MEMBRANE DYNAMICS

As if by magic

The endoplasmic reticulum (ER) contains dynamic subdomains — transitional ER (tER) sites — that are specialized for coat protein II (COPII)-vesicle production and that are distinct from the ER in terms of their function, biochemistry and morphology. Although these tER sites were described more than 25 years ago, how they are formed and maintained, and how their dynamics affect Golgi dynamics, has remained unclear. Now, though, in *Nature Cell Biology*, Glick and colleagues provide new insights.

The authors labelled tER sites of the budding yeast *Pichia pastoris* using a green fluorescent protein (GFP)–Sec13 construct (Sec13 is a COPII-coat subunit), and used three-dimensional time-lapse (4D) confocal video microscopy to monitor these tER sites. In both the mother cells and buds, they saw the apparent *de novo* formation of tER sites — small fluorescent spots appeared as if by magic and then increased in size. They also

noted that tER sites can fuse, and that they seem to have a 'preferred' size — they shrink after fusion and expand after *de novo* formation.

To study how tER dynamics relate to Golgi dynamics, Glick and co-workers used Sec7 — a late Golgi protein. They overexpressed a Sec7–*Discosoma* red fluorescent protein (DsRed) construct, and used two-colour 4D microscopy to monitor tER sites (GFP–Sec13) and the Golgi (Sec7–DsRed) at the same time. They consistently saw that tER-site formation is tightly linked to the apparent *de novo* formation of Golgi structures. In addition, they saw that late Golgi elements labelled with Sec7–DsRed often move to regions of polarized growth; that is, away from the tER and towards the bud.

Glick and colleagues have shown that tER sites and Golgi structures can apparently form *de novo* in *P. pastoris*, although they note that templates could be present that are invisible in their experiments. However, despite these uncertainties, their data "can be explained by assuming that tER sites give rise to Golgi cisternae that continually mature".

Rachel Smallridge

References and links

ORIGINAL RESEARCH PAPER Bevis, B. J. *et al.* Apparent *de novo* formation of transitional ER sites and Golgi structures in *Pichia pastoris*. *Nature Cell Biol.* **4**, 750–756 (2002)

FURTHER READING Glick, B. S. *et al.* Can the Golgi form *de novo*? *Nature Rev. Mol. Cell Biol.* **3**, 615–619 (2002)

WEB SITE

Benjamin Glick's laboratory: http://mgcb.bsd.uchicago.edu/index3.html?content=faculty/bGlick/index.html

CHROMOSOME BIOLOGY

Make it accessible

The cohesin complex regulates sister chromatid pairing in early mitosis and, subsequently, in metaphase–anaphase transition, arranges for the sister chromatids to separate again. To do this, cohesin needs to access nucleosomal DNA and, in *Nature*, Ramin Shiekhattar and colleagues now report the identification of a DNA-binding site for cohesin. In addition, they propose a role for a chromatin-remodelling complex in mediating cohesin's access to chromatin.

Shiekhattar and co-workers isolated a chromatin-remodelling complex that contains SNF2h (a member of the ISWI family of chromatin-remodelling proteins), subunits of the NuRD chromatin-remodelling complex, and the cohesin complex. The authors found that an essential subunit of the cohesin complex, hRAD21, immunoprecipitates specifically with SNF2h and the NuRD component Mi2, and that recombinant hRAD21 binds to SNF2h directly.

Next, Shiekhattar and colleagues used chromatin immunoprecipitation to find *in vivo* binding sites for hRAD21 and SNF2h on chromosomes and identified a DNA site that contains Alu repeats — a class of short repeat sequences that are dispersed throughout the genome. However, not all of the seemingly indistinguishable Alu sites bound hRAD21, which indicates that the histones associated with the Alu-repeat DNA might be modified differently. Indeed, the authors found a correlation both between methylation of lysine 4 of histone H3 and the binding of SNF2h to chromatin, and between the acetylation of histone H3 or H4 and SNF2h binding.

In addition, the fact that Alu repeats are rich in CpG dinucleotides makes them potential targets for DNA methylation. In cells treated with a DNA methyltransferase inhibitor, binding of both SNF2h and hRAD21 was strong, which indicates, in addition to histone modification, a regulatory function for DNA methylation.

So, what is the functional significance of chromatin-remodelling activity in cohesin binding? To answer this question, Shiekhattar and colleagues created a SNF2h mutant defective in ATP hydrolysis, which is essential for activity. Cohesin binding was reduced in the presence of mutant SNF2h, indicating that chromatin-remodelling activity has an active role in loading cohesin onto chromatin.

These data reveal an interesting new function for the chromatin-remodelling machinery in DNA replication. The precise mechanism by which chromatin-remodelling complexes mediate the binding of cohesin to chromosomes will be the focus of future studies.

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References and links

ORIGINAL RESEARCH PAPER Hakimi, M.-A. *et al.* A chromatin remodelling complex that loads cohesin onto human chromosomes. *Nature* **418**, 994–998 (2002)