Ghrelin and hormone dependent cancer

L.K. Chopin, P.L. Jeffery, A. Yeh, J.F. McNamara, R. Wight, A.C. Herington, School of Life Sciences, QUT, Brisbane, Qld, Australia

Ghrelin, a 28 amino acid peptide hormone, was discovered by Kojima *et al*. in 1999 and has since been found to exert a wide range of biological effects. Evidence is rapidly emerging to suggest that ghrelin, like other members of the growth hormone (GH) axis, may be involved in growth and development. Ghrelin appears to play an autocrine/paracrine role in some cancers. Prostate and breast cancer cell lines express ghrelin and the growth hormone secretagogue receptor (GHSR) type 1a, the functional form of the receptor. GHSR1b, a truncated form of the receptor that is believed to be non-functional, is expressed in breast and prostate cancer cells, but not in normal breast or prostate tissue. This indicates that this form of the receptor could have functional or diagnostic significance in these cancers. Our studies have shown that ghrelin treatment stimulates cell proliferation in prostate and breast cancer cell lines. Prostate cancer cell lines secrete ghrelin and ghrelin stimulates cell proliferation through MAPK signalling pathways. The MDA-MB435 breast cancer cell line also proliferates in response to ghrelin treatment. We have described a new isoform of ghrelin, termed exon 4 deleted ghrelin, in which the mRNA lacks exon 4. This leads to the production of ghrelin and a novel C terminal peptide. This isoform is upregulated in cancer tissues and could stimulate cell proliferation in hormone dependent cancers. Our studies provide a basis for future studies into the potential of the ghrelin axis for the development of diagnostic markers or as a target for cancer therapies.