The molecular basis of the anticancer activity of green tea

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A fascinating study reported in the prestigious Nature Communications shows that the main polyphenol in green tea, EGCG, interacts directly with the most important tumor suppressor gene p53 and increases its anticancer activity.

A multitude of population studies have shown that regular consumption of green tea is associated with a reduced risk of developing several types of cancer, in particular those of the breast, lungs, prostate and colon.

Most of these chemopreventive effects of green tea are attributed to its high content of polyphenols, particularly epigallocatechin-3-gallate (EGCG), which can reach 200 to 300 mg in a single cup of green tea. This catechin is well absorbed and reaches sufficient plasma concentrations to interfere with several processes involved in tumor progression, including the formation of a network of new blood vessels by tumors (angiogenesis), as has been reported (1).

GUARDIAN OF THE GENOME

According to recent research, low concentrations of EGCG, easily attained by regular consumption of green tea, may block cancer progression by specifically targeting the tumor suppressor p53 (2). P53 is often called the "guardian of the genome" because of its crucial role in detecting and eliminating damaged cells, whether because of attacks from toxic molecules, the presence of errors that creep in spontaneously in DNA or the activation of oncogenes. To prevent these abnormal cells from becoming cancerous, p53 sets in motion a sophisticated control system that will attempt to repair the cellular damage that has been detected or, if the damage is irreversible, force the cells to cause their own death by cell suicide (apoptosis). To become cancerous, abnormal cells often have to find a way to bypass this quality control system, and it is for this reason that the presence of an inactivated p53 protein is a very common phenomenon observed in more than half of human cancers. The importance of this protein is further illustrated by Li-Fraumeni syndrome, a rare genetic disorder involving this gene where patients are almost 100% likely to develop several types of cancer over their lifetime.

PREVENT THE DEGRADATION OF p53

A strategy often employed by cancer cells to inactivate p53 is to overexpress a protein (MDM2) that interacts with this tumor suppressor and causes its degradation. From a therapeutic point of view, one of the ways to restore the anticancer action of p53 is therefore to find molecules capable of preventing this p53-MDM2 interaction.

And this is exactly where EGCG might come in handy: Using a technique that allows the interaction between proteins to be studied in detail (NMR spectroscopy), the researchers demonstrated that EGCG specifically binds to the same region of the p53 protein as that used by MDM2. By preventing the binding of this protein to p53, EGCG therefore prevents the degradation of the tumor suppressor and stabilizes its anticancer function. Under the anticancer effect of green tea observed in population studies, there is a very strong molecular basis that goes far beyond the simple correlation of facts.

This study therefore represents another example of the multiple benefits associated with the regular consumption of plants, such as green tea, which contain high amounts of polyphenols. Including these foods in our eating habits, especially when part of an overall healthy lifestyle that includes no smoking, regular physical activity, and maintaining a healthy body weight, is the best current strategy to prevent cancer.

(1) Lamy S. et al. Green tea catechins inhibit vascular endothelial growth factor receptor phosphorylation, Cancer Res. 2002; 62:381-385.

(2) Zhao J. et al. EGCG binds intrinsically disordered N-terminal domain of p53 and disrupts p53-MDM2 interaction, Nat. Commun. 2021; 12:986.

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