Proceedings of the Nutrition Society (2015), **74 (OCE1)**, E46 doi:10.1017/S0029665115000610

Summer Meeting, 14–17 July 2014, Carbohydrates in health: friends or foes

Differences in the expression of microRNAs implicated in colorectal carcinogenesis and involved in the WNT signalling pathway in the macroscopically-normal epithelium of people at higher-risk of colorectal cancer

F. C. Malcomson[1], N. D. Willis[1], I. McCallum[1], L. Xie[1], S. Kelly[1], M. Bradburn[1], N. J. Belshaw[2], I. T. Johnson[2] and J. C. Mathers[1]

[1]*Human Nutrition Research Centre, Institute for Ageing and Health, Newcastle University, Newcastle upon Tyne NE4 5PL, UK and* [2]*Institute of Food Research, Norwich Research Park, Norfolk NR4 7UA, UK*

People with ulcerative colitis (UC) or adenomatous polyps (adenomas) are at increased risk of colorectal cancer (CRC)[1]. Altered expression of microRNAs (miRNAs), small non-coding RNAs that regulate gene expression post-transcriptionally, has been observed in those with UC[2] and adenomas[3]. Importantly, abnormally-expressed miRNAs contribute to the initiation and progression of CRC and are potential biomarkers for diagnosis and prognosis of this cancer[4]. This study aimed to investigate differences in the expression of a panel of miRNAs in the macroscopically-normal mucosa of people at higher-risk of CRC.

We quantified expression of 8 miRNAs that are (i) implicated in CRC, (ii) regulators of WNT signalling, a pathway frequently aberrantly activated in CRC[5], and/or (iii) whose expression is altered by butyrate treatment in healthy participants ($n = 56$) and in patients at higher CRC risk with quiescent UC ($n = 26$) or history of adenomatous polyps ($n = 12$). RNA was isolated from mucosal biopsies of macroscopically-normal tissue collected at 10 cm from the anal verge. cDNA was synthesised by reverse transcription and used to quantify the expression of *miR-17, miR-19a, miR-19b, miR-20a, miR-25, miR-93, miR-106b* and *miR-424* by quantitative PCR. For normally distributed data, the ANOVA General Linear Model was used to compare miRNA expression between the 3 risk groups, adjusting for age, sex and endoscopy procedure as covariates. Where data were not normally distributed, the non-parametric Kruskal-Wallis test was used.

Table 1. Median and range values for miRNA expression expressed as adjusted copies ($2^{-\Delta Ct} \times 1{,}000$) relative to the geometric mean of *RNU6* and *SNORD68* controls.

	Healthy Participants		Polyp Patients		UC Patients	
miRNA	Median	Range	Median	Range	Median	Range
miR-17	129	69–401	125	52–179	118	75–153
miR-19a	97	17–1728	156	19–751	89	29–464
miR-19b	69	15–3809	91	16–437	82	25–279
miR-20a	333*	107–1550	308*	152–424	279*	181–379
miR-25	116	13–9987	69	34–129	78	50–153
miR-93	77	10–1102	70	32–125	68	47–114
miR-106b	164	61–5548	162	77–242	144	109–180
miR-424	32**	9–1145	24**	7–50	69**	17–137

** $p < 0{\cdot}01$ and * $p < 0{\cdot}1$ for differences between risk groups (Kruskal-Wallis test).

We observed significantly higher *miR-424* expression ($p < 0{\cdot}01$), a miRNA reported to be increased in CRCs[6], and reduced *miR-20a* expression ($p = 0{\cdot}055$) in participants with quiescent UC (Table 1). *miR-20a* expression also appears to be reduced in polyp patients. Alterations in miRNA expression may be detected in the healthy tissue of people at higher-risk of CRC and may represent very early molecular changes contributing to the progression from normal mucosa to carcinoma.

This study was funded by the BBSRC (BB/H005013/1). Ethical approval for the study was granted on 10th December 2009 (REC No. 09/H0907/77).

1. Itzkowitz SH & Yio X (2004) *Am J Physiol Gastrointest Liver Physiol* **287**, G7–17.
2. Coskun M, Bjerrum JT, Seidelin JB (2012) *World J Gastroenterol* **18**, 4629–4634.
3. Oberg AL, French AJ, Sarver AL *et al.* (2011) *PLoS One* **6**, e20465.
4. Schetter AJ, Okayama H, Harris CC (2012) *Cancer J* **18**, 244–252.
5. Bienz M & Clevers H (2000) *Cell* **103**, 311–320.
6. Wang YX, Zhang XY, Zhang BF *et al.* (2013) *J Dig Dis* **11**, 50–54.