Starving Cancer

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A fascinating recent study suggests that a dietary intake reduced in one single amino acid, methionine, decreases the growth of colorectal tumors and improves their response to anti-cancer treatments.

A fundamental characteristic of cancerous cells is their ability to grow indefinitely. This uncontrolled growth requires a constant intake of energy and it is for this reason that cancer cells have a metabolism that is different from that of normal cells.

Theoretically it should thus be possible to prevent, or to at least impede, the growth of cancer by depriving the cancer cells of nutrients that are essential to their abnormal metabolism, an approach known as "metabolic therapy".

THE CASE OF SUGAR

When one considers the metabolism of cancer, one thinks immediately of sugar because it is undeniable that cancer cells exhibit a sugar metabolism that is clearly accelerated compared to that observed in normal cells (known as the Warburg effect).

Under certain very specific circumstances, it has been shown that restricting sugar (by use of a ketogenic diet, for example) effectively improves the response to certain classes of anticancer agents (PI3K inhibitors)[1]. However, just because the cancer consumes much sugar doesn't mean that providing less sugar will necessarily slow its growth, as was generally thought: other studies have shown that such a sensitivity to the presence of sugar is not observed in many types of cancer cells and is in reality quite rare. There must thus exist other metabolic pathways which permit tumors to sustain their uncontrolled growth.

A QUESTION OF AMINO ACIDS

Over the past few years, several studies have shown that the absence of certain amino acids (the precursors to proteins) in the diet, e.g. glycine, serine, methionine or even asparagine, can affect the growth of many types of cancers.

One of the more interesting cases is that of methionine, an amino acid containing an atom of sulfur which plays several fundamental roles in the control of metabolism and in the synthesis of constituents of DNA. This importance can also be seen by the fact that certain front-line anticancer treatments, such as 5-fluorouracil (5-FU) or even radiotherapy, produce their effects by targeting the metabolic pathways involving methionine, suggesting that a lack of this amino acid could disrupt the growth of tumors.

The results of a recent study appearing in the prestigious journal *Nature* run along these lines. By using animal models bearing colorectal tumors resistant to both chemotherapy and radiotherapy, the researchers observed that a diet low in methionine was associated with a marked diminution in the growth of these tumors and an increase in the therapeutic response to 5-FU and to radiation. These effects were correlated with a very rapid drop (less than 2 days) in methionine levels in blood, which deprives cancer cells of this important amino acid and

makes them more susceptible to the anticancer treatments. The normal cells themselves have the ability to recycle methionine and are thus less sensitive to a decrease in its dietary supply.

It is still too early to know if this restriction in the supply of methionine could improve the therapeutic response to cancer, but the preliminary results are encouraging. In a pilot study performed in parallel on men in good health, the authors showed that a diminution in dietary methionine did not cause any notable secondary effects. It is also interesting to note that it is quite possible to achieve these low levels of methionine by adopting a diet principally composed of foods of plant origin.

This is because methionine is principally found in foods of animal origins such as meat and dairy products, whereas fruits, vegetables and beans contain much less methionine[3].

There is much work remaining to be done on this topic, but these results allow us to foresee that in the medium term it will be possible to recommend that people being treated for cancer adopt certain diets specifically designed to maximize the therapeutic response and to improve their probability of survival.

(1) Hopkins BD et al. Suppression of insulin feedback enhances the efficacy of PI3K inhibitors Nature 2018; 560: 499–503.
(2) Gao X et al. Dietary methionine influences therapy in mouse cancer models and alters human metabolism. Nature 2019; 572: 397-401.
(3) Ables GP and JE Johnson. Pleiotropic responses to methionine restriction. Exp. Gerontol. 2017; 94: 83-88.
(4)

Food	Methionine Content (mg/100g)
Beef	680
Poultry	610
Veal, lamb and game	600
Seafood	590
Pork	575
Dairy products, eggs	410
Nuts and grains	320
Beans	200
Flour and pasta	160
Vegetables	40
Fruits	10

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