GERMAN CANCER RESEARCH CENTER
IN THE HELMHOLTZ ASSOCIATION

No. 56 Ocotber 18, 2005 (Koh)

A Boost for Radiation Therapy

Does a combination of radiation therapy and the inhibition of integrins (key molecules in angiogenesis) improve the chance of cure in cancer?

An increasing number of cancer patients are cured today by radiation therapy – alone or in combination with surgery or chemotherapy. At the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ), scientists of the Clinical Cooperation Unit "Radiation Oncology" headed by **Professor Dr. Dr. Peter Huber** are identifying ways to further enhance the effectiveness of this type of treatment. The research team is targeting a weak point of the tumor: the formation of new blood vessels, or angiogenesis.

Once a tumor has reached pinhead size, it needs a supply of blood by blood vessels. If this supply is cut off, tumor growth comes to a halt. To suppress the formation of new blood vessels, integrins are a suitable target. This protein family comprises about 20 members that are involved in cell-cell interaction and regulate contacts with the surrounding protein matrix. Integrins play a key role in the formation of new blood vessels.

The Heidelberg researchers have now tested a combination of radiotherapy and a drug named S247, a substance which specifically inhibits the function of integrins. Investigations in the culture dish have shown that the combination therapy is considerably more effective both against tumor cells and against blood vessel-forming endothelial cells than irradiation alone. The combination approach has also been tested in mice with transplanted human tumors (glioblastoma, skin and prostate cancer). In these experiments, the combined treatment slowed down tumor growth – with no noticeable toxicity – more than twice as much as either of the therapies alone. In addition, tumors in animals treated by the combination approach formed significantly less blood vessels.

The Heidelberg researchers were able to show that the synergistic effect of the combination treatment can be ascribed to the fact that integrin inhibition neutralizes the angiogenesis-promoting effect of radiation. As a survival strategy, endothelial cells respond to radiation by increasing their integrin production. This promotes their invasion of the tumor tissue. The S247 substance counteracts this effect, while at the same time promoting programmed cell of endothelial cells.

The researchers are now working to define the optimum time period between administration of the drug and irradiation. In a next step, they will carry out clinical studies to investigate whether integrin inhibitors also enhance the chances of cure in patients treated for cancer.

Amir Abdollahi et al: Inhibition of $\alpha_v\beta_3$ Integrin Survival Signaling Enhances Antiangiogenic and Antitumor Effects of Radiotherapy. Clin Cancer Research 11:6270, 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.).

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