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BOOK OF ABSTRACTS

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Integrative Structural Biology In Situ: Toward a Molecular Sociology of GLS Filaments in Mitochondria

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Understanding the organization and regulation of metabolic networks within their native subcellular environment demands a shift from reductionist to integrative strategies. In this talk, I will explore how combining classical structural biology methods with omics technologies and advanced cellular imaging can reveal emergent properties of complex biological systems embedded within cellular lamellae. This integrative approach allows not only the identification of macromolecular assemblies but also contextualizes them within their physiological milieu—spatially, temporally, and functionally.

As a case study, I will present our ongoing efforts to decipher the molecular sociology of glutaminase (GLS) filaments in mitochondria. GLS is a key metabolic enzyme whose polymerization into filaments is now recognized as a regulatory mechanism with potential architectural consequences. Using single-particle cryo-EM, cryo-electron tomography, proteomics, and endogenous tagging strategies, we aim to capture and interpret the structural and functional interactions of GLS filaments *in situ*. These efforts are guided by the hypothesis that filamentous assemblies of metabolic enzymes not only reflect catalytic regulation but also contribute to higher-order mitochondrial organization—affecting cristae morphology, metabolite flux, and membrane dynamics.

By bridging molecular structure, interactomics, and high-resolution cellular imaging, we seek to map filament-associated microdomains and their connectivity to other mitochondrial components. This project exemplifies how integrative structural biology can be extended beyond purified samples to the mesoscale of the cell, offering a new vantage point to study enzyme assemblies as structural regulators. Such in situ analyses are crucial for understanding how metabolic processes are orchestrated at the systems level, particularly under stress conditions that reprogram mitochondrial architecture and function.

This presentation will emphasize both conceptual advances and technical challenges, highlighting the need for cross-disciplinary frameworks to decode the physical and functional logic of macromolecular assemblies within cells.

Keywords: *In situ* structural Biology, integrative biology, enzyme filamentation, mitochondria