

Press release

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Overcoming a Genetic Defect

Kiel University coordinates European research project on alpha-mannosidosis

The European Union has approved a grant of about € 2.4 million to a team of European scientists, led by the Kiel biochemist Professor Paul Saftig, to carry out research on the rare hereditary disease alpha-mannosidosis. The project, HUE-MAN (Human Enzyme Replacement Mannosidosis), will be coordinated by Professor Saftig for the next three years at the Christian-Albrechts-Universität (CAU) in Kiel. The aim is to develop a drug that will compensate the patient's body for the genetic defect.

In Europe about 400 people - mostly children - suffer from alpha-mannosidosis. It causes coarse facial features, retards the development of speech and mental ability, weakens the immune system, and damages bones and muscles. Professor Saftig explains the importance of his research: "At present, without a very risky bone marrow transplant, many of these patients die between the ages of 10 and 20". The cause of this lysosomal storage disorder is a genetic defect. Lysosomal enzymes - cell constituents that are specifically programmed to break down metabolic waste products - normally decompose the waste products sufficiently to enable the cell to continue the process. If a certain gene, which controls one of these enzymes, is defective, that enzyme cannot be produced. The waste products, which in the case of alpha-mannosidosis are mannose sugars, build up in the cell and completely block its function. As a result, not only muscle cells, but also brain cells, cease to work.

The European team of scientists are building on their previous basic research in an EU project that has been completed. In that work they discovered that the "accumulated garbage" in the cell became dispersed when diseased mice were given injections of the missing enzyme at fortnightly intervals. "It is especially new and interesting that we even succeeded in treating the damage to the animals' central nervous system", explains the Kiel biochemist. However, there is still a long way to go before an effective drug can be developed. "Nevertheless, we hope that in three years we will have progressed far enough to begin the first clinical phase", says Saftig.

In addition to the Kiel researchers, about 15 other scientists are working on the project - in particular paediatricians from Göttingen and Mainz, from Norway, Great Britain, France and the Czech Republic, as well as from a pharmaceutical company in Denmark. Each one will be responsible for a specialist area: while Saftig will coordinate the project and develop drugs for animal tests, the paediatricians will study the detailed course of the disease in patients. For example, the Göttingen scientists will investigate changes to the neighbouring genes.

The € 2.4 million funding for the project has come from the European Union's Sixth Framework Programme *Life Sciences*. A proportion of this programme's funding is reserved for research into rare diseases. Of the total project grant of € 2.4 million, the amount allocated to the Christian-Albrechts University of Kiel is € 600 000. For the Institute of Biochemistry this will fund three new posts: a technical assistant, a post-doctoral student, and a secretary.

More information about the project can be found at the website:

www.uni-kiel.de/Biochemie/hue-man

Three photographs/figures related to the topic can be downloaded from:

<http://www.uni-kiel.de/download/pm/2006/2006-043-1.jpg>

Picture legend:

Professor Paul Saftig and Dr Judith Blanz, the senior collaborator in the project, examining a cell tissue sample.

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<http://www.uni-kiel.de/download/pm/2006/2006-043-2.jpg>

Picture legend:

The microscope image shows a muscle cell blocked by metabolic waste products. On the left beside it is shown a healthy muscle cell.

Copyright: CAU, photo: Paul Saftig

<http://www.uni-kiel.de/download/pm/2006/2006-043-3.jpg>

Picture legend:

The project's logo shows a child - representing the age-group most usually affected by mannosidosis - and nine stars symbolising the European Union as partner. Shown below is the structure of the mannose sugars that accumulate in the cells of patients.

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