

Dietary fiber improves the effectiveness of cancer immunotherapy

Richard Béliveau

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A study shows that the consumption of dietary fiber is associated with better survival in patients with metastatic melanoma who are treated with immunotherapy.

IMMUNE AWAKENING

As its name suggests, cancer immunotherapy is based on the destruction of tumors by stimulating the immune system. It has long been known that in several types of tumors, cancer cells create an immunosuppressive climate that paralyzes killer lymphocytes (white blood cells) and prevents them from attacking.

The discovery that certain antibodies could eliminate this paralysis and thus awaken the immune cells to enable them to eliminate cancerous cells therefore represented a major advance in the effective treatment of certain cancers, a discovery that was also rewarded with the Nobel Prize of Medicine, awarded in 2018 to Drs James Allison and Tasuku Honjo. A fully deserved distinction, because immunotherapy has made it possible to obtain a spectacular increase in the survival of certain patients suffering from very aggressive and advanced cancers which were previously considered incurable, in particular metastatic melanomas (1).

INVOLVEMENT OF THE GUT MICROBIOME

Despite the resounding successes of immunotherapy, it was soon noted that the therapeutic effectiveness of this approach could vary considerably from one patient to another. The numerous studies that have looked into this question have shown that the intestinal microbiome (the hundreds of billions of commensal bacteria present in the intestine) plays a major role in these inter-individual variations (2).

This contribution of the microbiome is biologically plausible, since it is well established that a diverse microbiome generates several compounds (short-chain fatty acids, for example) that improve the effectiveness of the immune system.

Since the composition of the microbiome is strongly influenced by factors associated with lifestyle, in particular the nature of the diet, it would therefore be possible to optimize the effectiveness of immunotherapy by adopting a diet that promotes implantation of friendly bacteria, which exert a positive influence on immunity.

FIBER ON THE MENU

Dietary fibers are the main ingredient of food origin capable of modifying the microbiome and, by extension, immunity: the fermentation of these fibers by intestinal bacteria allows the establishment of a varied bacterial flora, consisting of species that produce anti-inflammatory compounds influencing the immune system.



This immune modulation associated with fiber consumption seems to influence the efficacy of immunotherapy: by comparing the fiber intake of patients with metastatic melanoma who were treated with immune checkpoint inhibitors (the most common form of immunotherapy), American researchers observed that those who consumed a minimum of 20 g of fiber per day responded better to treatment (longer progression-free survival) than those who consumed less (3).

Importantly, however, this improvement in efficacy is not observed in patients who consume probiotic supplements, a strategy often used by cancer patients to improve gut health: on the contrary, the study shows that these supplements impair the efficacy of immunotherapy and slightly decrease patient survival.

This suggests that the large diversity of bacterial populations (several hundred) generated by the diversified diet is greater than the increase in a single bacterial population, caused by taking supplements.

These observations were confirmed using animal models with metastatic melanoma treated with immunotherapy: again, here, a fiber deficiency or the administration of probiotic supplements reduced the response to therapy as well as life expectancy, possibly due to a lower recruitment of killer T cells to the tumor microenvironment.

Overall, these results suggest that higher fiber intake is associated with establishment of a more diverse gut microbiome and improved tumor response to immunotherapy. Although this association remains to be better characterized, a diet rich in dietary fiber (vegetables, whole grains, and legumes) seems to represent a very interesting strategy for patients treated with these drugs and who seek to increase their probability of survival. The use of probiotic supplements cannot, however, be advised, as these do not appear to offer any improvement in survival and may even interfere with treatments.

- (1) Ribas A and JD Wolchok. Cancer immunotherapy using checkpoint blockade. *Science* 2018 ; 359 : 1350-1355.
- (2) Gopalakrishnan V et al. Gut microbiome modulates response to anti-PD-1 immunotherapy in melanoma patients. *Science* 2018 ; 359 : 97-103.
- (3) Spencer CN et al. Dietary fiber and probiotics influence the gut microbiome and melanoma immunotherapy response. *Science* 2021 ; 374 : 1632-1640.