Title: Long noncoding RNA EPCART regulates translation through PI3K/AKT/mTOR pathway and PDCD4 in prostate cancer

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Abstract
While hundreds of cancer-associated long noncoding RNAs (lncRNAs) have been discovered, their functional role in cancer cells is still largely a mystery. Increasing number of lncRNAs are recognized to function in the cytoplasm, e.g., as modulators of translation. Here, we investigated the detailed molecular identity and functional role of *EPCART*, a lncRNA we previously discovered to be a potential oncogene in prostate cancer (PCa). First, we interrogated the transcript structure of *EPCART* and then confirmed *EPCART* to be a non-peptide-coding lncRNA using in silico methods. Pathway analysis of differentially expressed protein-coding genes in *EPCART* knockout cells implied that *EPCART* modulates translational machinery of PCa cells. *EPCART* was also largely located in the cytoplasm and at the sites of translation. With quantitative proteome analysis on *EPCART* knockout cells we discovered PDCD4, an inhibitor of protein translation, to be increased by *EPCART* reduction. Further studies indicated that the inhibitory effect of *EPCART* silencing on translation was mediated by reduced activation of AKT and inhibition of mTORC1 pathway. Together, our findings identify *EPCART* as a translation-associated lncRNA that functions via modulation of PI3K/AKT/mTORC1 pathway in PCa cells. Furthermore, we provide evidence for prognostic potential of PDCD4 in PCa tumors in connection with *EPCART*.