Subject: Thesis Defense: James Davis, MS Biology
Date: Tuesday, October 7, 2025 at 10:37:11 AM Eastern Daylight Time
From: SSB Faculty List on behalf of Diane St. Germain
To: SSB-FACULTY-LIST-L@LISTSERV.GMU.EDU

Thesis Defense Announcement
To: The George Mason University Community

Candidate: James Davis

Program: M.S. in Biology

Date: October 20, 2025

Time: 10:00 AM Eastern Time (US and Canada)

Location: via Zoom

Join Zoom Meeting
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Committee Chair: Dr. Ancha Baranova

Committee Members: Dr. Mariaelena Pierobon, Dr. Aarthi Narayanan

Title: Optimizing Use of the Reverse Phase Protein Microarray to Capture Functional Interactions in Lung Cancer

Abstract: While genomic alterations drive tumorigenesis, at the molecular level cancer is driven by the aberrant activation of biochemical signaling cascades. Thus, many members of these signaling networks have become the direct target of anti-cancer therapeutics. However, due to the complex and highly dynamic nature of these networks, response to targeted treatments remains hard to predict and resistance is often acquired through the rerouting of these signaling cascades. Devising novel technologies able to accurately capture functional and dynamic interactions within these signaling networks can be transformative for understanding and predicting signal transduction patterns in cancer and for developing new therapeutic strategies. Through these biochemical interactions, protein and lipid kinases are phosphorylated and enabled to activate their downstream substrates, leading to controlled gene expressions, metabolic responses, and regulation of the overall cellular machinery. However, activation and interaction of signaling molecules are not driven by random encounter of freely diffusing interacting members, but by the assembly of heterotypic protein complexes. Capturing interacting members within these protein complexes can be easily achieved using affinity-based proteomic techniques. However, measuring broad-scale functional activation of interacting members remains challenging from a technical perspective. As a result, most high-throughput data exploring signal transduction are based on direct or indirect quantifications of protein expression levels or activation status of decoupled signaling molecules not necessarily capturing true signaling events in complex biological samples. To overcome this hurdle, we have developed a high throughput platform able to isolate whole native protein complexes from complex biological samples and capture activated binding partners in a two-step format. Bait proteins are first isolated using Co-immunoprecipitation and functional activation of binding partners are then measured using the Reverse Phase Protein Microarray. As a model system to optimize this new assay, we have dissected signaling dynamics elicited by the epidermal growth factor receptor (EGFR), a key oncogenic driver of lung cancer, in response to stimulation to its ligand EGF. Orthogonal methods like western blotting and proximity ligation assay (PLA) where then used to validate significant interactions and their subcellular localization. This study not only proves feasibility for this novel method to analyze complex protein-protein interactions but also highlights several EGFR binding partners that could provide the basis for future therapies against EGFR-inhibitor resistant non-small cell lung cancer.

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