GERMAN CANCER RESEARCH CENTER
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Inventory of Genes

Scientists at DKFZ screen fruit fly genome for cancer-relevant genes

Dr. Michael Boutros of the Deutsches Krebsforschungszentrum (German Cancer Research Center, DKFZ) and an international team of collaborators have been the first to screen an almost complete genome for genes that could play a role in cancer. The results have been published in the latest issue of the journal Science. Most cancers are linked to changes in the genetic material. As a result, the affected cells multiply uninhibited or cannot be killed by the immune system. Now that the sequence of the human genome has been almost completely deciphered, the next key challenge is to uncover the role of each individual gene. Based on these findings cancer researchers are hoping to be able to develop new therapies. For their investigation, Boutros and his colleagues used blood cells of the fruit fly Drosophila, a model organism that particularly lends itself to genetic studies.

Using advanced high-throughput techniques the researchers analyzed the function of almost 20,000 different genes. In the process, they identified more than 400 genes that are needed for cell proliferation and survival – key criteria for tumor development. Among those were numerous genes whose relatives in the human genome are involved in cancer. For example, mutations in the AML1 gene have been implicated in acute myeloid leukemia. While screening the Drosophila genome, the researchers discovered that the fruit fly counterpart of AML1 has a function in cell survival. Their findings support the hypothesis that a mutated AML1 gene prevents the cell from activating its natural program of self-destruction. Once cells start to multiply in an uncontrolled fashion, they become transformed into malignant tumor cells. Boutros, who heads the Boveri-Group “Signaling and Functional Genomics” at DKFZ, used a method called RNA interference, or RNAi, to selectively analyze the functions of individual genes. Scientists first selected from a database the sequence of information building blocks of all genes to be investigated. Based on this pattern artificial RNA copies are produced for each gene. The tailored RNA molecules are then applied to cells where they silence their natural gene counterparts. If, as a result, cells die or stop dividing, then the investigators know that the respective gene must play an important role in cell survival or proliferation. Since the method does not yet work genome-wide in human cells, researchers are using model organisms such as the fruit fly.

The more insights scientists get into the molecular basis of cancer, the more apparent it becomes that it is rarely based on changes in a few individual genes. Rather, several small steps together cause the complex interactions of genes and gene products to fail, ultimately leading to the transformation of a cell. According to Boutros, the next logical step after deciphering the genome is a systematic investigation of gene functions. “The aim is to produce a kind of map,” he explained. “Most of the 25,000 to 30,000 human genes are already marked on this map. As a next step, we have to decipher the street names, that means to understand the genes’ tasks and interactions.” Boutros and his group are also working on methods to use RNAi screening in human cells. This might allow, for example, to systematically determine the function of genes in tumor cells and compare them in different types of cancer.

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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.).

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

Dr. Julia Rautenstrauch
Division of Press and Public Relations
Deutsches Krebsforschungszentrum
Im Neuenheimer Feld 280
D-69120 Heidelberg
T: +49 6221 42 2854
F: +49 6221 42 2968