

P019 The importance of colonic butyrate transport to maintenance of tissue homeostasis.

Kristian Daly, Mark Cuff, Francis Fung, Soraya Shirazi-Beechey
University of Liverpool

Butyrate, a product of microbial fermentation of dietary fibre is known to regulate a number of genes involved in proliferation, differentiation and apoptosis of colonic epithelial cells, suggesting that butyrate may be protective against the onset of colorectal cancer. We used microarray analysis to assess the expression levels of 19,400 genes in HT29 human colon carcinoma cells treated with butyrate compared to untreated controls and have identified approximately 200 butyrate-responsive genes specifically involved in maintaining tissue homeostasis.

Furthermore, using real-time PCR, the butyrate response of a number of selected genes was quantitatively assessed in three different human colonic cell lines (HT29, HCT116 & AA/C1). We have previously shown that the colonic luminal membrane butyrate transporter, MCT1, is down-regulated in colon cancer tissues compared to normal controls, resulting in a reduction in the levels of intracellular butyrate, and that silencing of MCT1 expression in colonic cell lines, using siRNA, abrogates the butyrate-induced response of several key genes. In colon cancer tissue, in which MCT1 expression is significantly downregulated, we show that the expression of selected butyrate-responsive genes involved in the processes of proliferation, differentiation and apoptosis are also deregulated contributing to the genetic changes that characterize the adenoma-carcinoma sequence, and suggesting the importance of MCT1 and butyrate availability to the prevention of colorectal cancer.