Effective Cancer Immune Therapy Through Order in the Blood Vessels

Researchers at the German Cancer Research Center have discovered a key molecule that is responsible for the characteristic immature structure of blood vessels in malignant tumors. If this molecule is switched off in mice, vessels normalize so that immune cells are better able to get to the tumor tissue from the bloodstream. This significantly increases the effectiveness of immune therapies and, thus, considerably enhances the survival time of treated animals.

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Immune cells have difficulty entering the cancer tissue

Immune therapies are considered very promising in cancer medicine: Tumor-fighting immune cells are supposed to invade tumor tissue and eliminate cancer cells right there. Although this works well in the test tube, clinical application often fails because immune cells are unable to get into the tumor tissue from the bloodstream in sufficient numbers.

This is due, among other things, to the 'chaotic' tumor vasculature: To get supplied with nutrients, a tumor stimulates the formation of new vessels. However, the architecture of these newly formed blood vessels differs from the normal one; they are poorly organized and regarded as immature. Therefore, in many tumors, immune cells have difficulty entering the cancer tissue. Studies show, however, that patients survive longer when immune cells are able to invade the tumor.

Key molecule identified

In an article published in Nature, scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) and Heidelberg University Hospitals, jointly with Australian researchers, have now described a key molecule that is responsible for the immature state of the tumor vasculature. In mice suffering from cancer whose gene encoding the Rgs5 signal protein is switched off, the investigators observed a normalization of blood vessels in the tumor. Tumor-specifically activated immune cells that were transplanted into these animals were found to colonize the cancer tissue in large numbers. In contrast, in mice with normal Rgs5 status, there is no significant invasion of immune cells into the tumor.

Survival rates clearly showed the success of the immune therapy: While some of the Rgs5-deficient animals were still alive after 48 weeks into the investigation, all animals with normal Rgs5 formation had died from cancer after 35 weeks at the latest. Vaccination with tumor-specific proteins also resulted in improved survival times of Rgs5-deficient mice, while it showed no effect in control animals.

"We were surprised that a gene that apparently affects vascular structure has such a strong influence on the success of immune therapies. Rgs5 is, thus, a completely new, promising target structure for clinical tumor therapy," says DKFZ's Professor Günter Hämmerling, one of the scientists leading the study. "But we don't necessarily have to knock out Rgs5 to improve the success of immune therapies. Available therapeutics that normalize tumor vasculature should also increase the invasion of immune cells into tumor tissue."

Literatur:

Juliana Hamzah, Manfred Jugold, Fabian Kiessling, Paul Rigby, Mitali Manzur, Hugo H. Marti, Tamer Rabie, Sylvia Kaden, Hermann-Josef Gröne, Günter J. Hämmerling, Bernd Arnold und Ruth Ganss: Vascular normalization in Rgs5-deficient tumours promotes immune destruction. Nature 2008, DOI: 10.1038/nature06868

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