



 GENE EXPRESSION

Beyond pores

In eukaryotic cells the nuclear envelope is permeated by nuclear pore complexes (NPCs), which are large multiprotein channels consisting of multiple copies of ~ 30 different nucleoporins. These can be divided into scaffold nucleoporins (which are embedded in the nuclear membrane) and peripheral nucleoporins (which extend into the pore channels or as filaments into the cytoplasm and the nucleoplasm). In addition to functioning as transport channels, NPCs have been implicated in the regulation of gene expression and chromatin organization. In yeast, nucleoporins associate with promoters and 3' ends of actively transcribed genes, the expression of which increases on interaction with NPCs. However, the role of nucleoporins in the regulation of gene expression in higher eukaryotes, and whether nucleoporin–chromatin interactions occur exclusively at nuclear pores, is unknown. Two studies published in *Cell* now show that nucleoporins have a role in promoting transcription in *Drosophila melanogaster* and that this occurs in the nucleoplasm, away from nuclear pores.

Kalverda *et al.* mapped the interactions of nucleoporin 50 (NUP50), NUP62 and NUP98 with chromatin in *D. melanogaster* embryonic cells. They found that the three nucleoporins interact with a similar set of actively transcribed genes and that these genes are predominantly involved in development and the cell cycle.

In higher eukaryotes, many peripheral nucleoporins, including NUP50, NUP62 and NUP98, are mobile and move on and off NPCs. To distinguish between nucleoporin–chromatin interactions that occur in the nucleoplasm and at NPCs, the authors used a truncated version of NUP98 that localizes exclusively to the nucleoplasm and NUP98 fused to an integral membrane nucleoporin, which tethers to the NPC. They found that nucleoplasmic NUP98 accounts for most NUP98-bound chromatin domains and that these domains are different from those bound by NPC-tethered NUP98.

Furthermore, the genes that interact with nucleoplasmic NUP98 showed high levels of transcription, suggesting that nucleoplasmic nucleoporins activate gene expression. This was confirmed by the observation that NUP50- and NUP98-bound genes show reduced levels of expression following NUP50 and NUP98 knockdown, and are upregulated by the overexpression of nucleoplasmic NUP98.

Capelson *et al.* carried out immunofluorescence studies on polytene chromosome spreads using antibodies against components of the NPC. They detected specific binding patterns — that varied at different developmental stages — for each NPC component, suggesting that they are targeted to particular genomic sites and that target genes are important for development. Furthermore, staining of intact nuclei revealed that SEC13 and NUP88 (two peripheral nucleoporins) interact with chromatin away from the nuclear envelope, which confirms that they function in the nucleoplasm.

By comparing the chromatin binding patterns of nucleoporins with those of active RNA polymerase II (RNAPII), Capelson *et al.* showed that nucleoporins bind to actively transcribed genes, which suggests that they promote transcription. Indeed, SEC13 knockdown reduced target gene activation and RNAPII staining at SEC13-bound chromatin sites, confirming a role for peripheral nucleoporins in transcriptional induction.

Together, these studies show that nucleoporins activate genes in the nucleoplasm, and increase the evidence for NPC components having important roles beyond that of regulating transport across the nuclear envelope.

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ORIGINAL RESEARCH PAPERS Kalverda, B. *et al.* Nucleoporins directly stimulate expression of developmental and cell-cycle genes inside the nucleoplasm. *Cell* **140**, 360–371 (2010) | Capelson, M. *et al.* Chromatin-bound nuclear pore components regulate gene expression in higher eukaryotes. *Cell* **140**, 372–383 (2010)