GERMAN CANCER RESEARCH CENTER
IN THE HELMHOLTZ ASSOCIATION

9 January, 2013 (Sel)

Scientists Generate Oncolytic Viruses for Targeted Attack on Cancer Stem Cells

Researchers from the Paul Ehrlich Institute (PEI) have been the first to generate oncolytic viruses which specifically infect and kill CD133-positive cancer stem cells. Using such viruses, scientists at the German Cancer Research Center (DKFZ) and the National Center for Tumor Diseases (NCT) Heidelberg were able to substantially reduce tumor growth in cell cultures and in an animal model. Cancer Research reports on these research results in its online edition of January 4, 2013.

Tumors are usually not made up of a homogenous cell population whose cells all respond with the same sensitivity to different types of therapy. Instead, many tumor types are suspected to contain cancer stem cells, which usually respond poorly to chemotherapy and radiotherapy and are considered to be responsible for metastasis. Scientists are therefore trying to find ways of identifying and eliminating such cells, which are also known as tumor-initiating cells.

The cell surface protein CD133 is a candidate being discussed as a characteristic marker for such cancer stem cells. Researchers led by Professor Christian Buchholz at the Paul Ehrlich Institute in Langen modified a weakened and thus harmless measles virus, which is used as a vaccine, for targeted attack on cancer stem cells. The modified virus needs the CD133 surface protein as a receptor to penetrate the cell. The researchers were able to prove in mixed cell cultures that the modified virus infects only cells with this surface protein.

In collaboration with research groups led by Professor Hanno Glimm of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) and the National Center for Tumor Diseases (NCT) and by Professor Christel Herold-Mende at Heidelberg University, the scientists then tested the antitumor effect of their targeted virus using mouse models for glioma, colon cancer, and liver cancer. “The modified virus showed pronounced antitumor activity in all animal models tested. Tumor growth was substantially reduced or even entirely suppressed in individual cases,” Hanno Glimm reports. The scientists compared the effectiveness of their modified oncolytic measles virus with that of an oncolytic measles virus with no specificity for tumor cell subtypes, which is currently being tested in clinical trials. "We were surprised that the antitumor effect of the CD133-specific virus was at least as good as that of the standard virus. In the liver cancer model, it was even clearly superior and led to complete tumor remission", said Professor Buchholz. The scientists will pursue further research to find out why their targeted viruses turned out to be more effective in fighting tumors than conventional oncolytic viruses, which are supposed to attack all tumor cell subtypes.

Does the attack on CD133-positive cells really target only cancer cells? After all, this surface marker is not only found on cancer stem cells, but also on hematopoetic stem cells. Nevertheless, the oncolytic measles virus did not attack these cells. This is due to their innate immunity, which protects them from measles viruses. This immunity is defective in many tumor cell types so that the virus is able to replicate unchecked.

Use of these oncolytic viruses in cancer treatment would also profit from their booster effect. An infected cell produces new virus particles which spread upon the cell’s lysis and can infect more tumor cells.

Original publication: Bach P, Abel T, Hoffmann C, Gal Z, Braun G, Voelker I, Ball CR, Johnston ICD, Lauer UM, Herold-Mende C, Mühlebach MD, Glimm H, and Buchholz CJ:

Specific elimination of CD133+ tumor cells with targeted oncolytic measles virus (doi: 10.1158/0008-5472)

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. The staff of the Cancer Information Service (KID) offers information about the widespread disease of cancer for patients, their families, and the general public. 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. In the German Consortium for Translational Cancer Research (DKTK), one of six German Centers for Health Research, DKFZ maintains translational centers at seven university partnering sites. Combining excellent university hospitals with high-profile research at a Helmholtz Center is an important contribution to improving the chances of cancer patients. DKFZ is a member of the Helmholtz Association of National Research Centers, with ninety percent of its funding coming from the German Federal Ministry of Education and Research and the remaining ten percent from the State of Baden-Württemberg.

Dr. Stefanie Seltmann
Head of Press and Public Relations
German Cancer Research Center
Im Neuenheimer Feld 280
D-69120 Heidelberg
T: +49 6221 42 2854
F: +49 6221 42 2968