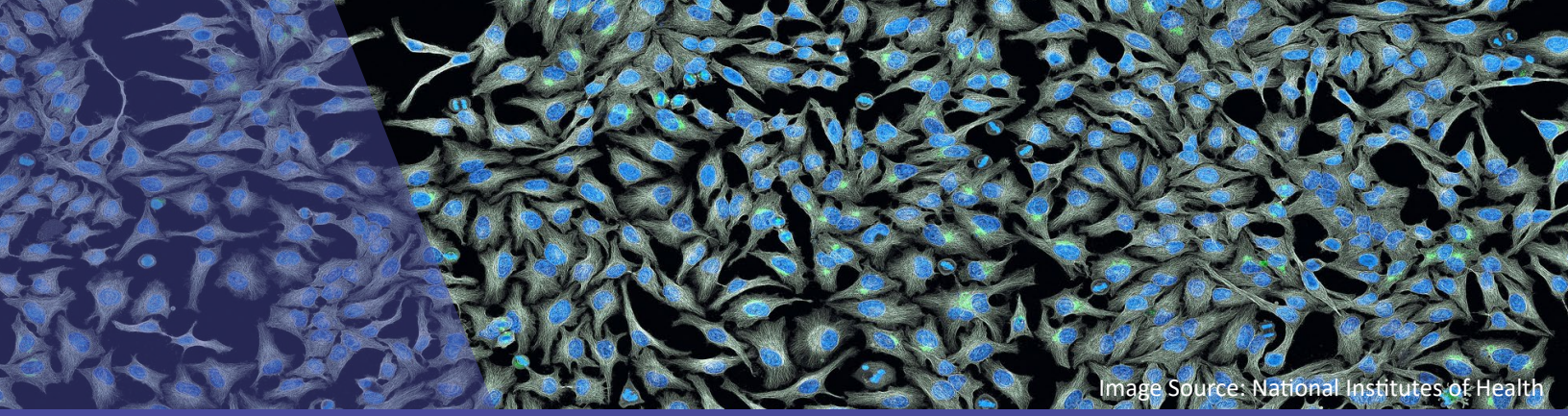

Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Lurie Cancer Center's Basic Research Seminar Series

Targeting Tumors with an RAS Degrader

Tuesday, February 11, 2025

11:00 a.m.- 12:00 p.m. CT

Baldwin Auditorium, 1st Floor

Robert H. Lurie Medical Research Center
303 E. Superior St., Chicago, IL

RAS small GTPases stimulate cell proliferation and promote survival. Mutations arise in RAS can occur in more than 30% of all cancers. Although once considered "undruggable", small molecules targeting this protein have been developed and approved for clinical cancer therapy. An alternative approach that also shows promise for targeting RAS is the development of RAS degraders, including PROTACs, linker-based degraders, and direct proteolysis degraders. We have developed a RAS degrader that directly cleaves RAS within its Switch I region resulting in targeted protein degradation. This degrader has been successfully delivered to cells as an engineered biologic and via an mRNA-nanoparticle delivery strategy. The biologic degrader reduces RAS levels in cells and reduced breast, pancreatic, and colon cancer when introduced i.p. into mice. The mRNA-delivery strategy reduced pancreatic tumors when directly injected to tumors. Our work establishes that a highly specific degrader targeting RAS can be successful delivered to cells by multiple strategies and can be safely used even when delivered to all cells.

Karla Satchell, PhD
Professor, Microbiology-Immunology
Northwestern University Feinberg School of Medicine

Hosted by: Marcelo Bonini, PhD

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Basic Sciences Research Division of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University
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