Expression and function of ghrelin and receptors in human endometrial cancer cell lines

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Purpose: Endometrial cancer is the most common malignant tumour in the female reproductive tract. This study has examined the expression and function of two new facets of the growth hormone axis, the growth hormone secretagogue receptor (GHS-R) and its endogenous ligand ghrelin, in endometrial cancer cells.

Methods: Four human endometrial cancer cell lines with different differentiation were used (Ishikawa, HEC1A, HEC1B and KLE). Ghrelin and its receptors GHS-R 1A and GHS-R 1b mRNA expression was detected by RT-PCR and quantified with qPCR by normalising to 18s rRNA. The protein expression of GHS-R1a was also detected by immuno-blotting with specific antibodies. Effect of ghrelin on endometrial cancer cell proliferation was determined by using the MTS dye method. Endometrial cancer cell lines were cultured in presence or absence of human n-octanoylated ghrelin at concentrations ranged from 0.1 to 1,000 nM for 24, 48 or 72 hours (n=3/time point).

Results: Ghrelin, GHS-R1a and GHS-R1b gene expression was detected in all cell lines. Quantification of mRNA level demonstrated that both receptor isoforms gene expression is highly and positively associated with the differentiation level of the cell lines. GHS-R1b gene expression of poorly differentiated KLE endometrial cancer cell line is 3.9-fold higher than that of well differentiated endometrial cancer cell line Ishikawa. Protein expression of GHS-R1a was detected in all four endometrial cancer cell lines. Ghrelin treatment significantly increased the cell proliferation of Ishikawa, HEC1B and KLE cell lines by 32%, 29% and 28% above untreated controls after 72 hours incubation.

Conclusion: This study demonstrates the expression of the GHS-R and ghrelin in endometrial cancer cell lines and circulating ghrelin may promote cancer cell proliferation.