

Dragnet Search for Cancer Genes

Research team to identify previously unknown genes that are relevant for signaling in leukemia and other types of cancer

Cancer is often caused by defects in the information pathways that regulate cell division. **Dr. Michael Boutros**, head of the Boveri group "Signaling and Functional Genomics" of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ), jointly with a team headed by **Dr. Martin Zeidler**, Department of Molecular Developmental Biology of the Max Planck Institute for Biophysical Chemistry in Göttingen, Germany, has investigated a signaling pathway called JAK/STAT, which plays an important role in leukemias and lymphomas. In doing so, they found a number of previously unknown genes and proteins that may become interesting for cancer treatment and diagnosis. The investigators were using the RNA interference method, which is the first to allow simultaneous investigation of all signaling cascade components across the whole genome. Their results will be published in the latest issue of the journal *Nature** of August 11, 2005.

Using the RNA interference method, the researchers have discovered genes coding for four known and 86 uncharacterized proteins. These include several genes that play a role in the development of leukemias. The researchers synthesized about 20,000 artificial RNA copies that can be used to block over 90 percent of gene activity in *Drosophila*. Thereby, they searched specifically for genes that positively or negatively regulate components of the JAK/STAT pathway. Since this method does not yet work genomewide in human cells, the scientists studied the genome of the fruit fly *Drosophila*. The JAK/STAT signaling pathway has been highly conserved in the evolution from fruit fly to man. Therefore, signaling cascades in fruit fly and man have similar structures. In a next step, Boutros and his team are planning to characterize some of the newly identified components molecular-biologically and biochemically in order to investigate their function in human cells.

JAK is short for "Janus Tyrosine Kinase"; JAKs are enzymes that switch on transcription factors in the nucleus, which, in turn, regulate the activity of genes. STAT (signal transducer and activator of transcription) is a transcription factor that influences genes which regulate cell division or differentiation.

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**Patrick Müller, David Kuttenkeuler, Viola Gesellchen, Martin P. Zeidler and Michael Boutros:
"Identification of novel JAK/STAT signalling components by genome-wide RNAi", Nature, August 11, 2005*

The task of the Deutsches Krebsforschungszentrum in Heidelberg (German Cancer Research Center, DKFZ) is to systematically investigate the mechanisms of cancer development and to identify cancer risk factors. The results of this basic research are expected to lead to new approaches in the prevention, diagnosis and treatment of cancer. The Center is financed to 90 percent by the Federal Ministry of Education and Research and to 10 percent by the State of Baden-Wuerttemberg. It is a member of the Helmholtz Association of National Research Centers (Helmholtz-Gemeinschaft Deutscher Forschungszentren e.V., HGF).

This press release is available at www.dkfz.de/pressemitteilungen

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