

Making cell division impossible: Optimized substance forces cancer cells into death

Many tumor cells have a defective cellular equipment. It is only by a special trick that they manage to distribute their chromosomes correctly to their daughter cells during cell division. Scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have now developed a substance that thwarts this trick and forces cancer cells into death during cell division. The group has now reported their results in the journal *Cancer Research*.

When normal cells divide, the chromosomes, i.e. the genetic material, are distributed evenly to exactly two daughter cells. This process is regulated by two polar bodies, or centrosomes. When cell division begins, they are located at the opposite poles of the cell and they start forming protein fibers to each chromosome. These are then each pulled under tension to one of the poles and, thus, distributed evenly to the two newly forming daughter cells. Cancer cells often have too many centrosomes. This should normally make it impossible for them to divide correctly and, as a result, lead to their death, but most of them have developed a trick to escape this fate: They form clusters of polar bodies at two poles.

“We already discovered this clustering as a potential target for cancer treatment a couple of years ago,” says Professor Alwin Krämer, head of DKFZ’s Clinical Cooperation Unit Molecular Hematology/Oncology. Conducting further research, the scientists found out that the antibiotic griseofulvin prevents clustering.

Professor Alwin Krämer and Dr. Marc S. Raab, head of the Max Eder Junior Research Group “Experimental Therapies for Hematologic Malignancies”, collaborating with an international research team, have now been able to optimize this substance for use in cancer treatment. Project partners included scientists of Heidelberg University Hospitals. “The optimized agent GF-15 reduces the tension of the protein fibers and thus prevents clustering. As a result, cell division proceeds in a chaotic manner and this eventually leads to the death of the cancer cell,” Raab explains. His junior research group is supported by the German Cancer Aid (Deutsche Krebshilfe).

The investigators first tested the novel inhibitor in the culture dish. The substance was effective in various cell lines derived from such different types of cancer as colon cancer, cervical cancer, brain tumors, and blood cancer. In normal cells, however, GF-15 did not show any effect. The group then tested the substance in mice with colon cancer or cancer of the bone marrow. The treated animals survived significantly longer than the untreated ones and they showed no serious side effects. “GF-15 has more favorable pharmacological properties than the original griseofulvin. It is more specific and more effective,” Krämer explains. Further tests will show whether GF-15 can really be further developed into an effective anti-cancer drug.

Raab MS, Breitzkreutz I, Anderhub S, Ronnest MH, Leber B, Larsen TO, Weiz L, Konotop G, Hayden PJ, Podar K, Fruehauf J, Nissen F, Mier W, Haberkorn U, Ho AD, Goldschmidt H, Anderson KC, Clausen MH, Krämer A. GF-15, a novel inhibitor of centrosomal clustering, suppresses tumor cell growth in vitro and in vivo. *Cancer Research*, 31. August 2012, doi:10.1158/0008-5472.CAN-12-2026

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.

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
presse@dkfz.de