Category: Quality Improvement Research

**Molecular Mechanisms of Cancer Prevention by Plant Flavone Apigenin**

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Bioactive molecules of plant origin play an important role in disease prevention. Several of them are potent cancer preventive/therapeutic agents. Apigenin (4′,5,7-trihydroxyflavone) a plant flavone, widely distributed in common vegetables and fruits has been identified as a potent anticancer molecule. Epidemiological and case control studies support the finding that flavone intake decreases the risk of several malignancies including prostate cancer. Maspin (SERPINB5), a unique member of the serpin (serine protease inhibitor) family controls cell motility, invasion and tumor metastasis. Loss of maspin has been frequently identified in clinical specimens and prostate cancer cell lines. Ongoing research in our laboratory has unraveled pathways affected by apigenin contributing to cancer preventive properties. Here we focused our research on how apigenin restores maspin expression in prostate cancer cells. Immunohistochemical analysis on benign and cancer specimens revealed progressive loss of maspin which correlated with Gleason score. Suppression of histone deacetylation along with p53 activation and its binding to maspin promoter on p53 consensus-binding site restored maspin expression. Exposure of human prostate cancer LNCaP and 22Rv1 cells, harboring wild-type p53, with 5-20μM of apigenin resulted in dose-dependent increase in maspin expression and p53 activation through acetylation of Lys305 residue by inhibiting class I HDACs. Apigenin-mediated increase in p53 acetylation enhanced its binding on maspin promoter, causing a decrease in tumor cell invasion and migration. Apigenin also caused accumulation of acetylated histone H3 in total cellular chromatin, increasing p53 accessibility to bind with the promoter sequences of maspin, consistent with the effects elicited by HDAC inhibitor. Similar observations were noted after feeding apigenin at 20- and 50-µg/day to 22Rv1 tumor xenograft implanted in nude mice. Our results demonstrate that loss of maspin is due to upregulation of class I HDACs and that apigenin-mediated increase in maspin is regulated, in part, by p53 activation in prostate cancer.