Researchers study effect of immune tolerance on certain cancer risks

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For a malignant tumor to form, cancer cells must evade the immune system's attack. Numerous studies have already shown that cancer spreads particularly aggressively if there is an unfavorable balance between suppressing and active immune cells in the tumor microenvironment. "But we didn't know whether this is a consequence of an aggressive tumor or rather its cause," says Rudolf Kaaks, epidemiologist at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ).

Kaaks and his co-workers had a unique opportunity to pursue this question: The DKFZ in Heidelberg is one of the study centers of the EPIC study, which investigates the links between diet and cancer in almost half a million people in the whole of Europe. In the initial EPIC examinations from 1996 to 1998, blood samples were taken from all study participants and subsequently frozen. From the 25,000 participants in Heidelberg, the researchers now picked the blood samples from about 1,000 individuals who had developed cancer in the course of the observation period (lung cancer, colon cancer, breast cancer, and prostate cancer). Their control group consisted of 800 participants who were not affected by a malignancy.

Sebastian Dietmar Barth and his colleagues from Kaak's department counted the suppressing regulatory T cells in the blood samples and determined the ratio of these cells to the total number of T cells, which also comprises the tumor-fighting cells. This ratio is called "immunoCRIT". As a rule, it holds true that the higher it is, the more the immune system is suppressed.

When comparing the cancer risk of EPIC participants with extremely high or extremely low immunoCRIT, the researchers found that if the value is strongly increased, the lung cancer risk rises by 100 percent, and the risk of colon cancer by approximately 60 percent. Women with very high immunoCRIT even have a triple increase in their risk of developing estrogen-receptor negative breast cancer. Here, however, the researchers think that for a definite statement the case number might be too low. In cases of prostate cancer and estrogen-receptor positive breast cancer, the DKFZ epidemiologists found no links between immunoCRIT and cancer risk.

When the tumor-fighting T cells are kept in check by inhibitory regulatory T cells, scientists speak of "peripheral immune tolerance". "With this study, we have demonstrated for the first time that the unfavorable ratio of immune cells already prevailed long before the onset of the disease," Kaaks says. "Hence it is more likely to be the cause than the result of cancer."

The DKFZ researchers conducted this study in collaboration with Epiontis, a Berlin-based company that specializes in the epigenetic tests that were used to determine the ratio of the various T cell populations.

The scientists do not yet know why immune tolerance has an effect on certain cancer risks. A possible explanation may be that, according to prior research findings, tumors of the lung and bowel tend to be colonized by particularly high quantities of immune cells. The Heidelberg epidemiologists now plan to extend their investigation to other types of tumor.

Source:
German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ)
