SPRING 2021

Biochemistry and Molecular Biology Brown Bag Series

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M.S. Student

"The effect of PI4KB inhibition on small GTPases containing polybasic domain"

Tuesday, April 6, 2021

11:00 AM

Please contact x3249 if you would like to attend but did not receive an emailed link.

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

Abstract

The effect of PI4KB inhibition on small GTPases containing polybasic domain

Despite well-documented role of Ras proteins as one of the cancer driver in human since 1982, efforts for developing any anti-Ras treatment have not yet been successful. Among 3 ubiquitously expressed Ras isoforms in mammalian cells, mutated K-Ras is the most prevalent in pancreatic, colorectal and lung cancers. Different approaches have been suggested for targeting this “undruggable” protein; one of approaches is preventing Ras localization to the plasma membrane (PM). It has been shown that Ras proteins through post-translational modifications can stably bind the PM, where Ras proteins are activated and stimulate their downstream effectors promoting cell proliferation, differentiation and survival. Constitutively activating mutations of Ras can lead to carcinogenesis. Therefore, removing Ras proteins from the PM can block the signaling cascade of oncogenic mutant Ras. In our previous study, we have shown that phosphatidylinositol 4-kinase IIIβ (PI4KB), which converts PI to PI 4-phosphate (PI4P) at the Golgi complex, regulates transport of protein and lipid. Inhibition or knockout of PI4KB translocates K-Ras from the PM to mitochondria while PtdSer, an essential phospholipid for K-Ras PM localization, redistributes from the PM to endomembranes. In aim 1 of my project, I will study the effect of PI4KB inhibitors as an anti-cancer agent in K-Ras-driven cancers cells including pancreatic, lung and colorectal cancer cell lines. It will identify PI4KB as a target for developing anti-K-Ras therapies. Moreover, our data suggest that K-Ras translocation to mitochondria upon PI4KB inhibition is via the polybasic domain of K-Ras. In aim 2, I will investigate the effect of PI4KB inhibition on the cellular localization of small GTPases containing a polybasic domain and their biological activities.