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DEVELOPMENT

NUP210 takes cell fate decisions

Nuclear pore complexes (NPCs) assemble at the nuclear envelope as combinations of ~30 different nucleoporins (NUPs). Some NUPs exhibit cell type-specific expression, and this implies that, along side their well-characterized role in nucleocytoplasmic transport, they may be involved in other cell functions. In *Developmental Cell,* Hetzer and colleagues describe a role for the transmembrane protein NUP210 in the regulation of gene expression during cell differentiation.

NUP gene expression analysis in differentiating C2C12 myoblasts revealed that, although it is absent from quiescent and proliferating myoblasts, NUP210 is upregulated in postmitotic myotubes. Interestingly, short hairpin RNA-mediated inhibition of NUP210 induction in differentiating myoblasts did not prevent their exit from the cell cycle but inhibited cell–cell fusion and increased cell mortality, thereby preventing myotube formation. Thus, NUP210 expression is induced during myogenesis and is required for the later stages of myoblast differentiation.

So, how does NUP210 expression promote myocyte differentiation? The authors identified NUP210 at the nuclear envelope as an NPC component, but they did not detect NUP210 at the plasma membrane, thus excluding a potential role in cell–cell fusion. Moreover, NUP210 was dispensable for global nucleocytoplasmic transport and the targeting of inner nuclear membrane proteins involved in myogenesis. Moreover, NUP210 depletion in postmitotic myotubes did not result in altered global nuclear transport rates. Together, these findings suggest that NUP210 promotes myoblast differentiation through a nuclear transport-independent mechanism, although its contribution to specific transport processes could not be excluded.

Strikingly, depletion of NUP210 in myotubes resulted in altered gene expression. 75% of the differentially expressed genes were found to be downregulated in the absence of NUP210. Several downregulated genes, such as growth differentiation factor 5 (*Gdf5*), neuraminidase 2 (*Neu2*) and chloride intracellular channel 5 (*Clic5*), have previously been linked to myogenesis, and deletion of GDF5, NEU2 or CLIC5 reproduced the phenotype of NUP210-deficient myoblasts. By contrast, overexpression of a NUP210–green fluorescent protein fusion protein in C2C12 cells induced *Gdf5*, *Neu2* and *Clic5* expression, as well as tubule formation, in the absence of differentiation conditions, and this effect depended on the expression of *Neu2* and *Gdf5*. Thus, NUP210 upregulation and its addition to the NPCs of differentiating myoblasts promote myotube formation through the induction of myogenesis-related genes.

Finally, the authors demonstrated a similar role for NUP210 in differentiating neuroprogenitor cells. So, they suggest that altering the composition of NPCs, through the addition of cell type-specific NUPs, such as NUP210, might be a general regulatory mechanism in cell differentiation.

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> “a role for … NUP210 in the regulation of gene expression during cell differentiation.”