Chemopreventive isothiocyanates selectively depletes mutant p53 in tumor cells

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Researchers at Lombardi Comprehensive Cancer Center at Georgetown University Medical Center have demonstrated that naturally-occurring compounds can selectively deplete mutant p53 and restore "wild type" function to p53 in a variety of tumor cells.

Mutations in the p53 tumor suppressor gene - which is involved in apoptosis and DNA repair - occur in about half of all human tumors. p53 often acts as a checkpoint preventing abnormal cells from continuing to grow and divide. However mutations in p53 gene are one way that pre-cancerous cells overcome normal cellular controls and replicate without restraint.

This study demonstrates for the first time that phenethyl isothiocyante (PEITC), a naturally-occurring compound, can selectively deplete mutant p53. The authors also made an intriguing observation that the depletion of mutant p53 in human cancer cells is accompanied by restoration of the wild type p53. PEITC is a member of the isothiocyanate family compounds found in cruciferous vegetables, such as watercress, broccoli and cabbage. PEITC has been shown to have cancer preventive activity.

The researchers found that PEITC not only decreases the level of mutated p53 protein in tumor cells, but also restores the "wild type" or normal activity to mutated p53. The effect of this is that tumor cell lines with mutant p53 became more sensitive to PEITC-induced cytotoxicity than tumor cells with wild type p53, suggesting that the normal p53

checkpoint control pathways have been restored in the mutant p53-expressing tumor cells. This novel finding suggests that the PEITC and other compounds in the isothiocyante family could play important role in both cancer prevention and treatment of human cancers with mutant p53.

Source: Georgetown University Medical Center (news : web)