BETAJUDO

Beta-cell function in Juvenile Diabetes and Obesity

Through the betaJUDO project, the University of Luxembourg has benefited from European research funding.

Diabetes: What happens in a young body?

In many countries of the western world, severe obesity is the primary cause for the increasing number of people who develop type 2 diabetes already in childhood and adolescence. As a partner of the EU project betaJUDO, the Luxembourg Centre of Systems Biomedicine (LCSB) of the University of Luxembourg is working to track down the causes and processes of this metabolic disorder. LSCB researchers are analysing extensive data material obtained in laboratory tests and clinical trials carried out by their project partners. The long-term goal is to develop drugs that will, if not cure, then at least halt the development of the disorder and associated health problems.

The cause of the increase of type 2 diabetes amongst children and adolescents is quite clear: obesity. But what exactly trigger diabetes in the bodies of overweight children? Researchers do not have enough information to answer this question. Previous studies have revealed that many of these children have high levels of insulin during early childhood, but that their insulin secretion then gradually diminishes until, ultimately, the blood glucose level can no longer be controlled. Experts suspect that insulin hypersecretion may be a portent of the metabolic disorder – and might hold the key to better handling obesity and diabetes.

In the betaJUDO project, partners from hospitals, research institutes and pharmaceutical companies work together to study the role played by insulin-producing islet cells in the pancreas in the course of the disorder. With its expertise in bioinformatics, the LCSB is chiefly responsible for data processing, analysis and security. “These tasks form an essential basis for well-substantiated results and their interpretation,” says Dr Katharina Paulmichl of the University Clinic of Child and Adolescent Medicine Salzburg, a clinician involved in the study.

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This is a Collaborative Project of the European FP7-HEALTH.2011.2.4.3-2 programme.i

Understanding disorder development

Data are firstly obtained from laboratory cell tests. The researchers have already established a cell system that depicts the course of insulin secretion over a period of time. Initially, the cells release a great deal of insulin upon corresponding stimulation. Over the course of a few days, the insulin secretion decreases. A process that takes several years in the body of a child thus happens in the lab in just a week.

The scientists are studying the metabolism of these cells on several levels. The project partners from the University of Geneva, for example, determine all proteins that are built within the cell at different points in time. Scientists from Uppsala University, Sweden, conduct lipidomics and transcriptomics studies. They measure the lipids, or fats, from the cell and determine which genes are activated in the cell and transcribed into the messenger molecule RNA.

“In this way, we are trying to understand what metabolic pathways in the cells are potentially affected by the disorder,” explains Dr Kirsten Roomp of LCSB. “In a second step, we study what happens when we administer various drugs to the cells.” The tested drugs are currently used for treating diabetes in adults since there are at present no drugs approved for child therapy.

In the clinical part of the project, data are collected from children who are undergoing medical treatment for obesity. Using the Oral Glucose Tolerance Test (OGTT), for instance, physicians follow how the insulin secretion of these children changes. They also study the distribution of brown fat cells in the body and the fatty acid levels in the blood. In addition, by performing DNA analyses, the researchers hope to identify genes that influence the onset of obesity and diabetes.

Luxembourg-based data analysis

To collect the results from the clinical tests at the respective locations in standardised form, the LCSB researchers have prepared a data management portal into which physicians can directly enter their measurement results. “We can thus unify and bundle the collected data from the respective project partners and amass a larger cohort for subsequent analysis,” says Dr Roomp. “We hope the laboratory tests will reveal similar metabolic mechanisms to which our DNA analyses also point. This would give us clues as to new therapeutic targets.”

The plan for the next project phase is to test a first active agent in a clinical trial. The project partners are currently selecting the best candidate in order to begin the clinical trial with the study of 50 obese children. “With a better fundamental understanding, and therapeutic strategies based upon it, we ultimately expect an improved treatment for obese children and adolescents,” says Katharina Paulmichl of Salzburg.

The Seventh Framework Programme for Research and Technological Development (FP7) was the European Union’s main financial instrument to support European research during the 2007-2013 period. The funding programme continues under Horizon 2020, the Framework Programme for Research and Innovation, supporting a wide range of research domains with a budget of €79 billion (2014-2020).i

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