Fall 2025

Biochemistry and Molecular Biology Brown Bag Series

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"MINPP1: A New Potential Therapeutic Target for KRAS-Driven Cancers"

Tuesday, October 7, 2025

11:00 AM

Location 135 Oelman Hall

Lab: Kwang-jin Cho, Ph.D.

Boonshoft School of Medicine
WRIGHT STATE UNIVERSITY

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

Abstract

KRAS is one of the most commonly mutated oncogenes in human cancers, with KRAS mutants found in 88% of pancreatic cancers, 50% of colorectal cancers, and 30% of non-small-cell lung cancers. Oncogenic KRAS mutants are constitutively activated, leading to cellular reprogramming that causes cancer cells to be dependent on KRAS activity for their growth and survival. This presents KRAS as an ideal therapeutic target for KRAS-driven cancers. Previous studies have found that disrupting the binding of KRAS with the plasma membrane (PM) is an attractive approach for inhibition of oncogenic KRAS. Multiple inositol polyphosphate phosphatase 1 (MINPP1), a key regulator of inositol polyphosphate metabolism, was recently identified as a regulator of KRAS localization in a genome-wide siRNA screening, with loss of MINPP1 inducing KRAS dissociation from the PM. We found that loss of MINPP1 induces KRAS dissociation from the PM, as well as perturbs KRAS signaling. Ongoing research suggests that one mechanism driving KRAS PM dissociation via MINPP1 loss is through abrogation of phosphatidylserine content of the PM, an essential phospholipid required for KRAS PM localization. MINPP1 loss also results in mislocalization of oncogenic HRAS and perturbs HRAS signaling, and therefore does not operate in an isoform-specific manner. Loss of MINPP1 across multiple PDAC cell lines harboring different oncogenic KRAS mutations also results in perturbation of RAS signaling, indicating that loss of MINPP1 has anti-oncogenic effects for KRAS-driven cancer. These results position MINPP1 as a potential novel pan-oncogenic therapeutic target for blocking the growth of KRAS-driven cancers.