Cabbages Which Block Tumor Growth

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A preclinical study reports that a compound found in large quantities within cruciferous vegetables, indole-3-carbinol, is able to slow tumor growth by reactivating certain suppressor genes in tumors.

CURBING CELL GROWTH

The uncontrolled growth of cancer cells is caused by two phenomena which are genetically distinct but complementary. The first of these is the appearance of mutations in certain genes (oncogenes) which activate the pathways involved in cellular reproduction, a bit like how stepping on the accelerator causes the car to move forward more quickly. In parallel, the cancerous cell should also eliminate certain genes called tumor suppressors which act like brakes and keep the growth of cells at a normal level.

The inactivation of tumor suppressors is particularly important for the development of cancer because elimination of this brake maximizes the effects of the oncogenes on cell growth: to make a simple analogy, even if the accelerator of a vehicle is pressed to the floor, the vehicle cannot go forward unless the brakes are released! Loss of function for tumor suppressors is thus an extremely common event in the development and progression of cancer: one recent analysis of DNA from over 2000 human tumors which had reached the metastatic stage showed that nearly all of them had mutations in each of the two copies of the 5 principal tumor suppressor genes (TP53, CDKN2A, APC, PTEN and RB1)[1]. This suggests that biallelic inactivation (mutations in both versions, each inherited from one of our parents) of tumor suppressors is an essential prerequisite for the formation of metastases.

CRUCIFEROUS VEGETABLES TO THE RESCUE

A very large number of studies have shown that regular consumption of cruciferous vegetables (cabbage, broccoli, turnip, watercress and arugula) is associated with a reduced risk for developing many types of cancers. These protective effects are due to certain molecules found exclusively in these vegetables, particularly the isothiocyanates such as sulforaphane or indole-3-carbinol (I3C), which affect some processes involved in tumoral progression (detoxification of carcinogens, reduction of oxidative stress and inflammation, halting the growth of cancerous cells).

One recent study suggested that I3C could also play an anti-cancerous role by preventing inactivation of the important tumor suppressor PTEN[2]. In normal cells, this protein is present at the cell surface where it acts like a brake to prevent certain pathways involved in cellular growth (phosphoinositide 3-kinase-AKT) from excess activation. To overcome this interference, many types of cancerous cells must thus inactivate this protein, either by eliminating a copy of the gene or by blocking its function as a growth suppressor by preventing it from reaching the surface of the cell.

In an article recently published in the prestigious journal *Science*, researchers showed that the absence of PTEN from the surface of cells was due to the action of an enzyme (WPP1) which modifies its structure and prevents it from being recruited to the surface[2]. Even more interesting, the authors found that I3C is capable of strongly inhibiting this enzyme, which thus prevents the inactivation of PTEN, allowing the suppressor to reach the membrane and thus block the growth of cancerous cells. In other words, I3C can reverse this important tumor suppressor's inactivation, which is essential for the progression of some cancers, thus contributing to the chemoprotective benefits well documented for cruciferous vegetables in studies done with human subjects.

(1) Priestley P et al. Pan-cancer whole-genome analyses of metastatic solid tumours. Nature, 2019; 575(7781):210–216.

(2) Lee YR et al. Reactivation of PTEN tumor suppressor for cancer treatment through inhibition of a MYC-WWP1 inhibitory pathway. Science 2019; 364(6441):eaau0159.

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