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Assistant Professor Yi-Wei Chang

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Dr. Yi-Wei Chang is an Associate Professor of Biochemistry and Biophysics and Associate Director of the Institute of Structural Biology at the University of Pennsylvania. His laboratory specializes the use of cryo-electron tomography (cryo-ET) to visualize macromolecular machines directly inside cells at molecular resolution. By capturing biological structures in their native cellular environment, his work reveals how pcomplex assemblies drive fundamental processes such as host-pathogen interactions.
Dr. Chang's research has uncovered key molecular machines that power secretion and invasion in apicomplexan parasites, providing structural insight into diseases such as malaria, toxoplasmosis, and cryptosporidiosis. His group also develops new technological and computational advances that expand cryo-ET into increasingly complex systems, including human tissues. Through integrative cellular structural biology, his lab bridges fundamental mechanism and translational opportunity, uncovering structural principles that inform the next generation of therapeutic strategies.

Integrative Cellular Structural Biology Reveals Invasion Mechanisms of Apicomplexan Parasites

Apicomplexan parasites, including Plasmodium, Toxoplasma, and Cryptosporidium, invade host cells using a specialized secretory organelle called the rhoptry. Despite its central role in infection, the molecular architecture and regulation of this eukaryotic secretion system were previously poorly defined. Using cryo-electron tomography, we resolved the supramolecular organization of the rhoptry secretion system directly inside intact parasites. We identified a conserved multi-component assembly at the apical membrane (the rhoptry secretory apparatus; RSA) that anchors an apical vesicle docking the rhoptry tips and priming secretion. Distinct structural states correlate with specific rhoptry morphologies, supporting a model of regulated discharge. By integrating proteomics, genetics, AI-based modeling, and targeted cryo-microscopy of parasites captured during host invasion, we define the molecular composition, evolutionary conservation, and functional organization of this machinery. Together, these findings establish a structural framework for understanding rhoptry-mediated host-cell invasion and highlight the power of integrative in situ structural biology.