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HOTAIR is a REST-regulated lncRNA that promotes neuroendocrine differentiation in castration resistant prostate cancer

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Abstract

Long non-coding RNAs (lncRNAs) are emerging as novel diagnostic markers of prostate cancer (PCa) and new determinants of castration-resistant PCa (CRPC), an aggressive and metastatic form of PCa. In addition to androgen receptor (AR) signaling, neuroendocrine differentiation (NED) is associated with CRPC. Recent reports demonstrate that the downregulation of repressor element-1 silencing transcription factor (REST) protein is a key step in NED of PCa cells. Here, we report HOTAIR as a novel REST-repressed lncRNA that is upregulated in NED PCa cells and in CRPC. HOTAIR overexpression is sufficient to induce, whereas knockdown of HOTAIR suppressed NED of PCa cells. Gene ontology (GO) analysis of differentially expressed genes under HOTAIR overexpression and in CRPC versus benign prostatic hyperplasia (BPH) suggests that HOTAIR may participate in PCa progression. Taken together, our results provide the first evidence of lncRNA HOTAIR as a driver for NED of PCa cells.

1. LncRNA HOTAIR is a novel target of REST.
2. HOTAIR is upregulated in CRPC during progression.
3. HOTAIR is a novel driver for NED of PCa cells.

Keywords: Long non-coding RNAs, castration-resistant prostate cancer, neuroendocrine differentiation, REST, HOTAIR