

Hunter College of the City University of New York
Department of Biological Sciences
Spring 2024 Inga Richter Seminar Series

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A Tour of the Pore: Structural and Functional Mapping of the Nuclear Pore Complex

Nuclear Pore Complexes (NPCs) serve as the gatekeepers of RNA and protein transport between the cytoplasm and nucleoplasm and organize many nuclear processes. Defects in NPCs are associated with a wide variety of diseases. We have recently determined a subnanometer precision structure for the entire 52 MDa yeast NPC by satisfying diverse data including stoichiometry, a cryo-electron tomography map, and chemical cross-links, to generate a comprehensive overview of the NPC's architectural and functional principles. I will describe how we show that the NPC is surprisingly modular, consisting of only 30 proteins of the nucleoporin family (Nups). These Nups assemble into sub-complexes that form higher-order structures: coaxial outer and inner rings form a symmetric core scaffold connected to a membrane ring, a nuclear basket and cytoplasmic RNA export platform. Flexible connector cables hold these discrete and relatively rigid modules together, and we show that these connectors are highly dynamic, an arrangement that imbues the NPC's scaffold with both strength and flexibility; moreover, they provide targets for phosphorylation-regulated disassembly in cells with an open mitosis. We also discovered that the scaffold also shares a common evolutionary ancestor with vesicle coating proteins, and our current structure displays features in the organization of these coatomer paralogs. We also find that three major NPC structural variants co-exist within individual nuclei, whose specific localizations there foreshadow possible functional adaptations at the nuclear periphery. Finally, our studies reveal elements of the organization underlying the central transporter that mediate the bidirectional trafficking function of this remarkable transport machine.

Monday, May 13, 2024, 12:30pm
Hunter College 926HN
Host: Hualin Zhong