**Molecular mechanisms regulating ECE-1 expression in prostate cancer**

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It is widely known that the mitogenic peptide endothelin-1 (ET-1) influences cancer invasion and metastasis. Plasma ET-1 levels are significantly elevated in men with metastatic prostate cancer (PC). ET-1 is also involved in the transition of hormonally regulated androgen-dependent disease to androgen-independent PC. ET-1 is produced from big ET-1 by endothelin-converting enzyme-1 (ECE-1), expression of which is upregulated in prostate cancer. In this study we examined the aberrant molecular regulation of ECE-1 expression in prostate cancer, focussing particularly on post-transcriptional regulation. We first utilised a reporter assay in which the 3' untranslated region (UTR), a region of the transcript commonly involved in post-transcriptional regulation, of ECE-1 was fused to the luciferase coding sequence and transfected into PC-3 prostate cancer cells. The full-length 3' UTR significantly decreased luciferase activity by 85% compared to empty vector. Whilst this decrease was greatest in PC-3 cells, it was also seen in normal prostate cells (RWPE1) and non-prostate cells (Huh7). We subsequently identified six ECE-1 transcripts with truncated 3' UTRs in PC-3 cells by 3'RACE analysis. The truncated UTRs generated greater luciferase activity than the full length UTR when utilised in a reporter assay. Furthermore, addition of the full length UTR to the ECE-1 coding region markedly suppressed ECE-1 protein expression when heterologously expressed in PC and non-PC cells suggesting that UTR truncation, a common feature of malignant cells, may result in increased ECE-1 expression in PC. Studies are ongoing to assess the role of factors which may interact with the ECE-1 3'UTR, such as microRNA, in the findings presented here. The identification of a key role for the 3'UTR in the regulation of ECE-1 expression may prove useful in the development of novel therapeutic strategies targeting the endothelin axis in prostate cancer. This work is supported by Yorkshire Cancer Research.