# IN BRIEF

## METABOLISM

### CDK4 suppresses gluconeogenesis

The role of insulin in glucose homeostasis has now been shown to involve the cyclin D1–CDK4 (cyclin-dependent kinase 4) complex. The authors find that CDK4 suppresses gluconeogenesis in a cell cycle-independent manner by inhibiting the transcription factor PGC1α. GSK3β inactivation downstream of insulin receptor stimulation prevented the phosphorylation and proteasomal degradation of cyclin D1 and enabled it to form an active complex with CDK4. Active cyclin D1–CDK4 phosphorylated and activated the acetyltransferase GCN5. Acetylation of PGC1α by GCN5 inhibits its transcriptional activity, which in this case decreased the expression of gluconeogenic genes and glucose production. Finally, the authors found that this pathway is triggered in the parenchymal hepatocytes of mice re-fed after a period of fasting (to suppress hepatic gluconeogenesis), and that it is chronically activated in diabetic mice by compensatory hyperinsulinaemia.

**ORIGINAL RESEARCH PAPER** Lee, Y. *et al.* Cyclin D1–Cdk4 controls glucose metabolism independently of cell cycle progression. *Nature* http://dx.doi.org/10.1038/nature13267 (2014)

## RNA METABOLISM

### Heat stresses splicing

It is unclear to what extent cells adapt to heat stress by adjusting pre-mRNA splicing. Using transcriptome-wide RNA sequencing in mouse fibroblasts, Shalgi *et al.* found that severe heat stress inhibits splicing of ~1,700 genes, with the strongest effect being intron retention. Ribosome profiling and subcellular fractionation revealed that the unspliced transcripts are not translated and remain in the nucleus. Splicing inhibition is not global, as splicing of ~600 genes remained unaffected; the products of these genes are mainly involved in protein unfolding and energy metabolism. The authors found that most unaffected transcripts are spliced co-transcriptionally and that this process is unchanged in heat stress, whereas the unspliced transcripts are mostly processed post-transcriptionally, a process inhibited in heat stress. Thus, co-transcriptional splicing is important in shaping global cellular splicing under heat stress, and possibly other adverse conditions.

**ORIGINAL RESEARCH PAPER** Shalgi, R. *et al.* Widespread inhibition of posttranscriptional splicing shapes the cellular transcriptome following heat shock. *Cell Rep.* http://dx.doi.org/10.1016/j.celrep.2014.04.044 (2014)

## TECHNIQUE

### Single-cell western blotting

Single-cell protein analysis techniques lack resolution, sensitivity or specificity, or require protein tagging. Western blotting avoids these pitfalls but is not amenable to single-cell analysis. Hughes *et al.* now couple western blotting with single-cell analysis, which enables the simultaneous analysis of ~2,000 individual cells. Their array-based technique uses a slide coated with polyacrylamide gel and patterned with thousands of microwells, into which a cell suspension is seeded by gravity-driven cell settling, resulting in single-cell occupancy in 40–50% of the wells. Intracellular proteins are then solubilized in the wells, subjected to thin-gel electrophoresis and immobilized. Subsequently, the serial stripping and re-probing of antibodies enables multiplexed analyses of proteins.

**ORIGINAL RESEARCH PAPER** Hughes, A. J. *et al.* Single-cell western blotting. *Nature Methods* http://dx.doi.org/10.1038/nmeth.2992 (2014)