetes. Fat is mobilized as soon as the body needs energy in a process called lipolysis, the biochemical mining of this energy storage. The process, which controls fat mobilization, is critical for the energy balance of the whole body. The new study performed by a team around Richard Moriggl at the Ludwig Boltzmann Institute for Cancer Research, the Veterinary University Vienna and the Medical University Vienna in collaboration with the Medical University Graz showed that the transcription factor STAT5 plays an unexpectedly important role in adipose tissue function.

Transcription factors are similar to genetic light switches and capable of switching genes on and off. Mice lacking STAT5 in fat cells have a markedly reduced ability to mobilize fat stores. As a result, STAT5-deficient mice have a higher body fat content than normal mice. The researchers were able to demonstrate that STAT5 is involved in the gene regulation of the lipid-cleaving enzyme ATGL. Thereby, a new mechanism that contributes to the regulation of fat depot catabolism was discovered.

Despite the increased body fat content, both young and elderly mice with missing STAT5 are metabolically "healthier" and remain insulin sensitive. This might be attributed to the reduced products of lipolysis in the blood. When fats are mobilized the bloodstream is full of free fatty acids, which are known to contribute to the development of insulin resistance in higher concentrations. The study thus provides a basis for further research into the extent to which the inhibition of STAT5 in adipose tissue might constitute a possible therapeutic intervention for diseases such as diabetes or coronary heart and cardiovascular disease.

Publication in Diabetologia:

Adipocyte STAT5 deficiency promotes adiposity and impairs lipid mobilisation in mice
D. Kaltenecker, K. M. Mueller, P. Benedikt, U. Feiler, M. Themanns, M. Schlederer, L. Kenner, M. Schweiger, G. Haemmerle and R. Moriggl
http://link.springer.com/article/10.1007/s00125-016-4152-8

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About the Ludwig Boltzmann Institute for Cancer Research (LBI-CR):

The LBI-CR focuses on developing new murine models for cancer and exploiting them to gain novel insights into the origins of the disease. The institute conducts cutting edge research into the underlying mechanisms of cancer using the modern power of genetics. With particular attention for signal cooperation in tumour cells the researchers analyse the molecular basis of cancer with the intention to translate recent progress in cancer research into novel therapeutic approaches. The Institute conducts its research in close cooperation with the Research Institute for Molecular Pathology, Medical University Vienna, Veterinary University, Children's Cancer Research Institute and the company Tissuegnostics.

About the Ludwig Boltzmann Gesellschaft:

The Ludwig Boltzmann Gesellschaft (LBG) is a non-university research organization headquartered in Vienna. It operates research institutes (Ludwig Boltzmann Institutes) in the fields of human medicine / life sciences, as well as the humanities, social and cultural sciences. It initiates innovative research topics together with academic partners and stake holder organisations, including companies, associations and ministries. The LBG is specialized in translational research - the bridge between basic research and application. In the humanities and social sciences institutes, the interdisciplinary research results are communicated to the specialist audience at conferences and scientific events, as well as made accessible to the general public through public activities.