Bon Appetit/Alamy

NUCLEAR ENVELOPE

Curving out a nuclear pore

Nuclear pore complexes (NPCs) consist of a cylindrical core lining a highly curved opening in the nuclear envelope and a basket-like structure attached to the nucleoplasmic side. This study identifies a role for the yeast basket nucleoproteins Nup1 and Nup60 in bending the inner nuclear membrane to facilitate pore formation.

Mészáros and colleagues identified a predicted amphipathic helix and an adjacent α-helical region at the amino termini of both Nup1 and Nup60. Deletion of the amphipathic helix of Nup1 led to mislocalization of the protein from NPCs to the nucleoplasm, which was more pronounced when the α-helical region of Nup1 was also deleted. Similar mislocalization occurred for mutant forms of Nup60, and the absence of the Nup60 N terminus also resulted in abnormal clusters of basket proteins Mlp1 and Mlp2. Thus, the N termini of Nup1 and Nup60 are required for their recruitment to NPCs.

Further experiments identified nuclear localization signals in the N termini of Nup1 and Nup60 that facilitate interaction with karyopherin complexes for nuclear import. A Nup60 amphipathic helix localized to the entire nuclear envelope rather than to NPC puncta, whereas a Nup60 fragment comprising the amphipathic helix and its adjacent α-helical region was sufficient to associate with NPCs. These results indicate that the α-helical region helps to target the lipid-binding amphipathic helix to NPCs.

Amphipathic helices can remodel membranes by hydrophobic insertion, functioning as a 'wedge' in one leaflet of the lipid bilayer. Consistent with this, yeast cells overexpressing a Nup1 or Nup60 fragment that comprised the amphipathic helix had highly curved membrane protrusions on the nuclear surface, termed expansion membranes, which were associated with NPC clustering. Mutations of the Nup1 or Nup60 amphipathic helix that decreased its affinity for lipids did not generate expansion membranes. Overexpression of the whole Nup60 N terminus (the amphipathic helix and α-helical region) resulted in the formation of more highly curved intranuclear membrane tubules, which suggests that the Nup60 α-helical region may increase the degree of membrane curvature that is induced by the amphipathic helix. *In vitro* experiments confirmed that the Nup1 and Nup60 amphipathic helices can bind directly to lipids and induce membrane curvature, as shown by the evagination of liposomes into tubular structures.

In support of the idea that such membrane remodelling induced by basket nucleoproteins is relevant to the integrity of NPCs, yeast cells expressing an N-terminal-deleted form of Nup1 under membrane stress had distinct herniations of the nuclear envelope that created membrane seals over the cytoplasmic face of NPCs. Synthetic lethality resulted when the Nup1 and Nup60 amphipathic helices were deleted in conjunction with the transmembrane nucleoprotein Pom34. In conclusion, the authors suggest that Nup1 and Nup60 contribute to a "network of membrane-shaping forces" that are required for NPC assembly and maintenance.

Kirsty Minton

ORIGINAL RESEARCH PAPER Mészáros, N. *et al.* Nuclear pore basket proteins are tethered to the nuclear envelope and can regulate membrane curvature. *Dev. Cell* **33**, 285–298 (2015)

> "the Nup1 and Nup60 amphipathic helices can bind directly to lipids and induce membrane curvature"

© 2015 Macmillan Publishers Limited. All rights reserved