Prostate cancer: saturated fats favor the progression of metastases

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A preclinical study shows that saturated fats in the diet stimulate prostate cancer cells and can contribute to the formation of incurable metastases.

In North America, one man out of six will develop a prostate cancer, which makes this cancer the most frequently diagnosed in our society. Fortunately, these cancers generally evolve very slowly and do not represent a major cause of death in the short term: for example, one study has shown that only 16% of Americans diagnosed with a prostate cancer between 1961 and 2008 had died as a consequence of this disease[1]. In other words, even after a diagnosis of prostate cancer, men were more at risk of dying from other chronic diseases associated with aging (cardiovascular diseases, diabetes) than from cancer.

FATAL METASTASES

The situation is, however, much less optimistic when the prostate cancer becomes aggressive and forms metastases. In these patients, existing therapeutic treatments do not allow us to counter the progression of the cancer and the disease is invariably fatal.

The incidence of metastatic prostate cancers is much more elevated in Occidental countries than in Asian countries, which suggests that certain factors associated with lifestyle contribute to the aggressiveness of prostate cancer. Amongst these, several observations have suggested that the Western diet, characterized by an elevated consumption of foods rich in fat (such as *fast food*)[2] could represent one of these factors. For example, the incidence of this cancer is multiplied 20-fold when Japanese people migrate from Japan to the West, with the drastic change in lifestyle and diet associated with this migration.

PRODUCTION OF FAT

This hypothesis has just been substantiated by the results of a preclinical study performed by a group of scientists at Harvard University[2]. Genetic profiles of samples from localized prostate cancers (non-invasive) were compared to those taken from invasive, metastatic cancers. It was found that the majority of metastases had lost two genes known to prevent the growth of tumors, named PTEN and PML. These genetic losses seem likely to be crucial for the progression of prostate cancer to metastases because analysis of prostate tissues removed from patients show a tight correlation between the absence of these two genes and death caused by metastases from the prostate.

An unexpected consequence of the loss of these two genes was a strong increase in the production of fats by the cancer cells. The research group found that the prostate cancer cells lacking PTEN and PML were characterized by a hyperactivation of lipid metabolism, most notably by a significant increase in the production of saturated fats. These fats are involved in the progression of prostate cancers because addition of an inhibitor of lipid synthesis (fatostatin) drastically diminished the formation of metastases in preclinical models.

TUMORS WHICH FEED ON FATS

This participation of saturated fats in the progression of prostate cancer to metastases does not seem to be limited to fats produced by the cancer cells themselves. By using transgenic mice in which the PTEN and PML genes had been eliminated, the authors of the study found that prostate tumors formed fewer metastases when the animals consumed their normal diet, weak in fats and composed principally of plants. On the other hand, when lard (a rich source of saturated fats) was added to their diet, they found that the cancer cells accumulated large quantities of saturated fats and that this accumulation was correlated with a marked increase in the number of metastases. In other words, the presence of large quantities of saturated fats in the diet acts as a sort of "trigger" which promotes aggressiveness in prostate cancer cells and induces the formation of metastases.

For men who have already developed a less invasive prostate cancer, a diet low in saturated fats, such as by limiting the consumption of industrially processed foods, could prevent the evolution of the cancer into metastases and thus avoid their dying prematurely as a result of this disease.

(1) Epstein, MM et al. Temporal trends in cause of death among Swedish and US men with prostate cancer. J. Natl. Cancer Inst. 2012;104:1335-1342.

(2) Chen M et al. An aberrant SREBP-dependent lipogenic program promotes metastatic prostate cancer. Nature Genet. 2018;50:206-218.

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