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Sulforaphane halts breast cancer cell growth

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Sulforaphane (SUL), a plant chemical found in cruciferous vegetables including broccoli, sprouts and kale, is one of nature's wonder compounds. Discovered more than a decade ago, it's a potent inducer of protective enzymes that provide defense against cancer-causing chemicals. Now, Keith Singletary and doctoral student Steven Jackson of the University of Illinois at Urbana-Champaign (http://www.uiuc.edu/index.html) have discovered that SUL can also halt human breast cancer cells in their tracks and identified a new mechanism of action for the compound [1].

Potent phytochemical

'SUL is the most active compound from cruciferous vegetables shown to have anticancer properties in animals,' says Thomas Kensler, a toxicologist at Johns Hopkins University. 'The phytochemical works by inducing upregulation of a series of genes, known as phase II genes, encoding mostly enzymes shown to be protective against reactive oxygen speices and electrophiles,' explains physician scientist, Paul Talalay, at Johns Hopkins University School of Medicine (http://www.hopkinsmedicine.org/som), who first isolated SUL from broccoli in the early 1990s.

It was already known that SUL could prevent normal cells from becoming cancerous, says Singletary. But now, he says 'there is more interest in how SUL and similar compounds can prevent proliferation of cells that are already cancerous.'

Halting cancer cell proliferation

To test this, Singletary and Jackson exposed malignant breast cancer cells in culture to SUL. Within hours, they discovered that the compound could halt human breast cancer cell proliferation by interfering with microtubule assembly, necessary for cell division. They then showed that SUL inhibited tubulin polymerization after exposing purified tubulin to the compound.

'What's intriguing about what we found is that not only does it slow down proliferation, but it also disrupts polymerization of microtubules,' says Singletary. It is a mechanism of action shared by current cancer therapies including Taxol.

In cell culture, they showed that sulforaphane blocked cells in the prometaphase stage and disrupted chromosome segregation in breast cancer cells. 'The chromosomes were separating inappropriately due to disruption in the mitotic spindles,' he says. However, 'in a living cell, there are many more aspects by which SUL could be affecting microtubule dynamics.'

Cancer prevention and vegetable intake

How their findings translate into human cancer prevention remains to be seen, he cautions. 'In humans, the relationship between crucible vegetable intake and subsequent bioavailability of SUL and other isothiocyanates is not well characterized. It needs to be better studied to extrapolate our findings.'

The link between cruciferous vegetable consumption and reducing cancer risk has been around for more than a decade, says Kensler. However, 'we don't know what levels we can achieve in mammary glands in women, so this may or may not be a relevant mechanism in the context of women eating diets rich in cruciferous vegetables,' he adds.

'It's a very interesting study, significant in terms of revealing a new mechanism of action in its antiproliferative activity against human cancer cells' says Yuesheng Zhang, a scientist at Roswell Park Cancer Institute in Buffalo, New York (http://www.roswellpark.org) who first isolated sulforaphane with Paul Talalay at Johns Hopkins University. 'These studies suggest that sulforaphane has the potential to become an anti-cancer agent in the future.'

Sulforaphane as anti-cancer agent

Simultaneously, Marilyn Morris and colleagues also at the University of Buffalo report the anti-proliferative effects of SUL and related compounds on normal and breast cancer cells, comparing their activity with the cancer therapeutic drugs daunomycin and vinblastine [2]. They found that higher concentrations of SUL were required to inhibit cell proliferation compared with the drugs in normal and cancer cells, and were higher than those found in plasma after ingesting cruciferous vegetables. Although increased dietary intake might be beneficial, she concludes, 'our findings suggest a potential use of these compounds as chemotherapeutic agents in cancer treatment.'

References

1 Jackson, S.J. and Singletary, K.W. (2004) Sulforaphane inhibits human mcf-7 mammary cancer cell mitotic progression and tubulin polymerization. *J. Nutr.* 134, 2229–2236

2 Tseng, E. *et al.* (2004) Dietary organic isothiocyanates are cytotoxic in human breast cancer MCF-7 and mammary epithelial MCF-12A cell lines. *Exp. Biol. Med.* 229, 835–842

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