



# CHEMISTRY & BIOCHEMISTRY / MOLECULAR & CELL BIOLOGY SEMINAR:

## Endoplasmic reticulum structure and function: from stress response to germline inheritance

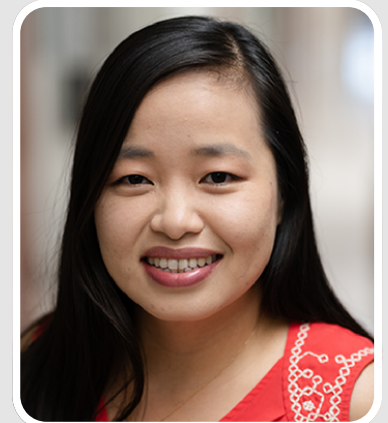
### Abstract:

The endoplasmic reticulum (ER) is a dynamic organelle organized as specialized domains adapted to its many essential functions in protein and lipid biogenesis, calcium signaling, and cellular homeostasis. How ER structure and functions are regulated across biological scales remains poorly understood. My research has addressed this question by studying ER organization at two ends of the spectrum: ER subdomain formation driven by molecular assemblies during ER stress signaling and ER specialization and function in *Drosophila melanogaster* ovary tissue.

At the molecular level, I investigated the dynamics and structure of the ER stress sensor IRE1 $\alpha$ , a key regulator of the unfolded protein response. Using quantitative light microscopy and correlative cryogenic light and electron tomography, I showed that activated IRE1 $\alpha$  forms two dynamically distinct oligomeric assemblies and remodels the ER into a specialized subdomain with narrow anastomosing membrane tubes. Within this environment, IRE1 $\alpha$  sensing domain assembles into ordered luminal helices that stabilize signaling and may explain its switch-like signaling output during the unfolded protein response.

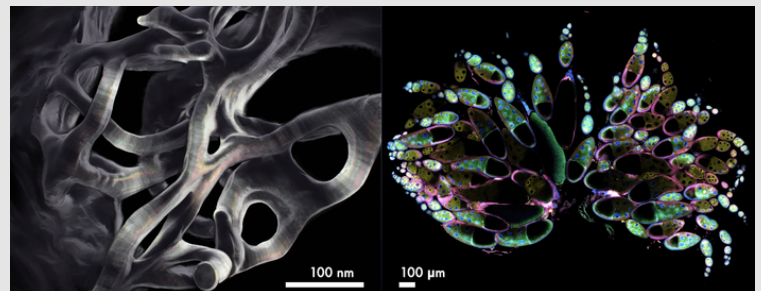
At the tissue level, I identified a novel ER subdomain forming extensive plasma membrane contacts in fly ovary tissue. This domain comprises ribosome-studded sheets enriched in translational regulators, RNA-binding proteins, and ER client proteins, suggesting a role in localized protein synthesis. A complementary genetic screen targeting over 200 ER-associated factors during oogenesis revealed surprising proteins and pathways required for proper ER functions and oogenesis during this developmentally relevant window.

Together, these studies lay the foundation for my future research vision to bridge ER molecular mechanisms with organismal physiology to illuminate how the ER promotes cellular, tissue, and organismal health, and how its dysregulations contribute to diseases.



**Han Tran**

HHMI Hanna Gray  
Postdoctoral Fellow  
Whitehead Institute



### About the Speaker:

Dr. Han Tran received her B.S. in Biological Sciences from San José State University and her Ph.D. in Biochemistry and Molecular Biology from the University of California, San Francisco. Co-mentored by professors Peter Walter and Shawn Douglas, she studied the dynamics and structure of the unfolded protein response sensor IRE1 $\alpha$  in cells. She is currently an HHMI Hanna Gray postdoctoral fellow in the Lehmann lab at the Whitehead Institute. Her research focuses on how structural and functional specializations of the endoplasmic reticulum in tissues contribute to oogenesis and embryogenesis.