



ROLE OF GASTRIN-RELEASING PEPTIDE IN THE NORMAL AND DISEASED KIDNEY

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Renal cell cancer is a problematic cancer in that it is often detected late in the disease when the results of surgical management are poor. There is currently no effective radiotherapy or chemotherapy. Many cancers produce their own growth factors and receptors. Activation of the receptor by the growth factor further stimulates the tumour's growth and spread throughout the body. Gastrin Releasing Peptide (GRP) is an established growth factor in certain lung and bowel cancers but little is known about its role in tumours of the kidney. The objective of this project is to determine the potential roles of the growth factor GRP in kidney cancers (Renal Cell Carcinoma, RCC). We will determine the expression of GRP and its receptors in RCC, the ability of GRP to stimulate proliferation, and the potential of antagonists to modulate the growth of RCCs. The role of GRP in the developing and normal kidney will also be assessed using a variety of in vitro and in vivo models.

We will use cell culture of RCC, mice with kidney cancers (xenografts), and human resected RCC.

A successful outcome will determine whether a functional GRP autocrine and/or endocrine mitogenic loop is present in RCC. In the longer term, this project will provide the basis for the development of assays for the early diagnosis and monitoring of RCC and the potential for novel treatments such as proGRP/GRP receptor antagonists, radiolabeled proGRP/GRP analogues for radiotherapy and cytotoxic proGRP/GRP analogues for chemotherapy.

Techniques:

- Cell culture
- Proliferation assays
- RT-PCR
- Radioimmunoassays and ELISA
- FACS analysis
- Animal models of disease
- Cancer patient samples

Publications:

Dumesny C, Whitley JC, Baldwin GS, Giraud AS, Shulkes A Developmental expression and biological activity of gastrin-releasing peptide (GRP) and GRP receptors in the kidney *Am J Physiol.* 2004; 287:F578-85.

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.

Patel O, Shulkes A and Baldwin GS. Gastrin-Releasing Peptide and cancer. *Biochimica et Biophysica Acta-Reviews on Cancer* 2006; 1766:23-41.