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Anti-neoplastic effects of non-digestible carbohydrates on WNT signalling in the bowel: a randomised controlled dietary intervention

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Colorectal cancer (CRC) is the third most common cancer in the UK. The majority of CRC cases develop sporadically[(1)], and the WNT signalling pathway is implicated in the aetiology of both sporadic and inherited forms[(2)]. Environmental factors, including diet, modify CRC risk and non-digestible carbohydrates (NDCs), such as dietary fibre and resistant starch (RS), appear to be protective[(3)]. These beneficial effects are believed to result from the production of butyrate, a short-chain fatty acid, by colonic bacteria and evidence exists for the modulation of WNT signalling by butyrate. This study aimed to investigate the effects of supplementing healthy participants with NDCs on WNT-related gene expression and its functional outcomes in the bowel. It is hypothesised that increasing NDC intake will increase colonic butyrate concentrations and modulate WNT signalling.

75 healthy participants were recruited as part of the DISC Study and supplemented with RS and/or polydextrose or placebo for 7 weeks in a 2*2 factorial design. Rectal mucosal biopsies were collected pre- and post-intervention. RNA was extracted from OCT-embedded biopsies and reverse transcribed to cDNA for the quantification of *CCND1*, *MYC* and *SFRP1* expression in duplicate by quantitative PCR.

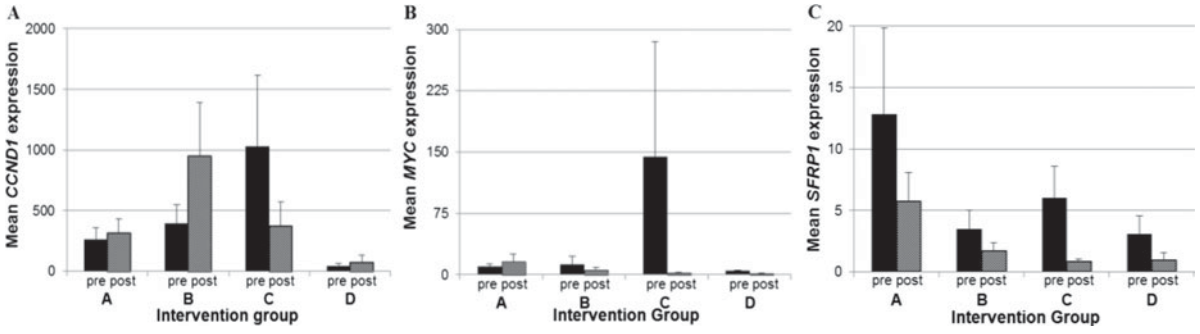

Fig. 1. Mean expression of *CCND1* (A), *MYC* (B) and *SFRP1* (C), expressed as adjusted copies ($2^{-\Delta Ct} \times 1000$) relative to the *18S* housekeeping gene ($n = 36$).

Preliminary results ($n = 36$) indicate differences in the expression of *CCND1*, *MYC* and *SFRP1* post-intervention for all four groups (Fig. 1). No statistically significant differences in baseline (pre-intervention) expression of *CCND1* ($P = 0.189$), *MYC* ($P = 0.447$) or *SFRP1* ($P = 0.338$) between the intervention groups were observed following analysis using the ANOVA General Linear Model. This study will be un-blinded in May to determine if any effects of NDC supplementation on WNT-related gene expression exist. In addition, effects of the intervention on proliferation and apoptosis, two functional outcomes of WNT signalling that are deregulated in CRC, are currently being investigated.

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