IN BRIEF

TRANSLATION

tRNA methylation controls translation rate

DNMT2 and NSUN2 methylate C5 cytosines outside the anticodon loop of several tRNAs, but the inconsistent phenotypes of single *Dnmt2*- and *Nsun2*-knockout mutants obscured the biological role of this tRNA modification. Here, Tuorto *et al*. generated *Dnmt2* and *Nsun2* double-knockout mice and found that lack of both tRNA methyltransferases hampers embryonic development, cell proliferation and differentiation. These effects did not depend on altered mRNA levels but on the global loss of tRNA methylation. Interestingly, the target specificities of DNMT2 and NSUN2 were complementary, and deletion of both enzymes reduced the levels of their few common tRNA targets. This, in turn, resulted in a decreased global translation rate, suggesting a central role for tRNA methylation in the control of protein synthesis.

ORIGINAL RESEARCH PAPER Tuorto, F. *et al.* RNA cytosine methylation by Dnmt2 and NSun2 promotes tRNA stability and protein synthesis. *Nature Struct. Mol. Biol.* 12 Aug 2012 (doi:10.1038/nsmb.2357)

TECHNIQUE

Getting ready for S phase

The study of cell growth and cell size regulation prior to cell cycle entry has been hindered by technical limitations. One recent advance was the development of an approach that dynamically monitors the mass of individual growing cells by using a suspended microchannel resonator (SMR) mass sensor. Here, Manalis and colleagues refine this technique, enhancing the precision of cell mass measurement, and also integrate a microscope, which enables the visualization of cell cycle progression using fluorescent cell cycle indicators. Using this approach, they reveal that there is an increase in growth rate during G1-to-S phase transition, suggesting that cell mass and cell cycle progression are tightly coupled. Importantly, despite initial variability in growth rates, all cells entered S phase with similar growth rates. This indicates that a growth rate threshold, rather than a critical size threshold, controls the G1-to-S phase transition.

ORIGINAL RESEARCH PAPER Son, S. *et al.* Direct observation of mammalian cell growth and size regulation. *Nature Meth.* 5 Aug 2012 (doi:10.1038/NMETH.2133)

PROTEIN STABILITY

The ADP ribosylation switch in BiP

The endoplasmic reticulum (ER) chaperone BiP binds unfolded proteins to prevent their aggregation and is upregulated following activation of the ER unfolded protein response. BiP ADP ribosylation has been suggested to contribute to the fast adaptation of the ER to the changing levels of unfolded proteins. Consistent with this, Chambers *et al*. report that BiP ADP ribosylation that is observed in the pancreas of fasted mice (low protein synthesis) is reversed following feeding (high protein synthesis). Moreover, they identify the conserved Arg470 and Arg492 residues as sites for ADP ribosylation in BiP. Interestingly, this modification alters the electrostatic properties of BiP, and mutations that mimic the charge changes induced by ADP ribosylation destabilize BiP–substrate binding. Finally, kinetic studies suggested that BiP ADP ribosylation, which correlates with low levels of newly synthesized proteins, allows protein folding, whereas BiP deribosylation during increased protein synthesis prevents aggregation of unfolded proteins.

ORIGINAL RESEARCH PAPER Chambers, J. E. *et al.* ADP ribosylation adapts an ER chaperone response to short-term fluctuations in unfolded protein load. *J. Cell Biol.* 6 Aug 2012 (doi:10.1038/jcb.20122005)