Spring 2026

Biochemistry and Molecular Biology Brown Bag Series

Shreya Dhengale

Platelet-activating factor-receptor signaling in the cytotoxic response to penfluridol-based combination approaches in lung cancer cells

Tuesday, February 10, 2026

11:00 AM

103 Biological Sciences Building

Lab: Ravi Sahu, Ph.D.

Boonshoft School of Medicine
WRIGHT STATE UNIVERSITY

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https://science-math.wright.edu/biochemistry-and-molecular-biology

Abstract

Non-small cell lung cancer (NSCLC) remains a leading cause of cancer-related mortality, underscoring the need for improved therapeutic strategies. Although epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) have advanced targeted therapy, their clinical efficacy is frequently limited by the development of resistance. Drug repurposing offers a cost-effective and time-efficient approach to enhance existing treatments. Penfluridol, an FDA-approved antipsychotic drug, has demonstrated anticancer activity through modulation of EGFR-related signaling; however, the role of platelet-activating factor receptor (PAFR) signaling, which crosstalks with the EGFR pathway, to penfluridol's anticancer effects remains unclear. In this study, we evaluated whether penfluridol enhances cytotoxic response to EGFR-TKI in NSCLC and examined the regulatory role of PAFR signaling. To that end, PAFR-expressing NSCLC cell lines were treated with penfluridol alone or in combination with EGFR-TKIs and a PAFR antagonist. Our studies demonstrate that penfluridol significantly inhibited NSCLC cell viability and migration in a dose- and time-dependent manner, and enhances EGFR-TKI's cytotoxic response. Notably, activation of PAFR attenuated penfluridol-mediated cytotoxic effects, identifying PAFR as a critical modulator of therapeutic response. Although studies to define downstream mediators are ongoing, these findings support the repurposing penfluridol to improve EGFR-TKIs cytotoxic response in NSCLC, and highlight PAFR signaling as a potential therapeutic target to overcome resistance.

Keywords: Penfluridol, NSCLC, PAFR, EGFR-TKIs, drug repurposing

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Anisha Addala

Exploring the role of the platelet-activating factor-receptor pathway in the cytotoxic response to antiangiogenic-based therapy in lung cancer

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Abstract

Given that angiogenesis supports tumor growth, therapeutic agents targeting this process have demonstrated improved response rates across multiple malignancies, including lung cancer. Apatinib, a clinically used antiangiogenic agent, inhibits vascular endothelial growth factor receptor 2 (VEGFR2), resulting in the suppression of tumor cell proliferation. However, despite initial therapeutic benefit, tumor cells frequently develop escape mechanisms through compensatory bypass pathways. The G-protein coupled, platelet-activating factor-receptor (PAFR) pathway has been implicated as one such bypass mechanism that promote tumor cell survival. In this study, we tested the hypothesis that inhibition of PAFR signaling can enhance the cytotoxic response to apatinib and apatinib-based combination approaches using NSCLC models. PAFR-expressing NSCLC cells were treated with apatinib alone or in combination with epidermal growth factor receptor (EGFR)-targeted agents (gefitinib and erlotinib), and PAFR antagonists. The studies demonstrate that apatinib inhibits NSCLC cell viability in a dose- and time-dependent manner. Significantly enhanced cell cytotoxicity was observed when apatinib was combined with gefitinib and erlotinib. Notably, triple combination therapy targeting EGFR, VEGFR, and PAFR produced significantly greater suppression of cell proliferation than double-agent combinations. In addition, PAFR agonist-induced cell migration was reversed by apatinib. Although studies to delineate the downstream signaling mechanisms are ongoing, these findings suggest that PAFR represents a potential therapeutic target to enhance the cytotoxic response of apatinib and apatinib-based approaches in NSCLC.