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Pore before seal

A checkpoint coordinates assembly of nuclear pore complexes (NPCs) with formation of the nuclear envelope (NE), according to Wolfram Antonin, Iain Mattaj, and colleagues (EMBL, Heidelberg, Germany).

NPC assembly begins with the binding of the Nup107-160 complex of nucleoporins to chromatin. The EMBL group looked at two other nucleoporins, gp210 and pom121. These nucleoporins span the nuclear membrane and thus might link NPC assembly on the two sides of the NE as it reforms after mitosis.

Although gp210 was not needed for NPC assembly or NE formation in frog egg extracts, pom121 was essential for both processes. After pom121 depletion, vesicles docked onto chromatin but did not fuse with each other to form a complete NE.

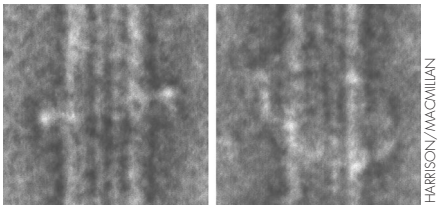
But if Nup107-160 was also depleted from the extracts, NE formation proceeded normally, albeit without insertion of NPCs. Thus pom121 is not absolutely required for NE formation, but pom121's absence can block NE membrane fusion events if Nup107-160 is present.

The assembly of Nup107-160 on chromatin happens early and does not require membranes. But prior NE formation does block the access of Nup107-160 to chromatin and thus its assembly. It may be essential to ensure that this initial assembly and its link to a transmembrane component and the outside world are complete before taking the step of sealing off the nucleus as a separate compartment. JCB

Reference: Antonin, W., et al. 2005. *Mol. Cell.* 17:83–92.

Kinetochores hold on with a ring

A complex that links a budding yeast kinetochore to a microtubule (MT) forms a ring around the MT, based on structures from two groups. The ring may help kinetochores to keep hold of an MT, even as the MT shrinks towards the spindle pole during anaphase.


HARRISON/MACMILLAN

DASH forms a collar around microtubules.

Stephen Harrison (Harvard Medical School, Boston, MA) and Peter Sorger (MIT, Cambridge, MA) are hoping to analyze the structure of the 60 or more yeast kinetochore proteins one subcomplex at a time. The current success with the 10-protein DASH complex, Harrison says, "came about on a dare to see if [first author JJ Miranda] could coexpress the whole thing in *E. coli*." Happily, the bold experiment worked, the purified complex bound MTs, and the electron micrographs clearly showed rings of DASH complex encircling an MT.

The ring structure immediately suggests a mechanistic possibility. "A major way in which evolution has made entities processive is by making rings," says Harrison. In this case, the outward splaying of MT protofilaments as the end of an MT falls apart should keep the ring on the intact section of the MT. This would effectively translocate the ring and thus the attached kinetochore towards the pole-attached end of the shrinking MT. Indeed, Stefan Westermann and Georjana Barnes (University of California, Berkeley, CA) used Miranda's construct to not only come up with a similar structure, but also to gain evidence for mobility of DASH rings along MTs. JCB

References: Miranda, J.L., et al. 2005. *Nat. Struc. Mol. Biol.* doi:10.1038/nsmb896.
Westermann, S., et al. 2005. *Mol. Cell.* 17:277–290.

Development is easy

Metazoan cell lineages can be collapsed to a set of rules that is surprisingly simple, according to Ricardo Azevedo (University of Houston, Houston, TX), Armand Leroi (Imperial College, Ascot, UK), and colleagues. Decoding the biochemical basis of the rules should provide a complete recipe book for development.

Azevedo brought three influences to the study: his background in evolutionary biology; his adopted field of worm biology; and computer science from collaborators. When he joined Leroi's worm lab he "was immediately struck by the lineage data," he says. "But there were more data to be extracted."

As in phylogenetic trees, there were repeating patterns. A handful had been noted by others, but no systematic study had been undertaken. This is where a simple computer algorithm helped out.

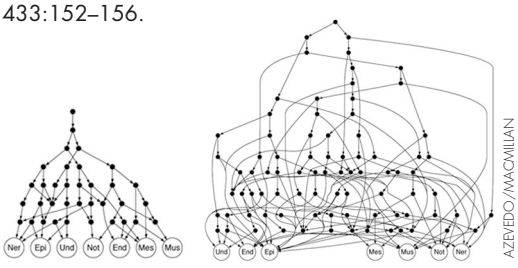
"For any particular cell division we can find another that forms the same pattern," Azevedo explains. "Then we collapse [those into one rule] until we can't do it any more because there is no more redundancy. That gives us the minimal number of states that is required."

In silico evolution of the simplified rule sets did not yield much further simplification, as long as the final distribution of cell types was constrained. Much simpler rule sets could be invented but only by going via intermediate states that had very different cell type distributions.

Azevedo thinks that simplicity arises as evolution strives to minimize the time and genetic information necessary for development. The tendency of evolution to modify what already exists, rather than invent new systems for each new function, may also favor simplicity.

In silico genetic circuits that generate lineages are allowing Azevedo to study the rules behind lineage formation. Eventually he hopes to understand what biochemical combinations of regulators form the basis for each of his rules, but that may have to wait for next-generation expression chips that can analyze individual cells. JCB

Reference: Azevedo, R.B.R., et al. 2005. *Nature.* 433:152–156.



AZEVEDO/MACMILLAN

An actual lineage (left) is much simpler than a randomly generated lineage (right).