Nature Reviews Genetics | AOP, published online 14 May 2013

IN BRIEF

STEM CELLS

Nuclear departure controls pluripotency exit

To investigate the mechanisms controlling exit from the pluripotent state during differentiation, Betschinger *et al.* carried out an RNA interference screen in mouse embryonic stem cells to identify gene knockdowns that could block differentiation. Among various hits, they found the folliculin (*Flcn*) and tuberous sclerosis 2 (*Tsc2*) genes. Further analyses showed that FLCN and TSC2 are involved in the nuclear export of a transcription factor, TFE3, that regulates pluripotency-associated genes; its export thus helps to control the pluripotency–differentiation switch.

ORIGINAL RESEARCH PAPER Betschinger, J. *et al.* Exit from pluripotency is gated by intracellular redistribution of the bHLH transcription factor TFE3. *Cell* **153**, 335–347 (2013)

EPIGENETICS

BPA and imprinting disruption

Various studies in mice have linked exposure to the environmental compound bisphenol A (BPA), which is common in plastics, to altered DNA methylation. Susiarjo *et al.* studied the effects on mice of continuous maternal exposure to BPA during oocyte maturation through to the first 9.5 days of embryonic development (an important period of epigenetic reprogramming). DNA methylation and gene expression analyses revealed that exposure to environmentally approved levels of BPA resulted in loss of imprinting (LOI) at some genetic loci in placentas. At higher levels of BPA, LOI also occurred in embryos, and histological abnormalities were observed in placentas. These effects were absent when exposure to BPA occurred only after the period of embryonic reprogramming.

ORIGINAL RESEARCH PAPER Susiarjo, M. *et al.* Bisphenol A exposure disrupts genomic imprinting in the mouse. *PLoS Genet.* **9**, e1003401 (2013)

NON-CODING RNA

R-loop stability controls expression

Using a forward mutagenesis screen, Sun *et al.* studied regulation of a set of antisense transcripts named *COOLAIR*, which are important for controlling flowering time in *Arabidopsis thaliana*. They found that a plant homeodomain protein called NDX1 regulates *COOLAIR* by binding to and stabilizing an RNA–DNA hybrid (known as an R-loop) that forms in the *COOLAIR* promoter; this loop impedes transcription. This provides an example of how regulatory long non-coding RNAs can themselves be regulated, and modulation of R-loop stability might be a more general mechanism of gene regulation.

ORIGINAL RESEARCH PAPER Sun, Q. *et al.* R-loop stabilization represses antisense transcription at the *Arabidopsis FLC* locus. *Science* **340**, 619–621 (2013)

GENE REGULATION

Determining global and specific regulation

Studies of gene regulation often focus on circuits involving specific transcription factors, but gene expression is also influenced by global factors, such as the growth status of the cell. Gerosa *et al.* used a combination of experimental and computational approaches to dissect the contributions of global and specific regulation of arginine biosynthesis in *Escherichia coli*. They uncovered principles of coordination between these modes — for example, through a growth-rate-dependent maximum expression level — that could be applicable to other biosynthetic pathways.

ORIGINAL RESEARCH PAPER Gerosa, L. *et al.* Dissecting specific and global transcriptional regulation of bacterial gene expression. *Mol. Syst. Biol.* **9**, 658 (2013)