Subject: Dissertation Defense - Alison Gomeiz, PHD Biosciences
Date: Friday, November 1, 2024 at 10:05:14 AM Eastern Daylight Time
From: SSB Faculty List on behalf of Diane St. Germain
To: SSB-FACULTY-LIST-L@LISTSERV.GMU.EDU

Dissertation Defense Announcement
To: The George Mason University Community

Candidate: Alison Gomeiz
Program: PhD in Biosciences
Date: Thursday, November 14th, 2024
Time: 10am EST
Location: Science & Tech campus, IABR, room 1004
Zoom link: https://gmu.zoom.us/j/96242012712

Committee Chair: Dr. Mariaelena Pierobon

Committee members: Dr. Barney Bishop, Dr. Emanuel Petricoin, Dr. Claudia Fredolini

Title: FA-MPINA (Formaldehyde-Crosslinked Multinodal Protein Interactome Network Array): A Novel, High-Throughput Method to Identify Functional Interactions Associated with Resistance to CDK4/6 Inhibition in Breast Cancer

Abstract:

The effect of genomic alterations on the biological process of tumorigenesis has been well-studied in recent years, resulting in increased clinical use of targeted therapies designed to inhibit mutated oncogenes. While these treatments are initially successful, a majority of patients develop aggressive, treatment-resistant disease. One strategy to address drug resistance is to broaden the scope of study to consider genomic-independent mechanisms such as functional protein behavior. Cancer signaling is mediated predominantly by transient kinase interactions and their phosphorylation events, which cannot be accurately captured by genomics data alone. Thus, it is of great interest to characterize these genomic-independent functional interactions, but their detection has been difficult to realize with existing proteomic techniques. In this study, we introduce the FA-MPINA (formaldehyde-crosslinked multinodal proteomic interactome network array): a novel, high-throughput method to capture functional protein interactions and their activation states from unmodified cell cultures. This assay couples co-immunoprecipitation with the reverse phase protein microarray to capture lowly abundant, post-translationally modified proteins in complex with the precipitated protein. Once optimized, we used FA-MPINA to explore genomic-independent events in breast cancer cell lines with established

resistance to CDK4/6 inhibitors as a translational model for breast cancer patients with acquired CDK4/6 inhibitor resistance, focusing on EZH2 binding partners. We isolated EZH2 from whole cells as well as the cytosolic and nuclear compartments of parental and resistant cells and probed for 75 potential interacting partners. We identified Akt as an interacting partner of EZH2 present exclusively in the cytosolic compartment of the resistant cell lines. This physical interaction between these two proteins was independently validated using proximity ligation assay. As expected, inhibition of Akt kinase activity or degradation of EZH2 using hydrophobic tagging eliminated Akt/EZH2 interactions. Through its successful application in this study, we demonstrate that FA-MPINA serves as a promising platform for the exploration of functional, genomic-independent biological behaviors.

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