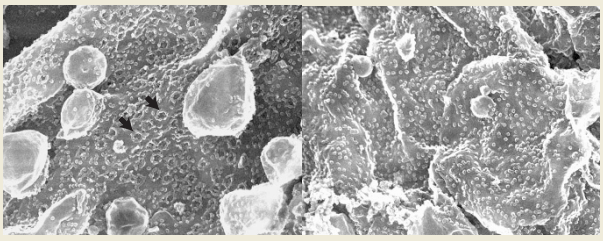
Nuclear pore assembly: locating the linchpin

Because the genome is enclosed within the nucleus of all eukaryotic cells, it is imperative that there is efficient communication between the nucleus and the cytoplasm. From yeast to humans, the nuclear pore complex (NPC) provides such a gateway. Despite its critical function in regulating nuclear import and export, however, we know little about how the NPC is assembled and incorporated into the nuclear envelope. Two groups have now identified the nucleoporin 107–160 sub-complex as a key building block of the pore, loss of which results in nuclei devoid of NPCs.

Part of the challenge in identifying the structural foundation of the NPC is its sheer complexity. The vertebrate NPC is ~120 million daltons, and only recently has the full list of its ~30 nucleoporins (each of which are present in at least eight copies) been revealed. From comparative analysis of yeast and vertebrate pores, certain conserved sub-complexes have been identified. The vertebrate Nup107–160 complex, for example, seems to be homologous to the yeast Nup84 complex, containing at least four equivalent proteins and one close neighbour: Nup107, Nup160, Nup96, Sec13, and Nup133.

In the new work, both Walther *et al.* (*Cell* **113,** 195–206 (2003)) and Harel *et al.* (*Mol. Cell* **11,** 1–20 (2003)) focused on post-mitotic NPC assembly. Intrigued that depletion of different members of the Nup107–160 complex by RNA interference resulted in cells with impaired pores, both groups used nuclear reconstitution in *Xenopus laevis* egg extracts to probe further. Using different antibodies, they depleted extracts of the Nup107–160 complex and assembled nuclei. Both found that loss of the Nup107–160 complex was sufficient to block pore assembly and, using scanning electron microscopy (see figure), they revealed that underlying these defects was a marked absence of NPCs in the nuclear envelope. Interestingly, Harel *et al.* also identified a sixth and vital member of the Nup107–160 complex, Nup85, which is conserved in the yeast Nup84 complex.



The Nup107–160 complex mediates pore assembly. Nuclei were assembled in either mock-depleted extracts (left) or Nup107-depleted extracts (right) and processed for scanning electron microscopy. Image reproduced from Walther *et al.* © (2003) with permission from Elsevier Science.

So where in the nuclear envelope assembly process does the Nup107–160 complex function? By varying the timing of 'add-back', Walther *et al.* found that the Nup107–160 complex is certainly required before nuclear envelope closure. By examining the kinetics carefully, they noticed that loss of the sub-complex prevents nucleoporin recruitment to the chromatin surface. On this basis, they propose that the Nup107–160 complex may mediate the formation of a 'pre-pore' complex on the chromatin surface, although such a model needs to be tested further and assessed for its relevance to NPC assembly in interphase cells. Another key question is whether the complex needs to be present on both sides of the nuclear envelope to facilitate new pore formation. However, with this linchpin in hand, we can now hope to gain new understanding of the foundations on which the nuclear pore is built.

ALISON SCHULDT

The cutting edge of mitochondrial fusion

Michael P. Yaffe

Mitochondrial membrane fusion contributes to the shape and distribution of mitochondria in the eukaryotic cytoplasm. Recent work shows that a key component of the fusion reaction, Mgm1p, is activated by a novel mitochondrial protease related to the *Drosophila melanogaster* signalling protein Rhomboid.

Mitochondria are dynamic organelles. Their morphology and distribution change in response to cellular activity, nutritional status and developmental programmes[1]. Although they possess characteristic, internal structural features and function as essential centres of energy metabolism in almost all eukaryotic cells, their external shapes display great variability. Such alterations of mitochondrial morphology are sculpted by the fusion and division of mitochondrial tubules[2]. These processes underlie both the subtle rearrangements of mitochondrial networks that occur during cellular growth and division and the marked re-organisations of mitochondria that sometimes accompany differentiation, cellular senescence or apoptosis[1,3]. Recent research has identified many of the proteins that mediate mitochondrial fusion and division, but the regulation of these key processes is poorly understood. Now, two independent studies by McQuibban *et al.*[4] and Herlan *et al.*[5] describe intramembrane proteolysis as a novel mechanism for the activation of

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