IN BRIEF

METABOLISM

Small nucleolar RNAs U32a, U33, and U35a are critical mediators of metabolic stress

Michel, C. I. *et al. Cell Metab.* **14**, 33–44 (2011)

Small nucleolar RNAs (snoRNAs) are non-coding RNAs with roles in ribosomal RNA (rRNA) modification and gene expression. This study links snoRNAs to lipotoxic and oxidative stress. First, the authors identified a locus (ribosomal protein L13A (*RPL13A*)) that was crucial for lipotoxicity-induced cell death. Further analysis showed that cell death was promoted by three snoRNAs found in *RPL13A*: U32A, U33 and U35A. These accumulated in the cytoplasm following treatment with saturated fatty acids (which are lipotoxic), and their knockdown protected against cell death caused by lipotoxic or oxidative stress *in vitro*. The effects of U32A, U33 and U35A were independent of the C/D box (which mediates rRNA methylation in canonical snoRNAs), indicating that they are noncanonical. A role for the three snoRNAs as mediators of metabolic stress-induced cell death was further supported by an *in vivo* model of oxidative stress.

EPIGENETICS

Thymine DNA glycosylase is essential for active DNA demethylation by linked deamination–base excision repair

Cortellino, S. *et al. Cell.* **146**, 67–79 (2011)

The pathways of active demethylation of 5-methylcytosine (5mC) in mammals have long been elusive. One pathway that is thought to be involved is the deamination of 5mC to T, which causes G•T mismatches that are removed by DNA glycosylases, such as T DNA glycosylase (TDG). Now, Cortellino *et al.* show that loss of TDG is embryonic lethal and that TDG-null cells are hypermethylated at specific CpG islands. They find that TDG associates with two proteins that have been linked to DNA demethylation: activation-induced deaminase (AID) and growth arrest and DNA damage-inducible 45α (GADD45α). Furthermore, they show that TDG can deglycosylate 5-hydroxymethyluracil (5hmU), the deamination product of 5-hydroxymethylcytosine (5hmC), which may also be an intermediate in DNA demethylation. They propose that TDG acts immediately downstream of the deaminase-mediated conversion of 5mC to T and 5hmC to 5hmU, and that this integration of both pathways may explain why TDG is essential for development.

DEVELOPMENT

The F-box protein Ppa is a common regulator of core EMT factors Twist, Snail, Slug, and Sip1

Lander, R., Nordin, K. & LaBonne, C. *J. Cell Biol.* **194**, 17–25 (2011)

The transcription factors Twist, Snail, Slug and SMAD-interacting protein 1 (SIP1) are core regulators of epithelial–mesenchymal transition (EMT). Lander *et al.* injected Twist mRNA into early *Xenopus laevis* embryos and concluded that, as Twist protein levels decreased during neural crest development, Twist stability might regulate its activity. Indeed, Twist was targeted for ubiquitylation by Partner of paired (ppa), an F box protein that acts as part of a Skp–cullin–F box E3 ubiquitin ligase. Twist and ppa co-overexpression and ppa depletion in embryos increased and decreased Twist degradation, respectively. Furthermore, ppa was also found to target sip1. These findings, together with previous observations that ppa targets Snail and Slug for ubiquitylation, indicate that ppa is a common regulator of these structurally unrelated, but functionally linked, EMT factors.