

## Fighting Fat With Fat

**Coordinated by the German Cancer Research Center (DKFZ), a European research consortium is searching for ways to use brown fat tissue for combating widespread diseases such as type 2 diabetes and metabolic syndrome.**

Gross overweight or obesity is spreading like a pandemic. In 2006, WHO estimated that half of all adults and one fifth of all children in Europe are overweight. Of these, about one third is considered obese. In 2009, these figures were confirmed for Germany in a microcensus by the Federal Statistical Office: Fifteen percent of Germans were classified as obese. Today, over ten times more children in Europe are obese than in 1970. Obesity is responsible for numerous diseases including such severe ones as type 2 diabetes, cardiovascular diseases, and cancer.

Obesity results when the body stores excess energy in the form of fat molecules in white fat tissue. Large deposits of white fat can be found, for example, at the stomach, hips and buttocks. However, apart from white fat cells, there is a second type of body fat, the brown fat tissue. Unlike energy-storing white fat tissue, brown fat tissue burns energy by converting it to heat.

Until recently, scientists believed that in humans, only babies have active brown fat. In 2007, several research groups discovered this tissue type also in adult humans. Last year, a research team led by Stephan Herzig of DKFZ showed that prostaglandin, an inflammatory hormone in our body, stimulates the formation of brown fat-like cells within white fat.

These findings could lead to a completely new way of fighting obesity. Activating or regenerating only small amounts of brown fat tissue would significantly increase the breaking down of white fat, consumption of glucose (blood sugar) and, thus, an individual's output of energy. This is also confirmed by the observation that lean people have – relatively speaking – more brown fat tissue than overweight people. Researchers are therefore looking for ways of stimulating brown fat to proliferate or to produce more heat by dietary measures or drugs. Some scientists have even considered transplanting brown fat cells. "Estimates suggest that an additional 50 grams of brown fat tissue would be enough to increase an adult person's energy output by 20 percent," said Herzig, who leads a joint research department of DKFZ, Heidelberg University and Heidelberg University Hospitals. "What we are trying to achieve here is not to help people attain what they believe to be a perfect body shape. Instead, our aim is to treat severely obese people by repairing a defective glucose tolerance, i.e., improving the effect of insulin, and thus to combat type 2 diabetes."

To this end, Herzig's group has teamed up with 19 partner institutes from 12 European countries. The European Union will provide funds of six million euros for this research project over the next four years. The consortium has named itself "DIABAT", a made-up word combining "diabetes" and "BAT", the acronym for "brown adipose tissue", or brown fat tissue. Coordinator Stephan Herzig is pleased: "This is the first time that research into the promising properties of brown fat tissue is being supported on a large scale in Europe."

The participating research institutes, which include three biotechnology companies, have defined various tasks which they endeavor to accomplish with the support of the EU funds. This includes, among other things, identifying the stem cells or precursor cells of brown fat cells and unraveling their molecular profile. Several research groups will develop methods for isolating such precursor cells from the body and growing them in the culture dish. Further

research in mice will be pursued to investigate whether brown fat cells thus obtained can prevent or slow down diabetes. Another important task is to search for substances that activate brown fat cells or encourage their formation in white fat tissue. Promising substances found will be tested in clinical trials within the DIABAT project.

For the various research endeavors it is essential to find the brown fat tissue in the body. However, brown fat cells occur in small, scattered tissue islands that are difficult to image. Therefore, DIABAT teams plan to enhance suitable imaging technologies and to identify biomarkers that make it possible to trace even the slightest changes in the amount of brown fat.

“The DIABAT consortium brings together an impressive variety of scientific expertise and know-how – from metabolism researchers and molecular biologists over nutrition experts through to clinicians and radiologists,” says Stephan Herzig. “Together, we are a powerful troop ready to embrace one of the greatest health challenges of our Western society.”

DIABAT Coordinator:

Prof. Dr. Stephan Herzig,

head of the joint research department “Molecular Metabolic Control” of the German Cancer Research Center, the University of Heidelberg and Heidelberg University Hospitals.

The German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) with its more than 2,500 employees is the largest biomedical research institute in Germany. At DKFZ, more than 1,000 scientists investigate how cancer develops, identify cancer risk factors and endeavor to find new strategies to prevent people from getting cancer. They develop novel approaches to make tumor diagnosis more precise and treatment of cancer patients more successful. Jointly with Heidelberg University Hospital, DKFZ has established the National Center for Tumor Diseases (NCT) Heidelberg where promising approaches from cancer research are translated into the clinic. The staff of the Cancer Information Service (KID) offers information about the widespread disease of cancer for patients, their families, and the general public. The center is a member of the Helmholtz Association of National Research Centers. Ninety percent of its funding comes from the German Federal Ministry of Education and Research and the remaining ten percent from the State of Baden-Württemberg.

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