New insights into nuclear pore complex structure

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The nuclear pore complex (NPC) is the sole gateway between the cell nucleus and the cytoplasm, and it mediates all trafficking between theses two compartments. Much effort has been put into identifying and characterizing the transport receptors that participate in nucleocytoplasmic transport, how these interact with the NPC, and how the directionality of nucleocytoplasmic transport is regulated by the small GTPase Ran. In contrast, comparably little progress has been made in understanding the NPC on its ultrastructural level. In this context, we are mapping the molecular topography of the different NPC proteins (nucleoporins) within the 3-dimensional NPC architecture by immuno-electron microscopy (EM) to understand the functional role of distinct nucleoporin domains in nucleocytoplasmic transport. By doing so, we have recently determined the domain topography of Nup153 within the NPC of *Xenopus* oocyte nuclei. Accordingly, Nup153 is anchored to the NPC by its N-terminal domain at the nuclear ring moiety and by its zinc-finger domain to the distal ring of the nuclear basket, whereas its C-terminal FG-repeat domain is highly mobile and could be detected even at the cytoplasmic periphery of the NPC's central pore. Based on this unexpected domain topography of Nup153 within the NPC, we are now investigating the Nup153 topography in different transport states to elucidate the functional role of the three distinct domains in nucleocytoplasmic transport. Similarly, we are also dissecting the domain topography of the two nucleoporins CAN/Nup214 and p62 by immuno-EM. This structure-based approach will provide novel insights into the role of specific nucleoporin domains in nucleocytoplasmic transport, which, in turn, is a prerequisite towards a rational understanding of the molecular mechanisms governing nucleocytoplasmic transport.