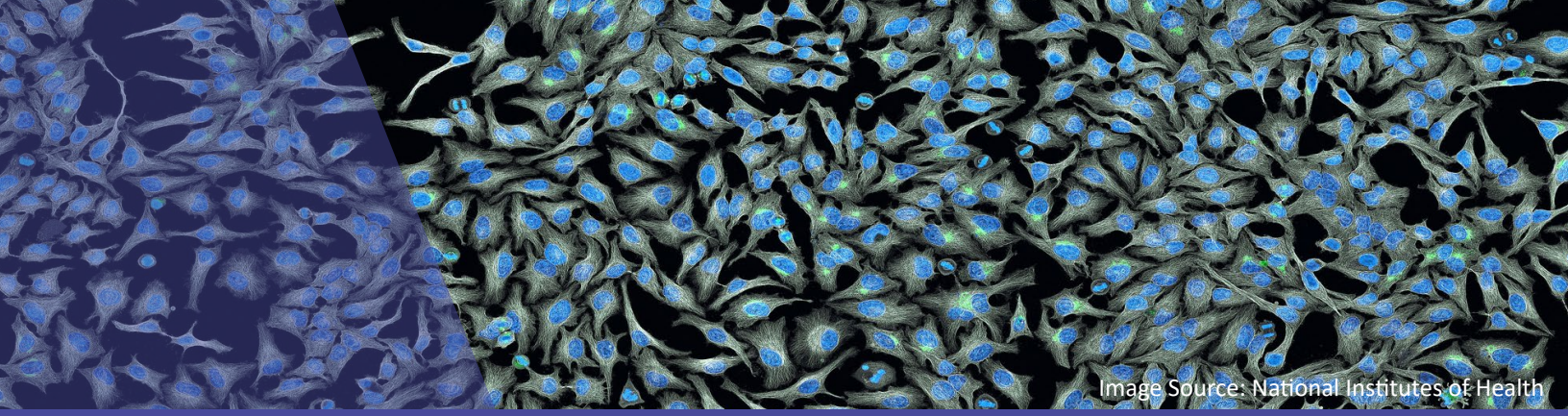

Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Lurie Cancer Center's Basic Research Seminar Series

Role of Site-Specific ADP-Ribosylation in Cancer

Tuesday, October 15, 2024

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

Host: Debabrata Chakravarti

ADP-ribosylation (ADPRylation) is a reversible post-translational modification (PTM) of proteins resulting in the covalent attachment of a single ADP-ribose (ADPR) unit [i.e., mono(ADP-ribose) or MAR] or polymers of ADPR units [i.e., poly(ADP-ribose) or PAR] derived from β-NAD+ on a variety of amino acid residues (e.g., Glu, Asp, Ser). ADPRylation is catalyzed by the PARP family of mono(ADP-ribosyl) transferases (MARTs) and poly(ADP-ribose) polymerases (PARPs), consisting of 17 members that have distinct structural domains, activities, subcellular localizations, and functions. Historically, PARPs and ADPRylation have been studied in the context of DNA repair, focusing on PARP-1 and PARylation in cancer. New findings on the diverse roles of PARPs in cellular processes beyond DNA repair have linked ADP-ribosylation to metabolism, inflammation, immunity, stress responses, hormonal signaling, and viral infections. Although the functions of PARylation are well studied, little is known about the functions of MARylation. Recent studies, including work from the Kraus lab, have begun to reveal novel and interesting functions for cytoplasmic MARTs, such as PARP-7, PARP-12, PARP-14, and PARP-16, in molecular and cellular functions including RNA processing, translation, stress granule formation, unfolded protein response, and regulation of the cytoskeleton. In our work, we are elucidating the functional links among compartment-specific NAD+ synthesis, PARP/MART activity, ADP-ribosylation, and major cellular processes, including transcription, splicing, and translation. Our work has placed a particular emphasis on identifying, confirming, characterizing, and functionally analyzing specific sites of ADP-ribosylation in biologically relevant PARP substrate proteins in physiological and disease, including breast and ovarian cancers.

Lee Kraus, PhD

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