IN BRIEF

CHROMOSOME BIOLOGY

H2A.B facilitates transcription

Although the mammalian histone variant H2A.B has unique structural and biochemical properties *in vitro*, its *in vivo* functions are unclear. Using chromatin immunoprecipitation followed by sequencing (ChIP–seq) and methylated DNA IP (MeDIP), Chen *et al.* now show that H2A.B is enriched in coding exons and introns, and is mainly associated with CpG-hypermethylated loci. H2A.B-bound genes are more highly expressed than unbound genes, and H2A.B depletion in mouse embryonic stem cells reduced the expression of these genes. In addition, H2A.B was exclusively enriched in the parentally methylated, expressed alleles of imprinted genes. Its depletion reduced their expression by suppressing transcription elongation, which was evident by the arrest of Ser2-phosphorylated RNA polymerase II on methylated regions following H2A.B depletion. Thus, these results show that H2A.B facilitates transcription elongation in highly methylated genes, including in imprinted genes.

ORIGINAL RESEARCH PAPER Chen, Y. *et al.* H2A.B facilitates transcription elongation at methylated CpG loci. *Genome Res.* http://dx.doi.org/10.1101/gr.156877.113 (2014)

CELL DEATH

At the crossroads of cell death pathways

Tumour necrosis factor (TNF) can activate caspase 8-mediated apoptosis or receptor-interacting protein kinase 3 (RIPK3)-dependent necroptosis. To study the connection of these two pathways, Newton *et al.* engineered mice to express a catalytically inactive version of RIPK3 (RIPK3^{D161N}). *Ripk3*$^{D161N/D161N}$ mice died mid-gestation from caspase 8-dependent apoptosis; *Casp8*$^{-/-}$ embryos also die mid-gestation, but double mutant *Casp8*$^{-/-}$ *Ripk3*$^{D161N/D161N}$ mice were viable. Tamoxifen-induced expression of RIPK3^{D161N} in adult transgenic mice caused severe intestinal lesions, which is indicative of caspase 8-mediated apoptosis. Culturing embryonic fibroblasts of these mice with tamoxifen caused increased apoptosis and enabled the isolation of a complex containing RIPK3^{D161N} and caspase 8. As removal of RIPK3 kinase activity promotes caspase 8-dependent apoptosis, these results indicate that by supressing caspase 8-dependent apoptosis, RIPK3 activity dictates whether a cell dies by necroptosis or apoptosis.

ORIGINAL RESEARCH PAPER Newton, K. *et al.* Activity of protein kinase RIPK3 determines whether cells die by necroptosis or apoptosis. *Science* http://dx.doi.org/10.1126/science.1249361 (2014)

METABOLISM

p66SHC inhibits anabolic metabolism

Increased insulin signalling can result in rapid cell growth and increased survival owing to a rise in glucose consumption. Soliman *et al.* studied the role of p66SHC (the p66 isoform of the adaptor protein SHC (SRC homology 2 containing)), a mediator of growth factor signalling, in cell metabolism. By measuring glucose uptake and catabolism in p66SHC-deficient and wild-type cells, and comparing their metabolite profiles, they found that p66SHC inhibits glycolytic metabolism, lipid biosynthesis, amino acid biosynthesis and pyrimidine metabolism. The authors further showed that the effects of p66SHC are partly mediated by the inhibition of mTOR signalling in response to insulin. Their data indicate that p66SHC has a prominent role in inhibiting glycolysis and anabolic metabolism in favour of oxidative respiration.

ORIGINAL RESEARCH PAPER Soliman, M. A. *et al.* The adaptor protein p66Shc inhibits mTOR-dependent anabolic metabolism. *Sci. Signal.* **7**, ra17 (2014)