

**Title** Broccoli consumption interferes with prostate cancer progression: mechanisms of action  
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### **Abstract**

Epidemiological studies suggest that people who consume more than one portion of broccoli per week are at lower risk of both the incidence of prostate cancer and developing aggressive extraprostatic prostate cancer, and this is modulated by *GSTM1* genotype. In order to determine the mechanistic basis of chemoprotection by broccoli in vivo, we quantified with microarrays changes in global gene expression within prostate biopsies obtained from volunteers diagnosed with high-grade prostatic intraepithelial neoplasia (HGPIN), a condition that is considered pre malignant. Firstly, we found significant differences in expression profiles between *GSTM1* positive and null individuals who had been on the broccoli-rich diet for six months, but no differences in expression between *GSTM1* genotypes that had been on the pea-rich diet. These differences were associated with TGF $\beta$ 1 and EGF signalling pathways. Secondly, through comparison of sequential biopsy samples, we found more changes in gene expression had occurred in individuals on a broccoli-rich diet than in those on a pea-rich diet, and these changes were associated with mRNA processing, TGF $\beta$ 1 signalling, EGF signalling and insulin signalling. In this manner, low levels of dietary isothiocyanates can have profound effects on signalling pathways associated with inflammation and carcinogenesis providing for the first time in vivo a mechanistic explanation for chemoprotection of broccoli.