MiRNA-149-5p and platelet-activating factor-receptor signaling impacts lung cancer growth and the efficacy of targeted therapy

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Lung cancer remains one of the highly aggressive malignancies associated with poor prognosis and increased mortality rates. Of two major types, non-small cell lung cancer (NSCLC) is the most prevalent type and detected in 80-85% lung cancer cases. Several studies have shown the involvement of multiple signaling pathways in affecting the growth and treatment efficacy using NSCLC models. To that end, the roles of microRNAs (miRs) in essentially all biological processes are evident. The altered expression of miRs has been documented in various disease conditions, including cancer. While multiple mechanisms have been identified in mediating miRs effects, the involvement of miR-149-5p in Platelet-Activating Factor-Receptor (PAFR)-induced effects on lung cancer growth and therapeutic potential has not been studied. Given the oncogenic and tumor-suppressive roles of miRNA-149-5p and the oncogenic effect of PAFR signaling in various cancer models, our studies sought to determine the potential link between miR-149-5p and PAFR signaling in NSCLC models. Using A549 and H1299 cell lines, we first verified the tumor- suppressive role of miR-149-5p and the growth proliferative effect of PAFR signaling. Our next studies demonstrated that overexpression of miR-149-5p significantly attenuated PAFR agonist, CPAF-mediated increased proliferation of NSCLC cells. These findings were confirmed by the expression analysis of miR-149-5p, cyclin D1 and forkhead box protein M1 (FOXM1) via qRT- PCR. Our next studies examined the effects of the PAFR and miR-149-5p on targeted therapy (i.e., erlotinib and gefitinib) responses. We found that both these therapies inhibit the survival of A549 and H1299 cell lines in a dose- and time-dependent manner. Importantly, activation of the PAFR significantly blocked this effect. These findings indicate that miR-149-5p blocks PAFR-mediated increased cell proliferation and that PAFR activation attenuates the cytotoxic effects of targeted therapy.

Recent Publications:

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Biography

Ravi P Sahu is a professor in Wright State University. The major research interests of my laboratory are we explore molecular biology, immunology and pharmacological approaches, including microvesicle particles analysis, gene deletion/overexpression, gene array, qPCR, western blotting and flow cytometry with multiple novel cellular systems, relevant mouse models including genetic knockout and transgenic, as well as human samples for our research. Our basic and translational research projects involve collaborations with colleagues, including Physician-Scientists and Pathologists and primarily use melanoma, lung and pancreatic cancer models.

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