Transcriptomic analysis reveals downstream effectors of the oncogenic lncRNA EPCART in prostate cancer

Hana Hien Le1 , Annika Kohvakka1 , Hanna Rauhala1 , Leena Latonen2 , Tapio Visakorpi1, 3 1Tampereen Yliopisto Kaupin Kampus, Tampere, Finland, 2 Itä-Suomen Yliopisto, Koulutus ja kehittämispalvelu Aducate, Kuopio, Finland, 3Fimlab Laboratoriot, Tampere, Finland

Background: Long non-coding RNAs (lncRNAs) have emerged as important regulators of prostate cancer (PCa) progression. We have previously identified the lncRNA EPCART as an androgen receptor (AR)- and ERG-regulated oncogene that promotes PCa growth through PI3K/AKT/mTOR signaling. However, the transcriptional programs downstream of EPCART remain largely unknown. Method: In this study, we stably overexpressed different variants of EPCART in LNCaP PCa cells using lentiviral transduction. Cell growth was monitored over time. Transcriptomic alterations following EPCART induction were characterized by RNA sequencing and differential gene expression analysis. Functional pathway enrichment was performed using Reactome, and the results were compared with those from an independent RNA-sequencing dataset generated from EPCART-knockout LNCaP cells. Results: EPCART overexpression resulted in increased cell growth in LNCaP cells in comparison with control. In addition, EPCART overexpression resulted in extensive transcriptomic remodeling. Reactome enrichment analysis revealed significant activation of the Integrated Stress Response, suggesting that EPCART promotes cellular adaptation to oncogenic stress. Comparative analysis of different EPCART variant overexpression models identified a shared transcriptional signature, including upregulation of ADAM9, RUFY3, and LENG8, genes involved in extracellular matrix remodeling, cell migration, and RNA metabolism. Consistently downregulated genes included UGT2B28, UGT2B10, RIPOR2, ADAM7, and ZNF43, indicating alterations in androgen metabolism and invasive behavior. Conclusion: Our findings demonstrate that EPCART regulates transcriptional programs beyond its previously reported role in translational control. By activating the integrated stress response and modulating genes involved in invasion and androgen metabolism, EPCART may facilit