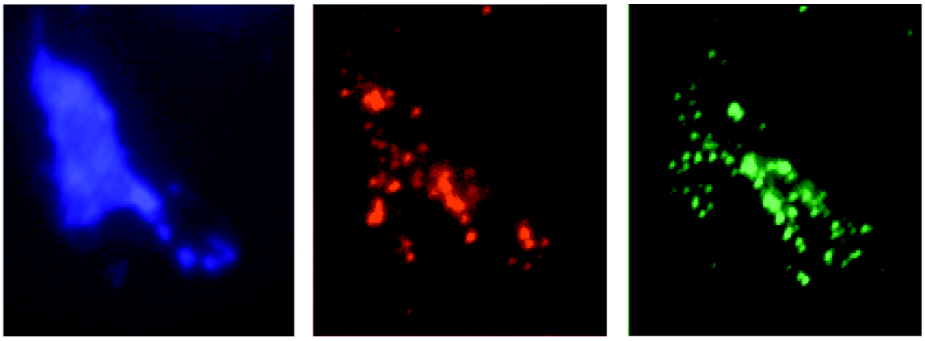
disassembly, releasing the cargo to the cytoplasm. Different receptors recognize different classes of proteins, tRNAs or U snRNPs.

Although much less is known about mRNA export, a fundamentally different mechanism may be at work. This may be because of the greater size of the cargo, as mRNAs are exported as large ribonucleoprotein complexes (mRNPs). Some of the proteins bound to the mRNA are removed from mRNPs immediately before translocation through the NPC, but others are removed on the cytoplasmic side of the NPC and then shuttle back into the nucleus. By analogy with protein transport, it was thought that proteins bound to mRNAs would contain NESs and be recognized by one or more export receptors. The export of intron-containing HIV-1 mRNAs requires the NES-containing viral Rev protein and the export receptor Crm1 (also known as Xpo1 in budding yeast), and probably proceeds by this mechanism, as does the export of 5S ribosomal RNA.

Cargoes have been identified for most importin-family receptors in *Saccharomyces cerevisiae*. Analysis of mRNA export in strains mutant for each receptor indicates that Xpo1/Crm1 is the only candidate for participation in mRNA export. In *xpo1-1* mutant cells, poly(A)$^+$ RNA accumulates rapidly in nuclei after a shift to the non-permissive temperature, indicating that Xpo1/Crm1 may recognize mRNP complexes and mediate their export[2]. Strong mRNA-export defects are also seen in strains carrying mutations of Ran or its effectors, a finding that is consistent with a mechanism for mRNA export similar to that used for protein transport. Two recent studies[3,4], however, suggest that Crm1/Xpo1 has no direct role in mRNA export. First, the rate of protein synthesis is unaffected by mutation of *XPO1*, implying that mRNA export continues in mutant cells at a rate sufficient to maintain a normal rate of protein synthesis. Second, over-expression of Dbp5, a shuttling DEAD-box protein and essential

# Matchmakers for sister-chromatid cohesion



During cell division, a cell must faithfully duplicate its chromosomes and distribute them equally to both daughter cells. These processes, including the establishment and destruction of sister-chromatid cohesion, have to be tightly controlled as any error can result in cells with aberrant chromosome numbers, which may die or become tumour cells. Sister-chromatid cohesion is established during S phase and persists until anaphase, when sister chromatids, having been correctly aligned on the metaphase plate, are pulled apart to opposite poles of the mitotic spindle. In budding yeast, sister-chromatid cohesion is mediated by a complex, known as cohesin, containing the proteins Scc1p, Scc3m, Smc1p and Smc3p. Shortly before S phase, cohesin binds to centromeres and specific sites along chromosome arms, and remains bound until Scc1p is cleaved at the onset of anaphase, disrupting cohesion and allowing sister-chromatid separation.

But how is the cohesin link between sister chromatids established in the first place? It is known that at least two more proteins, Eco1p and Scc2, are required. As neither is part of the cohesin complex itself, it seems they function as matchmakers rather than forming linkage structures themselves. Eco1p is thought to have a role in S phase, after cohesin has bound to chromosomes, in the formation of tight cohesive structures between sister chromatids, but not in the maintenance of these bonds at later stages of the cell cycle. Now, a paper by Ciosk and colleagues (*Mol. Cell* **5,** 243–254; 2000) sheds light on the function of Scc2p. The authors identify Scc4p as a new binding partner of Scc2p and show that both proteins are required for the initial binding of cohesin to chromosomes. In the absence of either Scc2p or Scc4p, the cohesin complex assembles normally but fails to bind to chromosomes. Interestingly, Scc2 and Scc4 themselves bind to chromosomes, presumably as a complex. The picture shows chromosome spreads with DNA stained in blue (left panel) and Scc2p in green (right panel).

How then does the Scc2p–Scc4p complex mediate cohesin binding to chromosomes? Ciosk and colleagues show that the localization pattern of cohesin does not match that of Scc2p–Scc4p (see middle panel, Scc1p stained in red). It is therefore unlikely that the Scc2p–Scc4p complex simply marks chromosomal sites for cohesin loading. The authors also demonstrate that the Scc2p–Scc4p complex is no longer required after S phase to maintain cohesion, again implying that Scc2p–Scc4p is not simply a cohesin receptor. One might speculate that Scc2p–Scc4p facilitates cohesin binding by changing either the conformation of the cohesin complex or the structure of chromatin. Binding of both cohesin and the Scc2p–Scc4p complex to chromatin is highly salt-resistant, indicating that higher-order structures may be involved. One could therefore imagine that the binding of Scc2p–Scc4p to chromosomes exerts a long-range effect that allows cohesin binding at a distant site. Whatever the precise mechanism turns out to be, these new findings increase our understanding of the matchmakers that form the temporary bonds between sister chromatids at the appropriate stage of the cell cycle, and future work will no doubt shed further light on this crucial process.

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