that microtubules remain attached to anaphase kinetochores that cannot produce tension. The high concentration of Ran-GTP in interphase nuclei might also prevent inadvertent checkpoint activation.

A paradigm is emerging from these studies, in which structural components of particular cellular machines are re-used for different functions in different contexts and at distinct times in the cell cycle. The teleological question is whether the cell has evolved such multiple uses for reasons of economy, through an accident of evolutionary history, or perhaps to provide an additional layer of control over the order of events. In this case, we now need to solve the puzzles of what regulates the movement of proteins between the kinetochore and the NPC, and determine the function of Ran-GTP in spindle checkpoint signalling. □

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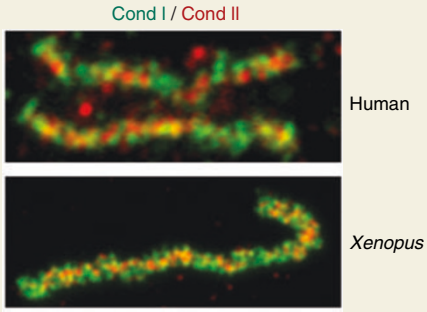
Architects of the chromosome

Chromosome condensation represents the first critical step in mitotic progression. A central component in this process is condensin, a multiprotein complex that converts amorphous interphase chromatin into a compact, well-organized, structure. Although the broad role of condensin has been appreciated for several years, a precise mechanistic understanding of its function has remained elusive. Now, a study by Tatsuya Hirano and colleagues (*Cell* **115,** 109–121 (2003)) provides intriguing insights into the role of condensin by suggesting that a distinct condensin complex may also function in concert with the original complex to regulate chromosomal architecture in vertebrate cells.



A pair of chromosomes stained with antibodies specific for condensin I (green) and condensin II (red).

The canonical condensin complex (now referred to as condensin I) consists of five subunits: two core subunits are members of the SMC (structural maintenance of chromosomes) ATPase family, and two out of three accessory subunits share a degenerate repeating motif, the HEAT repeat. Each subunit is necessary for establishing and maintaining mitotic chromosome architecture both *in vitro* and *in vivo*, and each is also essential for viability in a number of organisms. The two core SMC subunits are known to adopt a V-shaped conformation, with ATP-binding sites at the distal ends to which the three non-SMC subunits bind. ATP hydrolysis then allows condensin to introduce superhelical tension into DNA strands. There have also been some hints that condensin may be involved in maintaining chromosomal architecture.

In a new development, Hirano and colleagues now identify a second condensin complex, condensin II, which may function with condensin I to fulfil such an architectural role. By screening databases for HEAT-containing sequences, the authors identified and cloned a molecule that could be co-immunoprecipitated with the core SMC subunits. Furthermore, they identified two other subunits that bind to the SMC core but which are distinct from the previously identified accessory subunits. Thus, condensin II shares the two core SMC subunits with condensin I, but contains three distinct accessory subunits.

The authors then use RNA interference (RNAi) to examine the *in vivo* function of individual subunits in human cells. Depletion of either core subunit resulted in fuzzy chromosomes with no discernable chromatids. In contrast, depletion of condensin I-specific subunits resulted in swollen chromosomes, whereas depletion of condensin II subunits resulted in curly chromosomes. Next, the authors turned to *in vitro* analysis of condensin function in *Xenopus laevis* egg extracts. Immunodepletion of condensin I resulted in masses of decondensed chromatin lacking chromosomal organization, whereas after immunodepletion of condensin II, chromosomes formed, but had an abnormal, wavy, morphology. Finally, immunolocalization studies of chromosomes assembled *in vivo* (see Figure, top panel) and *in vitro* (see Figure, bottom panel) showed that condensins I and II were both localized along chromatid arms, but each to distinct regions.

The authors propose that either condensins I and II form independent spirals along chromosome arms, or that they alternate in a single spiral. In both models, however, condensin I is the main organizer of chromatin fibres, whereas condensin II provides the additional architectural function. Much work will be required to address the specific functions of, and interactions between, the two complexes. However, this study represents a significant advance in the field and suggests that a fine balance between these two condensin complexes is essential for the establishment and maintenance of chromosome architecture.

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