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DIFFERENTIATION

Nuclear pores at the core

In recent years, views of the functions of the nuclear pore complexes (NPC) have broadened: in addition to regulating transport between the nucleus and cytoplasm, they have roles in gene regulation and chromatin organization. The importance of transport-independent functions of the NPC is emphasized by a recent paper showing that an NPC component is required for cellular differentiation.

Several studies have shown that the expression of some NPC proteins varies among tissues, and mutations in NPC components can cause diseases with tissue-specific phenotypes. D'Angelo *et al.* explored the observation that the transmembrane nucleoporin NUP210 (also known as GP210) — one of the three NPC components that are integral membrane proteins — is absent in proliferating mouse myoblasts but is highly expressed during differentiation of these cells into myotubes. They ablated *Nup210* expression during myoblast differentiation using RNAi and found that this inhibited myotube formation. The authors confirmed that NUP210 is only present at the nuclear envelope during this process, so it seemed to be influencing differentiation while it was associated with the NPC.

However, when the authors checked the distribution of inner nuclear membrane proteins and the efficiency of nucleocytoplasmic transport, they found that depletion of NUP210 had no effect. Instead, microarray analysis of gene expression in NUP210-knockdown myotubes revealed 255 genes that had significant changes in expression (191 were downregulated and 64 were upregulated). The downregulated genes included several with known roles in myogenesis. The authors showed that reducing expression of these genes by RNAi inhibited myotube formation, but individually ablating expression of each had a weaker effect than that caused by NUP210 reduction. Therefore, the role of NUP210 in myogenesis seems to be through the simultaneous regulation of several important differentiation genes.

D'Angelo *et al.* went on to show that NUP210 is also crucial for the differentiation of mouse embryonic stem cells into neuroprogenitors, thus implicating the NPC in diverse cell differentiation programmes. As the NPC is viewed as a site of transcription, one possible mechanism is that NUP210 modulates the activity of transcriptional regulatory proteins; this will provide an avenue for future enquiries.

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ORIGINAL RESEARCH PAPER D'Angelo, M. A. *et al.* A change in nuclear pore complex composition regulates cell differentiation. *Dev. Cell* 19 Jan 2012 (doi:10.1016/j.devcell.2011.11.021)

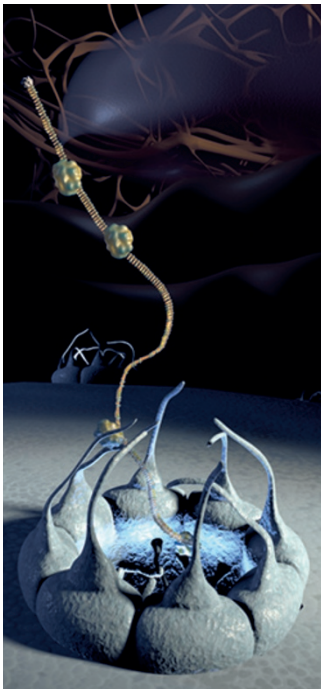

Image from the *Nature Reviews Genetics* animation on RNA interference, which was produced in association with Arkitek Studios. http://www.nature.com/nrg/multimedia/rnai/index.html