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Triple Approach Is Promising Against Cancer Cells

A trimodal treatment strategy combining chemotherapy, radiation therapy, and a protein kinase inhibitor is much more effective against cancer cells than any combination of only two treatment methods. This is the result of a preclinical study* performed by PD **Dr. Dr. Peter E. Huber**, head of the clinical cooperation unit "Radiation Oncology" at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ), jointly with investigators at Heidelberg University Hospitals. The study, which is the first to investigate trimodal cancer therapy, has revealed very promising results in cell studies and animal model experiments.

Today, a dual therapy combining simultaneous or sequential chemotherapy and radiation is the standard treatment for many tumors. Heidelberg researchers have now added an inhibitor studied only in preclinical trials so far. The inhibitor targets a number of protein kinases in blood-vessel-lining cells. Proteinkinases are enzymes that participate in signal transduction processes and, thus, in the control of cell growth. Inhibiting these enzymes prevents a process called angiogenesis, i.e., the formation of new blood vessels to supply a tumor with blood. Envisioning the future, Huber said: "From a clinical perspective, protein kinase inhibitors may be used as broad-spectrum medications for many types of cancer in therapy combinations."

The novel triple approach has proven clearly superior to dual strategies in tests both in human skin cancer cells and in mice injected with the same skin cancer cells. Thus, the trimodal combined therapy was more effective in inhibiting the multiplication of cancer cells *in vitro* and triggered the suicide program in more vessel lining cells than any combination of two treatments. In addition, the treatment significantly slowed down tumor growth in mice and also led to less invasion of tumor cells into neighboring muscle tissue.

The research team of DKFZ and Heidelberg University Hospitals also compared different treatment sequences of the trimodal approach. The investigations revealed that radiotherapy is more effective against a tumor following prior antiangiogenic therapy, because this prevents a growth-promoting effect of radiation therapy on blood vessels. According to Huber, the triple combination of chemotherapy, radiation, and antiangiogenesis effected by a protein kinase inhibitor has substantial potential in cancer treatment. The superiority of the triple therapy combination revealed in this preclinical study will be verified in 2006 in a clinical trial including between 20 and 30 patients with pancreatic cancer at Heidelberg University Hospitals. "It is very well possible that the trimodal therapy will take the place of the traditional dual treatment strategy for many types of cancer such as lung cancer or malignant brain tumors," said Huber.

* Peter E. Huber, Marc Bischof, Jürgen Jenne, Sabine Heiland, Peter Peschke, Rainer Saffrich, Hermann-Josef Gröne, Jürgen Debus, Kenneth E. Lipson, and Amir Abdollahi: "Trimodal Cancer Treatment: Beneficial Effects of Combined Antiangiogenesis, Radiation, and Chemotherapy". Cancer Research, Vol. 65, No. 9, pp 3643-3655, May 1, 2005.

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