We were very interested to read the papers by Gibson et al. (1999) and the ENDO project group (Van Loo et al. 1999) in the February issue of the British Journal of Nutrition. They give a useful introduction to the field and list over a dozen different potential health advantages of altered gut bacteriology. When we last attempted to prepare a list of physiological actions of fermentable substrates on the hindgut we gave up after thirty. One of these actions, which was not mentioned in the two papers, was the stimulation of cell proliferation in the intestinal mucosa by the production of short-chain fatty acids (SCFA). There is substantial confusion on the actions of the SCFA, as in vitro studies have shown them to be powerful stimulators of differentiation and apoptosis; however, in vivo they are clearly powerful mitogens (Goodlad et al. 1989), moreover there is poor evidence for pro-apoptotic effects in vivo. The implications of this significant proliferative effect are as yet still unclear, but increased proliferation is traditionally regarded as a potential risk factor in the development of carcinogenesis (Wasan et al. 1996). Fermentation in the colon also has other biological–cellular actions on the process of crypt fission (McCullough et al. 1998), which we have implicated as a critical event in the initiation–development of colorectal carcinogenesis (Wasan et al. 1997).

It would appear that this consensus paper is somewhat biased towards the positive evidence, and one must be clearly aware that most clinical dietary interventions have not had the intended beneficial outcomes. This is especially worth stressing in light of the unanticipated results of most of the randomized human β-carotene studies, vitamins C and E and fibre-polyp prevention studies. In these human clinical trials, either no benefits were seen or, more worryingly, detrimental, (i.e. pro-carcinogenic) effects were observed, which led to the early closure of some of the studies (ATBC, 1994). Thus no prospective human clinical study has ever confirmed the purported theoretical benefits. Indeed, worryingly, a fair proportion of dietary fibre studies in animals have also shown pro-carcinogenic effects (Hill et al. 1996).

A further complication may be that the addition of fermentable substrate supplements to a ‘Western’ diet may result in a feast or famine pattern of fermentation (McBurney et al. 1987) in which there are sudden surges in bacteriological activity followed by a lack of substrate, in which case the colonic flora must either ferment each other (cannibalism) or the colonic epithelial mucosa and mucins.

We therefore agree with the ENDO group that there is a great need for more in-depth research, but would caution against over enthusiasm in instigating human trials based on the currently available scientific data.

**References**


