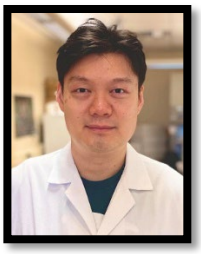
PURDUE UNIVERSITY | Department of Industrial and Physical Pharmacy

Industrial & Physical Pharmacy Seminar

IPPH 69600

Wednesday, September 6, 2023
3:30 PM in RHPH 164

"Plasma Membrane integrity and lipids as modulators for Innate Immunity in Solid Tumors"



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The plasma membrane plays a crucial role in maintaining cellular viability, and damage to it can be devastating, often leading to necrosis. Nonetheless, our research, as well as that of others, has demonstrated that cells possess multiple mechanisms for repairing the membrane, including ESCRT-III, which enables them to maintain their integrity to some extent and even recover from damage. Intriguingly, we have also discovered that cells that have survived near- necrotic experiences can detect the sub-lethal membrane damage and use it as a signal to release chemokines and cytokines that activate downstream immune responses, such as inflammation. We have identified the signaling pathway underlying this cellular response, including the plasma membrane damage sensors, the downstream kinase cascades, and the transcription factor complex that controls the chemokine/cytokine production. We have named this pathway the PMI (Plasma Membrane Integrity) pathway, as it is initiated by sensing perturbations in plasma membrane integrity. At the molecular level, this pathway is similar to the well-established yeast cell wall integrity signaling pathway (CWI), suggesting an evolutionarily conserved mechanism for responding to cellular barrier damage. Lastly, we have found that the patients' solid tumor cells use the PMI pathway to produce pro-tumor cytokines that promote metastasis. Conceptually, the identification of the PMI signaling pathway suggests that the partial loss of plasma membrane integrity represents a distinctive cell- identifiable innate immune activation pattern, resulting in immune modulations to the microenvironments. We will also discuss how we modulate the phospholipid in boosting anti-tumor immunity.