IN BRIEF

REPROGRAMMING

Direct cell reprogramming is a stochastic process amenable to acceleration

Hanna, J. *et al. Nature* 8 Nov 2009 (doi:10.1038/nature08592)

The overexpression of certain transcription factors can lead to the reprogramming of somatic cells to induced pluripotent stem (iPS) cells, but only a few cells actually become reprogrammed. To investigate this, Hanna *et al.* used a system in which somatic cells (in this case B cells) have the same integration pattern of these transcription factors, which are expressed following drug treatment. Reprogramming (assessed by the expression of the pluripotency factor NANOG tagged with green fluorescent protein) was observed in 3–5% of the cells after 2 weeks in culture and increased to >92% after 18 weeks, indicating that it is a stochastic process during which all cells can become iPS cells. Inhibition of p53 or its effector p21 accelerated reprogramming by increasing the rate of cell division. By contrast, ectopic expression of NANOG increased the reprogramming rate independently of cell division by a cell-intrinsic mechanism. So, this study identifies two modes of generating iPS cells: cell division-dependent and cell division-independent reprogramming.

CELL CYCLE

DNA damage checkpoint maintains Cdh1 in an active state to inhibit anaphase progression

Zhang, T. *et al. Dev. Cell* **17**, 541–551

This study reveals that the DNA damage checkpoint does not prevent the segregation of damaged chromosomes only by inhibiting the cleavage of cohesin (which binds sister chromatids) but also by other, parallel mechanisms. Specifically, they describe a mechanism that prevents spindle elongation, which is characteristic of progression from early to late anaphase. When yeast DNA is damaged, Rad53 phosphorylates, and therefore inactivates, the polo kinase Cdc5. The inactivation of Cdc5 prevents it from phosphorylating and inactivating the ubiquitin ligase Cdh1. This results in the ubiquitylation and degradation of the kinesins Cin8 and Kip1 by Cdh1, leading to inhibition of spindle extension. Further studies will be required to determine whether a similar mechanism operates in other organisms.

TRANSCRIPTION

Profiling the human protein–DNA interactome reveals ERK2 as a transcriptional repressor of interferon signaling

Hu, S. *et al. Cell* **139**, 610–622 (2009)

Hu *et al.* used microarray analysis to assess the ability of 4,191 human proteins, of various functional classes, to interact with 460 DNA motifs. Surprisingly, as well as doubling the number of transcription factors for which consensus sites have been identified, many proteins were detected that were not previously known to interact with specific DNA motifs, including sugar and protein kinases. Electromobility shift assays and chromatin immunoprecipitation confirmed that extracellular signal-regulated kinase 2 (ERK2; also known as MAPK1), which is known to regulate transcription factor activity, associates with a GAAAC sequence through residues Lys269 and Arg261. Furthermore, the authors found that ERK2 represses the expression of interferon-γ-induced genes through a promoter element that also binds the transcription factor CCAAT/enhancer binding protein-β, suggesting crosstalk between conventional transcription factors and unconventional DNA binding proteins in gene regulation.