

Two ERC grants go to the German Cancer Research Center

Two DKFZ researchers at a time are awarded a prestigious European Research Council (ERC) Advanced Grant this year. One of the grants is awarded to a project of Prof. Michael Boutros, who endeavors to show, for the first time, the interaction of all genes in cells of a higher organism. Prof. Bruno Kyewski is awarded an ERC grant for his studies of how immune cells learn tolerance of the body's own structures.

Launched in 2007, the European Research Council (ERC) supports investigator-initiated frontier research with the aim of promoting visionary projects and opening up new interdisciplinary fields of research. For excellent established researchers, the ERC has yearly calls for proposals for its ERC Advanced Grants, which are awarded in a highly competitive scheme. "It is a tremendous success for DKFZ that two of our scientists at a time have been selected in this year's round of calls," said Prof. Dr. Otmar D. Wiestler, Chairman of the Management Board of DKFZ.

One of two awardees is molecular biologist **Prof. Dr. Michael Boutros**, who leads a joint department at DKFZ and Medical Faculty Mannheim of Heidelberg University. In the project that has been awarded the ERC grant, Boutros aims to generate, for the first time, a genetic interaction map in order to gain a fundamental understanding of how genes interact.

The links between particular genetic mutations or genetic variants and the development of disease are often very difficult to identify: Many genes can amplify, reduce or even cancel out each others' effects. Therefore, the effect of individual genetic variants often also depends on what other genes are affected. Michael Boutros and colleagues have developed a new method that uncovers these combined effects of genes. Using a technique called RNA interference, they silenced a set of genes one at a time and two at a time in all pair combinations. By systematically cataloging all interactions among important genes, the scientists obtain a detailed list of interaction partners for each gene, much like a list of friends in a facebook profile. If two facebook users have many friends in common, the odds are that those two people know each other – even if they themselves are not facebook friends. Similarly, by comparing the interaction profiles of genes, the researchers can now predict which genes affect the same cellular processes.

In cancer cells and cells of the fruit fly *Drosophila*, the investigators intend to map these interactions across the whole genome. In doing so, they are particularly interested in the interaction of genes that are involved in cell signaling, because defective transmission of growth signals plays an important role in the development of cancer. The ERC will support the project with funds amounting to €2.5 million for a period of five years.

Michael Boutros studied biology and biochemistry in Aachen and Witten/Herdecke, both in Germany, and New York, U.S.A. He subsequently held research positions at the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany, and at Harvard Medical School, U.S.A. Since 2003, he has been working at DKFZ as a researcher and head of the Division of Signaling and Functional Genomics.

Immunologist **Prof. Dr. Bruno Kyewski** studies the immune system's essential feature: its ability to discriminate between self and non-self. If this mechanism becomes dysfunctional, autoimmune diseases may arise. The immune system's T cells are educated in the thymus to tolerate self proteins. In the past few years, Kyewski has been able to uncover a key aspect of tolerance induction: Body cells normally produce only those proteins which they

need for their particular tasks. However, as Kyewski found out, the cells of the thymus epithelium additionally produce a wide array of proteins that they do not need themselves and which were previously thought to be produced exclusively in other body cells. Using this molecular trick, the thymus epithelium can present an enormous range of self proteins to the immune cells.

In four different autoimmune diseases, Kyewski and colleagues have already shown that tolerance induction is dysfunctional if a particular self protein is not sufficiently presented in the thymus. Kyewski is awarded the ERC grant for taking a closer look at this striking feature of thymic epithelial cells. The immunologist seeks to understand how the production of proteins from other body tissues is regulated in the thymus. At least 10 to 20 percent of all genes of the human genetic material is read by the thymic epithelial cells and translated into proteins. However, each one of these cells has a share of only one to three percent in this. So how does a thymic epithelial cell “know” for which proteins it is responsible? Is there a pattern behind this or is it left to chance? These questions are also of great interest for cancer research because immune cells are also taught tolerance to tumor antigens by the thymus epithelium.

Bruno Kyewski studied medicine in Bonn, Germany, and Zurich, Switzerland. He subsequently pursued research at the Max Planck Institute of Immunobiology in Freiburg, Germany, and at Stanford University, U.S.A. In 1984 he joined DKFZ, where he has led the Division of Developmental Immunology since 2004.

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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