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YOU ARE INVITED TO ATTEND THE DEFENSE OF THE DOCTORAL DISSERTATION

"REGULATION OF THE LONG NONCODING RNA PACER IN CYCLOOXEGANASE SIGNALING AND IMPACT ON INFLAMMATORY LUNG CANCER"

By

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Friday, November 7th, 2025
2:00 P.M.
International Center for Public Health, auditorium

Join Zoom Meeting

https://rutgers.zoom.us/j/95911972085?pwd=xfm6jLFpvngf1mZ3YbR0oWMp72C5bi.1

Meeting ID: 959 1197 2085
Password: 423659

ABSTRACT

Chronic Inflammation-driven eicosanoid signaling is a predominant feature of lung adenocarcinoma (LUAD). Sustained cyclooxygenase-2 (COX-2) signaling can drive tumor proliferation, invasion, and immune evasion, yet current COX-2-targeted therapies are limited by drug toxicity and therapeutic resistance. Among the regulatory long noncoding RNAs (lncRNAs) influencing COX-2 is a lncRNA called PACER (PTGS2 antisense NF-κB1 complex-related RNA). This study seeks to better understand the mechanism of PACER regulation, define its role in LUAD progression and phenotype, and determine how sequence conservation, secondary structure, and molecular interactions drive PACER's regulation of COX-2 signaling.

Here, we show that PACER expression was markedly increased in LUAD tumors compared with normal lung tissue and showed a strong positive correlation with COX-2 using bioinformatic tools. Knockdown of PACER reduced COX-2 levels in LUAD cells, confirming a direct regulatory relationship. Inflammatory stimuli and PGE_2 treatment upregulated both PACER and COX-2 RNA, while COX-2 inhibition with celecoxib suppressed PACER, supporting a PGE_2-driven feedback loop. These findings suggest that disruption of this PACER signaling may attenuate this continuous proinflammatory signaling in LUAD patients' tumors. We also investigated the roles of several transcription factors in PACER signaling, suggesting that PACER and COX-2 share complex, interdependent transcriptional regulation.

Stable knockdown of PACER in LUAD cells suppressed proliferative, migratory, and invasive phenotypes, underscoring its role as an amplifier of COX-2 signaling. Comparative bioinformatic and structural analyses identified conserved sequences within the PACER transcript that harbor several potential miRNA and hnRNPK KH3-binding motifs. Our structural studies utilizing SHAPE-MaP generated the first structural determination of PACER. This analysis showed that PACER adopts a compact, modular architecture in vivo characterized by stabilized long-range interactions and flexible regulatory domains. Our homology and structural studies identified a region of the PACER transcript with several conserved motifs surrounding a known NF-κB binding domain and other punitive interaction domains.

Taken together, our findings establish PACER as an important regulator of LUAD phenotype through modulation of COX-2 mRNA transcription and provide evidence of structural features that may mediate PACER's biological roles. Our analyses suggest that PACER is an evolutionarily conserved, modular lncRNA whose secondary structure and conserved motifs enable dynamic RNA-protein and, potentially, RNA-miRNA interactions that reinforce inflammatory signaling. These results position PACER as an important regulator of inflammation-driven tumor phenotype in LUAD and as a potential therapeutic target for disrupting the chronic activation of COX-2-dependent inflammatory pathways.