



INTERACTION BETWEEN GASTRIN-RELEASING PEPTIDE AND ITS RECEPTOR

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Gastrin releasing peptide (GRP) has been identified as a mitogen involved in the progression of many cancers including colon, breast, and lung. GRP exerts its effect through the GRP receptor (GRP-R). We have shown that multiple form of GRP accelerate the progression of colon cancer in vivo and in vivo suggesting a potential role for GRP-R antagonists in the management of colorectal cancer. GRP-R belongs to the G-protein coupled 7 transmembrane receptor family. This study will characterize the amino acids within the GRP-R that are responsible for high affinity binding of GRP.

The study involves identifying conserved amino acids using sequence comparison tools. Using site directed mutagenesis conserved amino acids will be mutated and their effect on GRP binding investigated using radiolabelled GRP.

The effects of these mutations will then be tested on a range of receptor activation assays including inositol phosphates, calcium mobilisation, cell proliferation and migration. The outcome will be a better understanding of the mechanism of action of GRP which will form the basis for the development of high affinity antagonists.

Techniques:

- Cell culture
- Proliferation assays
- Radioimmunoassays and ELISA
- Receptor characterisation
- Western blots
- Recombinant peptides
- Cell transfections
- RT-PCR

Publications:

Patel, O., Shulkes, A. and Baldwin, G.S. Gastrin-releasing peptide. In: Cancer Encyclopedia, Ed M Schwab 2nd edition, Springer, Berlin, 2007

Patel O, Dumesny C, Giraud AS, Baldwin GS, Shulkes A Amidated and glycine-extended gastrin-releasing peptide stimulate proliferation and migration of a colorectal cancer cell line via the same receptor. *Biochem Pharmacol.* 2004;68:2129-42.

Oneel P, Dumesny C, Shulkes A, Baldwin GS C-terminal fragments of the gastrin-releasing peptide precursor stimulate cell proliferation via a novel receptor. *Endocrinology* 2007; 148:1330-9.