DEUTSCHES KREBSFORSCHUNGSZENTRUM IN DER HELMHOLTZ-GEMEINSCHAFT

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DNA Defects and Cancer –
Repair or Fatal Damage?

The DNA, the carrier of hereditary information in our cells, is permanently faced with attacks: by environmental influences such as UV radiation, X-rays and gamma radiation, or by aggressive oxygen radicals which are a product of metabolic processes in our own bodies. This often results in damages in the hereditary material, which may trigger aging processes or cause cancer. Scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) are now studying the molecular mechanisms underlying these processes. The Baden-Württemberg State Foundation (Landesstiftung Baden-Württemberg) will support the research project with funds of 750,000 euros over the next three years.

Our body has a number of repair systems which prevent that damages in the DNA lead to mutations, i.e., permanent changes in the hereditary information. Such repair systems help to recognize and eliminate damages. Depending on the size of the damage, different programs are activated: In a first step affected cells are “neutralized” in the sense that they are prevented from dividing and, thus, from multiplying their defective DNA. Minor defects are repaired, while programmed cell death (apoptosis) or the cell aging program (senescence) is started in cells with irreparable damages. As a result, the cells die or permanently lose their ability to divide.

The organism’s responses to damages in the DNA are based on a complex network of signaling chains. If it is not functioning properly, this can result in cancer or premature aging (progeria). Dr. Thomas Hofmann’s research project at DKFZ aims to identify the molecular events which cause cell death or cell aging after DNA damages.

“The HIPK2 enzyme plays a central role in these processes,” Hofmann explains. While the enzyme is silent in healthy cells, it becomes active when there are irreparable DNA damages and sends affected cells into death. Cancer treatment also makes use of these processes: Radiation therapy and chemotherapy are intended to cause so much damage to the DNA of tumor cells that eventually the natural cell death program is initiated and causes the tumor cells to die. “The next step for us is to find the precise mechanisms that cause HIPK2 to become active,” Hofmann continues. “This might provide new approaches for cancer treatment if we can deliberately activate the enzyme so as to cause tumor cells to commit suicide.”

The Baden-Württemberg State Foundation (Landesstiftung Baden-Württemberg) has already funded some of Hofmann’s previous projects and will provide funds amounting to 750,000 euros over the next three years for research into “The role of DNA repair response in aging and cancer”.

A picture showing Dr. Thomas Hofmann at work in the laboratory is available at:
http://www.dkfz.de/de/presse/pressemitteilungen/2009/images/Hofmann_1.jpg