

P012 Sp3-mediated up-regulation of BAK effects butyrate-mediated apoptosis

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There is strong epidemiological evidence to suggest that dietary fibre acts as a chemopreventive for colorectal cancer. Animal studies suggest that this may be through production of butyrate in the colon, which may trigger apoptosis, or sensitize epithelial cells to damage.

We have analysed the mechanisms by which butyrate triggers apoptosis. Our data show pro-apoptotic concentrations of butyrate trigger up-regulation of bak protein and no change in Bax. Butyrate-mediated apoptosis is dependent upon protein synthesis, implying up-regulation of Bak may be a key event.

We have analysed the Bak promoter by nested deletion and identified an 8bp region responsible for gene activity. Analysis of the region by EMSA suggests it is an Sp1/Sp3 binding site. Comparison of EMSA with untreated nuclear extract and butyrate-treated nuclear extract indicates that increase in Sp3 binding rather than Sp1 is mediating response to butyrate. Use of pan-anti-acetyl lysine antibody in EMSA assay suggests the increased binding may be through acetylation of Sp3.