

MicroRNA expression in the macroscopically-normal epithelium of people at differential risk of colorectal cancer

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Colorectal cancer (CRC) is the third most common cancer in the UK. The majority of CRC cases are sporadic⁽¹⁾, and the presence of adenomatous polyps or ulcerative colitis (UC) increases CRC risk. In preparation for a study of the effects of a dietary intervention, the present study investigated the expression of 5 microRNAs (miRNAs) reported to be altered in CRC, involved in the WNT pathway and/or implicated in the inflammatory process in people at higher-risk of CRC.

Colorectal mucosal biopsies were collected from normal participants ($n = 10$), participants with quiescent UC ($n = 9$) and participants with prior history of adenomatous polyps ($n = 9$). RNA was extracted from formalin-fixed paraffin-embedded (FFPE) biopsies and reverse transcribed to synthesize cDNA used to quantify the expression of a panel of miRNAs: miR-101, miR-335, miR-122a, miR-135a and miR-145, in duplicate by quantitative PCR. Statistical analysis was performed using the ANOVA General Linear Model.

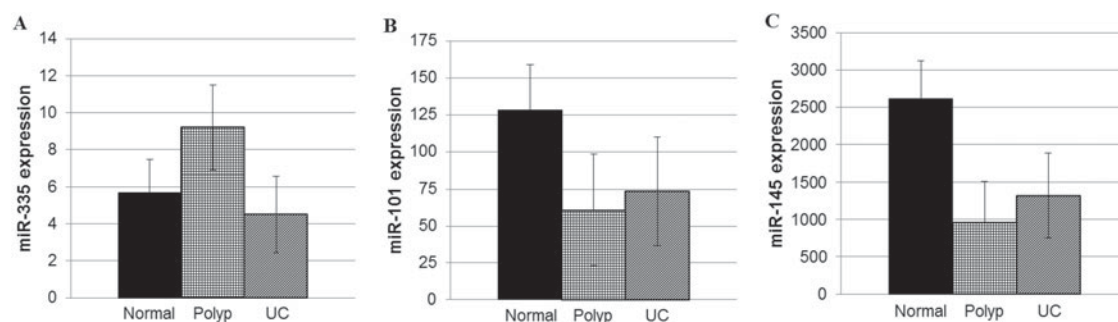


Fig. 1. Mean expression of miR-335 (A), miR-101 (B) and miR-145 (C), expressed as $2^{-\Delta Ct} \times 1000$ relative to the *SNORD68* control.

With relatively small participant numbers, no statistically significant differences were observed for the expression of the selected miRNAs between the 3 groups. However, miR-335 expression, frequently upregulated in CRC, appeared to be increased in polyp patients (Fig. 1A). Participants with UC, an inflammatory disease, appeared to have slightly reduced miR-335 expression, consistent with previous evidence that miR-335 is down-regulated by inflammatory cytokines⁽²⁾. In addition, miR-101 and miR-145, both down-regulated in CRC^(3,4), appeared to be reduced in higher-risk participants (Fig. 1B and C).

This study has quantified miRNA expression in FFPE tissue biopsies of normal colorectal mucosa and found evidence of potential differences in those at higher CRC risk. To investigate underlying mechanisms, the methodology developed in this study will be used to measure miRNA expression in healthy participants supplemented with non-digestible carbohydrates, thought to be protective against CRC.

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