



PROGASTRIN RELEASING PEPTIDE IN PROSTATE CANCER: RELATIONSHIP TO DISEASE PROGRESSION AND OUTCOME

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Prostate cancer is the most commonly diagnosed cancer in men. However, despite PSA testing to detect cancerous cells, currently no clinical or biological parameters can distinguish insignificant from potentially lethal prostate cancers.

Gastrin Releasing Peptide (GRP) is the prototypical neuroendocrine growth factor. GRP is a potent mitogen for carcinomas such as lung, colon, pancreas, medullary thyroid, breast and prostate. We have shown that this precursor gives rise to biologically active fragments that stimulate proliferation in colorectal and prostate cancer cell lines. There is also evidence that proGRP products may be the predominant form in tumour tissues such as prostate cancer. Our overall hypothesis is that regions of the proGRP molecule distinct from the region that produces GRP are biologically active in the prostate, are important in the development of prostate cancer, and may serve as a molecular biomarker in the diagnosis and therapy of prostate cancer.

A unique battery of assays will be used to measure different parts of the proGRP molecule. We will measure the circulating concentration of proGRP peptides in patients with prostate cancer, and in surgical patients before and after prostate cancer resection. We will also quantify and identify proGRP derived peptides produced by prostate cancer cell lines and resected tumours. The ultimate objective of this work is to develop an additional biomarker for prostate cancer that can be used in conjunction with the PSA.

Techniques:

- Cell culture
- Radioimmunoassays and ELISA
- Immunohistochemical staining
- Cancer patient samples

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.

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.

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