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The amelioration of western diet induced molecular changes in the colon by curcumin

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Colorectal cancer (CRC) is a third most commonly diagnosed cancer and fourth leading cause of cancer related mortality worldwide. Most CRC cases are sporadic with dietary factors strongly implicated in their development. Over-expression of the epidermal growth factor receptor (EGFR) pathway is associated with the development of multiple cancer types, including CRC. Activated EGFR initiates downstream signaling cascades that stimulate cell proliferation, migration and survival and inhibit apoptosis. Multiple studies have demonstrated that there is a strong association between western diet, EGFR over-expression and the tumorigenesis of CRC. The EGFR pathway itself is regulated via upstream targets such as C-X-C chemokine receptor 4 (CXCR4) and a disintegrin and metalloproteinase 17 (ADAM17) and are necessary for normal EGFR activation. ADAM17 is also upregulated in EGFR-overexpressing cancers. Curcumin, an active compound found in the spice turmeric, has demonstrated promising antiproliferative, anti-inflammatory, anti-neoplastic, and antioxidant properties in the colon and has been shown to suppress the growth of cancer cells in animal models and human cell line culture. The hypothesis of this study was that 100 mg/kg body weight of curcumin could prevent the molecular changes in the colon induced by a western diet. Using an established Wistar rat model of obesity, real time RT-PCR and Western immunoblotting analysis we demonstrated that a 16-week western diet significantly upregulated the expression of the ADAM17/EGFR pathway within the distal colon and this upregulation was prevented by supplementing the western diet with curcumin. This study provides new evidence to suggest that dietary curcumin may be used to prevent the overexpression of the ADAM17/EGFR pathway and potentially ameliorate diet-induced CRC.

Figure 1: Outline of ADAM17/EGFR pathway demonstrating targets involved in EGFR activation and downstream actions of the receptor.

Recent Publications

1. Bliss E and Whiteside E (2018) The gut-brain axis, the human gut microbiota and their integration in the development of obesity. Frontiers in Physiology 9:900.
2. Wanyonyi S, DuPreez R, Brown L, Paul N and Panchal S (2017) *Kappaphycus alvarezii* as a food supplement prevents diet-induced metabolic syndrome in rats. Nutrients 9(11):1261.
3. Seim I, Whiteside E, Chopin L, et al. (2016) Multi-species sequence comparison reveals conservation of ghrelin gene-derived splice variants encoding a truncated ghrelin peptide. Endocrine 52(3):609-617.

Biography

Amanda Dieckmann is a second year PhD student at the University of Southern Queensland. Her PhD project focuses on targeting early markers within the ADAM17/EGFR pathway to prevent the development of diet induced colorectal cancer. She was awarded with an Australian Research Council scholarship and her research is supported by a philanthropic donation from the Brazil Foundation. In addition to her research, she is also an Assistant Teacher in Human Anatomy and Physiology, Molecular Biology and Biomedical Science.

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