IN BRIEF

CELL CYCLE

Cohesin release is required for sister chromatid resolution, but not for condensin-mediated compaction, at the onset of mitosis.

Losada, A. *et al*. *Genes Dev*. **16**, 3004–3016 (2002)

Cohesin and condensin are protein complexes that mediate sister-chromatid cohesion and condensation, respectively, in preparation for sister-chromatid separation. In metazoans, cohesin is released during prophase, which occurs at the same time as condensin association. Losada *et al.* now show that two mitotic kinases, aurora B and polo-like kinase Plx1, cooperate to dissociate cohesin from chromatin at the onset of mitosis, which is essential for sister-chromatid resolution, but not for condensin-mediated compaction.

DNA REPLICATION

An ACF1–ISWI chromatin-remodeling complex is required for DNA replication through heterochromatin.

Collins, N. *et al*. *Nature Genet.* **32**, 627–632 (2002)

The mechanism that enables the DNA replication machinery to penetrate heterochromatin is poorly understood. However, Collins *et al.* now provide evidence that an ACF1–ISWI chromatin-remodelling complex is required for replication through highly condensed regions of chromatin. Depletion of ACF1 or the ISWI isoform SNF2H causes a delay in DNA replication in S phase. In addition, chemically decondensing the heterochromatin abolishes the requirement for ACF1 and SNF2H.

DEVELOPMENT

Identification of a Wnt/Dvl/β-catenin→Pitx2 pathway mediating cell-type-specific proliferation during development.

Kioussi, C. *et al*. *Cell* **111**, 673–685 (2002)

This paper describes a cell-specific proliferation strategy during cardiac and pituitary development, which requires the tissue-restricted transcription factor Pitx2. Activation of the Wnt/Dvl/β-catenin signalling pathway results in the rapid induction of *Pitx2*, and the binding of Pitx2 to the promoter of growth-control genes, such as *Cyclin D2*, that act in G1. Pitx2 then recruits a series of coactivator complexes required for promoter stimulation in a temporal and growth-factor-specific manner.

SIGNALLING

The protein kinase complement of the human genome.

Manning, G. *et al*. *Science* **298**, 1912–1918 (2002)

Most protein kinases belong to a single superfamily, the members of which contain a eukaryotic protein kinase (ePK) catalytic domain. Manning *et al.* have now catalogued the protein kinase complement of the human genome (the 'kinome') and identified 478 ePKs and 40 'atypical' protein kinase genes. Among these 518 putative protein kinases, 71 have not been previously reported or described as kinases. Importantly, 244 kinases map to disease loci or cancer amplicons.

INFLAMMATION

A combined effort

In response to injury, epithelial cells recruit inflammatory cells and somehow manage to confine them to a restricted area. How this occurs is now clearer, following a report by Li *et al.* in *Cell* that provides evidence that the proteinase matrilysin (which is also known as matrix metalloproteinase 7), the proteoglycan syndecan 1 and the chemokine KC act in concert to direct inflammatory cells to sites of injury in the lung.

Having observed increased matrilysin expression in lung alveolar epithelial cells in a bleomycin-induced mouse model of lung fibrosis, the authors used matrilysin-null (*MAT*$^{-/-}$) mice to assess the role of matrilysin in injury. *MAT*$^{-/-}$ mice showed less extensive alveolar fibrosis and were protected against bleomycin-induced lethality compared with wild-type animals. The authors consistently saw less neutrophils in the lumen of *MAT*$^{-/-}$ lung alveoli — they all remained in the interstitial perivascular space.

So, matrilysin might be regulating the activity of a neutrophil chemotactic factor derived from epithelial cells; neutrophils, macrophages and interstitial cells don't express matrilysin. A candidate chemoattractant was KC, which the authors indeed found to be low (at the protein level) in *MAT*$^{-/-}$ broncho-alveolar lavage (BAL) but to accumulate in the lung tissue overall, compared with wild-type mice.

The indication, then, was that matrilysin somehow affects the movement of KC into the lumen. But KC isn't a direct matrilysin substrate, so what was the intermediate? On the basis of published information, syndecans were likely suspects — and syndecan 1 is also expressed in lung epithelial cells. In response to bleomycin, a marked increase in soluble syndecan 1 in BAL, but reduced staining for syndecan 1 in alveoli, occurred in wild-type animals. No such change occurred in *MAT*$^{-/-}$ mice. Cell-culture studies showed that matrilysin can cleave syndecan, and immunoprecipitation experiments then showed that KC binds to the ectodomain of syndecan 1 in BAL of wild-type mice. Further experiments, using bleomycin-treated syndecan 1-null mice, indicated that syndecan 1 was needed to mobilize KC.

An attractive model is that injury induces epithelial cells to synthesize, secrete and deposit KC onto syndecan 1. Matrilysin then cleaves this, freeing the syndecan ectodomain–KC complex, which entices neutrophils to the alveolar space.

Katrin Bussell

References and links

ORIGINAL RESEARCH PAPER Li, Q. *et al.* Matrilysin shedding of syndecan-1 regulates chemokine mobilization and transepithelial efflux of neutrophils in acute lung injury. *Cell* **111**, 635–646 (2002)