

[Seminar] Cholesterol orchestrates pro-tumorigenic signaling networks in the plasma membrane

Date-Time:

Tuesday, November 17, 2026 - 11:20 to 12:00

Location: Seminar room C700, Lab 3



Description

Title: Cholesterol orchestrates pro-tumorigenic signaling networks in the plasma membrane

Speaker: Prof. Wonhwa Cho

Liberal Arts and Sciences Science Endowed Chair, UIC Distinguished Professor and Head,
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Summary

Although altered cholesterol metabolism is a hallmark of cancer, the precise spatial mechanisms driving oncogenesis remain elusive. Using spatiotemporally resolved quantification, we demonstrate that metabolic reprogramming selectively elevates cholesterol at the inner leaflet of the plasma membrane (IPM) across diverse cancer types. Integrated computational, biophysical, and live-cell imaging analyses reveal that elevated IPM cholesterol triggers cryptic, stimulus-independent oncogenic signaling by directly driving the recruitment and spatial assembly of key signaling protein complexes. Systematic profiling shows that while IPM cholesterol levels are differentially upregulated across distinct cancer types, they remain strictly uniform within specific cancer subtypes. Combined proximity labeling and IPM cholesterol titration further identify distinct thresholds of IPM cholesterol that selectively tune the recruitment of specific kinases, phosphatases, and scaffolding proteins. Consequently, IPM cholesterol acts as a central rheostat, orchestrating cancer-type-specific, cell-intrinsic signaling networks that enforce key malignant hallmarks, including stemness and acquired drug resistance. Crucially, these non-canonical, cholesterol-driven pathways bypass conventional therapies targeted against canonical signaling. To exploit this vulnerability, we developed lipid-protein interaction inhibitors and site-specific cholesterol depletion strategies to selectively dismantle IPM cholesterol-mediated oncogenic networks. These targeted approaches demonstrate robust in vitro and in vivo efficacy and high specificity across multiple cancer models, establishing a new therapeutic framework for precision oncology.

Short Bio

B. S., 1980, Chemistry, Seoul National University, Seoul, Korea

M. S., 1982, Chemistry, Seoul National University, Seoul, Korea

Ph. D., 1988, Chemistry, The University of Chicago, Chicago, IL

Postdoctoral Fellow, 1988-1990, Chemistry, California Institute of Technology, Pasadena, CA

Assistant professor, 1990-1996, University of Illinois Chicago, Chicago, IL

Associate professor, 1996-2000, University of Illinois Chicago, Chicago, IL

Professor, 2000-present, University of Illinois Chicago, Chicago, IL

Head of Chemistry Department, 2017-present, University of Illinois Chicago, Chicago, IL

Liberal Arts and Sciences Science Endowed Chair, 2017-present, University of Illinois Chicago, Chicago, IL

UIC Distinguished professor, 2018-present, University of Illinois Chicago, Chicago, IL

Avanti Award in Lipids, Biophysical Society, 2018

Elected Fellow, American Association for the Advancement of Science, 2018

BPS Award in the Biophysics of Health and Disease, Biophysical Society, 2026

Short abstract

Altered cholesterol metabolism is a hallmark of cancer, but its spatial mechanisms remain poorly understood. We show that metabolic reprogramming selectively elevates cholesterol in the inner leaflet of the plasma membrane across diverse cancer types. This inner-leaflet cholesterol recruits and assembles signaling protein complexes, activating cryptic, stimulus-independent oncogenic pathways. Distinct cholesterol thresholds tune the recruitment of kinases, phosphatases, and scaffolding proteins, thereby shaping cancer-type-specific signaling networks that promote stemness and drug resistance. We further develop lipid–protein interaction inhibitors and site-specific cholesterol depletion strategies that dismantle these networks with strong in vitro and in vivo efficacy, suggesting a new framework for precision oncology.