



# THE ROLE OF THE GASTRIN FAMILY IN THE DEVELOPMENT OF COLORECTAL CANCER

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Colorectal cancer (CRC) is the second most common cause of worldwide cancer mortality among men and women with an annual incidence of approximately 1 million cases and annual mortality of more than 500,000. Progastrin, the precursor of the classical hormone gastrin, has been shown to act as a growth factor for the colonic mucosa and to accelerate the development of colorectal cancers. However, neither the active region of the molecule nor the mechanisms of action are known. This project will involve the expression of a number of different progastrin-derived peptides as glutathione-S-transferase fusion proteins in *E. coli*, and their purification by reverse phase HPLC after cleavage of the fusion protein with thrombin. The study will further determine the biologic activity and the mechanism of action of these peptides.

We will also investigate the ability of these peptides to stimulate tumour growth in a number of mouse models of colorectal cancer and determine the effects of putative inhibitors. Transgenic mice lacking gastrin or gastrin receptors will be used as well. We can measure the concentration of the different gastrin peptides in the tumours and the circulation so the concentration of gastrin peptides will be determined in patients with colon cancers before and after removal of the tumour.

## Techniques:

- Recombinant peptides
- Proliferation assays
- Western blots
- Cell transfection
- RT-PCR
- Animal models of disease
- Transgenic mice
- Cell culture
- Radioimmunoassays and ELISA

## Publications:

Aly A, Shulkes A, Baldwin GS Gastrins, cholecystokinins and gastrointestinal cancers *Biochim Biophys Acta* 2004;1704:1-10.

Pannequin J, Kovac S, Tantiongco JP, Norton RS, Shulkes A, Barnham KJ, Baldwin GS. A novel effect of bismuth ions: Selective inhibition of the biological activity of glycine-extended gastrin. *J Biol Chem* 2004; 279:2453-2460.