

Architecture Of The Cytoplasmic Face Of The Nuclear Pore

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The nuclear pore complex (NPC) is the sole bidirectional gateway for nucleocytoplasmic transport. Despite recent progress in elucidating the NPC symmetric core architecture, the asymmetrically decorated cytoplasmic face, essential for mRNA export and a hotspot for nucleoporin-associated diseases, has remained elusive. Here, we report a composite structure of the entire human cytoplasmic face obtained by combining biochemical reconstitution, crystal structure determination, docking into cryo-electron tomographic reconstructions, and physiological validation, accounting for a third of the NPC's mass. Whereas an evolutionarily conserved ~540 kDa hetero-hexameric cytoplasmic filament nucleoporin complex is anchored by species-specific motifs above the central transport channel, attachment of the pentameric NUP358 bundles depends on the double-ring arrangement of the coat nucleoporin complex. Our results and the predictive power of our composite structure provide a rich foundation for elucidating the molecular basis of mRNA export and nucleoporin diseases.