Selective Depletion of Mutant p53 by Cancer Chemopreventive Isothiocyanates and Their Structure Activity Relationships.

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Isothiocyanates (ITCs) derived from cruciferous vegetables induce apoptosis in cancer cells. We demonstrate that certain naturally occurring ITCs selectively deplete mutant p53 but not the wild-type and do so via a transcription-independent mechanism. Direct p53 binding followed by conformational changes appears to be a mechanism by which mutant p53 is depleted. Structure-activity relationship studies (SARs) using naturally occurring and synthetic ITCs show that depletion is influenced by the ITC side-chain moiety. Furthermore, we show that cells with p53 mutations are more sensitive to Cytotoxicity induced by Phenethyl isothiocyanate (PEITC) than those with the wild-type protein. 2,2-Diphenylethyl ITC, a synthetic ITC, is one of the most potent depletors of mutant p53 studies and induces apoptosis to the greatest extent in mutant p53 breast cancer cells. Collectively, this study shows that mutant p53 depletion may be an important novel target for cancer chemoprevention and therapy by natural and synthetic ITCs.

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