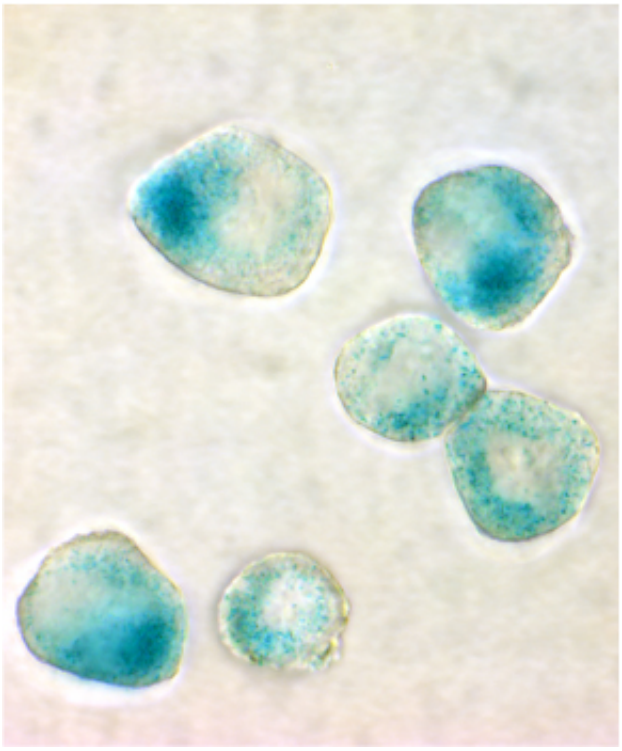
New therapeutic approach to fight cancer discovered

September 4 2013



Seneszenz-typisch blau angefärbte Tumorzellen eines Lymphdrüsenkrebses nach Chemotherapie.

Resting cancer cells can be selectively destroyed by inhibiting their energy metabolism. This is the recent discovery by researchers at Charité Universitätsmedizin Berlin and the Max Delbrück Center for Molecular Medicine (MDC) in Berlin-Buch, together with other cooperation partners from Germany. The findings of their study have been published

in the scientific journal *Nature*.

Chemotherapy does not kill all cancer cells, but instead, some cells enter a state known as senescence (programmed growth arrest). While in this state, the tumor cells are inactive and no longer divide. Nevertheless, senescence comes with hidden dangers. For instance, senescent cells produce protein messenger substances that can cause harmful inflammatory reactions. Moreover, senescent cells may pose a risk of cancer recurrence. Researchers working around Prof. Dr. Clemens Schmitt, Director of the Center for Molecular Cancer Research and Executive Supervising Medical Doctor at the Department of Hematology, Oncology and Tumor Immunology at the Charité, have now discovered a way to target senescent cancer cells for destruction.

"We have demonstrated a major increase in energy metabolism in senescent tumor cells after chemotherapy, and that the cells truly crave for sugar," explains Prof. Schmitt. "Moreover, we could show that these cells not only produce more energy, but are dependent upon their major increase in metabolism," he added. When the researchers inhibited sugar metabolism in the cells, they died off. By contrast, short-term inhibition of energy metabolism has little effect on resting or dividing cells in normal tissues. The researchers regard the cause for the high energy consumption in senescent cells as representing another unique feature: the moment the cells enter the state of senescence, they produce large quantities of protein messenger substances. These substances must then be digested, a highly energy-consuming process, since some of the proteins are toxic. Thus, if either energy production in the senescent cells or their digestive processes is blocked, they cannot survive.

"What is unique about this research study is the new understanding of a potential target structure for treating malignant diseases: as a rule, current and very promising so called "targeted" agents specifically inhibit the activity of an altered molecule that is present in cancer cells,"

explains Prof. Schmitt. Contrary to this, the researchers with their new therapeutic approach are proposing to use a cancer-specific state, i.e. cellular senescence resulting from chemotherapy, as the therapeutic target of a downstream metabolic therapy to destroy tumor cells, and not just a single molecule. "This represents a highly promising research approach at the interface between preclinical research and clinical trials," states Schmitt. "The idea behind our approach could be very relevant in future strategies for treating cancer patients; in view of this clinical potential, we are currently conducting further investigations," he adds.

In addition, the oncologist emphasizes the interdisciplinary character of the research findings, primarily developed in Berlin, and says, "This important study has been made possible by the excellent research landscape in Berlin and the close collaboration between transnational clinical researchers from the Charité with primary scientists from the MDC – brought even closer together in the newly founded "Berlin Institute of Health."

More information: Dorr, J. et al. Synthetic lethal metabolic targeting of cellular senescence in cancer therapy, *Nature*, 2013 Aug 14. DOI: 10.1038/nature12437

Provided by Charité - Universitätsmedizin Berlin