



THE BIOLOGY OF GASTRIN-RELEASING PEPTIDE

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Gastrin Releasing Peptide (GRP) is a neuroendocrine growth factor. Previously we have shown that peptides derived from the carboxy terminal region of the GRP precursor (proGRP) stimulate proliferation and migration of colon, prostate and renal cancer cells. To elucidate the developmental role of proGRP-derived peptides *in vivo* we will generate global proGRP knock-out and conditional GRP knock-in mouse models. This study also involves the generation of tissue specific proGRP knock-out mice by breeding the parent strain with various Cre recombinase mice to understand the biological activity of proGRP in tissues.

The project also involves understanding the regulation of the GRP promoter. by using a luciferase reporter system to identify which transcription factor binding sites in the GRP promoter region are important for regulation of GRP mRNA transcription.

A third aim is to understand proGRP processing *in vivo*. This study involves transfecting neuroendocrine cells with a vector expressing proGRP. We plan to detect native proGRP-derived peptides with region-specific ELISA, and purify them by high pressure liquid chromatography to determine structures.

This project will provide an opportunity to determine the biology of GRP and other proGRP-derived peptides in normal tissue. Members of the GRP family of peptides are growth factors in a number of cancers such as lung and prostate, so these studies will have long-term significance in oncology and may provide the basis for the development of novel chemotherapy.

Techniques:

- Animal models of disease
- Immunohistochemistry
- Biochemical assays
- RT-PCR
- Molecular Biology

Publications:

Dumesny C, Patel O, Lachal S, Giraud AS, Baldwin GS, Shulkes A Synthesis, expression and biological activity of the prohormone for Gastrin Releasing Peptide (ProGRP). *Endocrinology* 2006; 147:502-9.

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

Patel O, Dumesny C, Shulkes A, Baldwin GS Recombinant C-Terminal fragments of the Gastrin-Releasing Peptide precursor are bioactive *Cancer Letters* 2007; 254:87-93.