

## DNA packaging controls access to genetic information

**The genetic information in the nucleus is found packaged into nucleosomes for the most part. The position of these structures influences which genes are active and which are not. Scientists at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have now been the first to determine the positioning of all nucleosomes in the genome of embryonic stem cells and to compare it with further developed cells. The scientists will investigate whether position changing of nucleosomes is linked to the development of cancer.**

The DNA molecule of a single cell, if stretched out, is a thread of about two meters in length. In order to fit into the nucleus, which is only six micrometers in size, the DNA thread is wrapped around regularly spaced packaging proteins. These structures of DNA and protein are called nucleosomes. The downside of this packaging is that genetic information becomes almost inaccessible in these places and is therefore more difficult to read. The stretches between nucleosomes, however, are free and thus more easily accessible. Hence, the arrangement of nucleosomes tells us a lot about a cell's genetic program.

The DKFZ Research Group "Genome Organization and Function" led by Associate Professor (PD) Dr. Karsten Rippe has systematically studied the positioning of nucleosomes. Using the most advanced DNA sequencing methods, the group mapped the positioning of all nucleosomes in the genome of embryonic stem cells. For each cell, this amounts to almost 30 million nucleosomes. As expected, they found genetic information that was not needed in a packaged state. By contrast, frequently read genes were usually free of such structures.

The investigators aimed to find out how the arrangement of nucleosomes in embryonic stem cells changes as they further develop into other cell types. Even though the genetic information remains the same in all cells, completely different genes may have to be read depending on a cell's specialization. To study this question, the group compared embryonic stem cells with cells that were later to develop into skin and brain cells. "To do this, we analyzed about two billion nucleosomes," Karsten Rippe explains. "We have found out that the way they are arranged has completely changed in further developed cells. For example, the distance between individual nucleosomes has grown."

Just how the nucleosomes are shifted back and forth along the DNA is a question which remains to be answered in detail. However, the study shows that this process plays an important role in cell development. Errors occurring in the process might also be responsible for diseases such as cancer. In the German "CancerEpiSys" research network, the scientists are currently studying cancer cells of leukemia patients. One of the goals of this research effort is to produce a nucleosome profile of these cells. The researchers are hoping to draw conclusions about which type of cancer goes along with which changes in the organization of nucleosomes.

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A picture for this press release is available at:

[www.dkfz.de/de/presse/pressemitteilungen/2012/images/nucleosome\\_chain\\_binding.jpg](http://www.dkfz.de/de/presse/pressemitteilungen/2012/images/nucleosome_chain_binding.jpg)

Chain of nucleosomes with a protein binding to the linker DNA between two nucleosomes.

Source: Gernot Längst, University of Regensburg

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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