

ABSTRACT:

Breaking barriers: Unleashing potent anti-tumor immunity through advances in CD8 T cell and NK cell modulation

While immune checkpoint inhibitors have significantly advanced cancer therapy, overcoming resistance remains a major challenge, driving the need for new treatment strategies. This talk will present recent progress in cancer immunotherapy, focusing on enhancing immune responses and addressing resistance. One key area of research is targeting the protein tyrosine phosphatases PTPN2 and PTPN1, which play crucial roles in regulating inflammation and anti-tumor immunity. We have investigated the mechanism of action of AC484, a novel small-molecule inhibitor of PTPN2 and PTPN1. In vitro studies show that AC484 boosts interferon signaling and activates various immune cell populations. In mouse models resistant to FDA-approved anti-PD-1 therapy, AC484 alone induces strong anti-tumor responses by enhancing the activity of natural killer cells and CD8+ T cells in the tumor microenvironment. These findings suggest that inhibiting PTPN2 and PTPN1 represents a promising new strategy for cancer immunotherapy, currently being tested in clinical trials (ClinicalTrials.gov identifier NCT04777994). AC484 is, to our knowledge, the first active-site phosphatase inhibitor to reach clinical trials for cancer immunotherapy.

BIOGRAPHY:

Dr. Ebrahimi-Nik is an immunologist with over a decade of experience investigating tumor-immune system interactions. Her research focuses on developing innovative immunotherapies, particularly the modulation of CD8 T cells, NK cells, and personalized cancer vaccines. Currently, she leads a lab at the Ohio State University, Medical Oncology and Pelotonia Institute for Immuno-Oncology, where her team studies the molecular mechanisms that enhance immune responses against tumors.

Dr. Ebrahimi-Nik has published in top journals such as Nature and Nature Communications, and has recently filed for several patents in cancer immunotherapy. She earned her DVM and PhD from Ferdowsi University of Mashhad, Iran, with her PhD thesis conducted in collaboration with the University of Connecticut. Following her postdoctoral training at the University of Connecticut, she served as a senior research scientist at the Broad Institute of MIT and Harvard, where she led research on PTPN2 inhibitors, which is now in phase I clinical trials for patients with advanced cancer.

UPCOMING SEMINARS:

10/31- Dr. Svenja Illien-Junger- *Emory University*
11/7- Dr. Jeff Lichtman- *Harvard University*
11/14- Dr. Kelly Langert- *Loyola University Chicago*

DEPARTMENT OF BIOMEDICAL ENGINEERING

2024 FALL SEMINAR SERIES

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Department of Internal Medicine

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THURSDAY October 24, 2024
11am-12pm
PWEB 150



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