IN BRIEF

NON-CODING RNA

A class of their own

The transcription and processing of long intervening noncoding RNAs (lincRNAs), which are a class of lncRNAs expressed independently of protein-coding genes, are poorly understood. Schlackow et al. studied 285 lincRNAs that are highly expressed in HeLa cells using mNET-seq, which enables monitoring of the kinetics of transcription and co-transcriptional processes. The levels of co-transcriptional splicing in lincRNAs were considerably lower than in mRNAs, and transcription termination occurred at multiple positions along the transcripts. lincRNAs were weakly polyadenylated, and transcription termination and transcript stability were almost entirely independent of 3' cleavage and polyadenylation. Although lincRNAs and mRNAs are often similarly abundant at the chromatin, lincRNAs were less abundant in the nucleoplasm, as they were cleaved at multiple positions and then degraded by the nuclear exosome complex. The exosome was recruited to lincRNAs by DGCR8, independently of the microRNA-processing function of DGCR8.

ORIGINAL ARTICLE Schlackow, M. et al. Distinctive patterns of transcription and RNA processing for human lincRNAs. Mol. Cell **65**, 25–38 (2017)

DEVELOPMENT

Metabolism regulates lymphangiogenesis

Wong et al. report that metabolism — more specifically, fatty acid β -oxidation (FAO) — promotes lymphatic development. They found that FAO is high in lymphatic endothelial cells (LECs; which line lymph vessels) and that inhibition or LEC-specific loss of CPT1A, which is a rate-controlling enzyme of FAO, impaired the differentiation of LECs from their precursors, venous endothelial cells, both in vitro and in mice. The transcription factor PROX1 and vascular endothelial growth factor receptor 3 (VEGFR3) are known inducers of LEC differentiation through the upregulation of lymphatic genes. The authors report that PROX1 upregulates FAO by inducing CPT1A expression, thereby increasing the levels of FAO-derived acetyl-CoA, which is used by p300 to acetylate histone H3 at Lys9 at key lymphatic genes, including VEGFR3. Moreover, they propose that selective activation of lymphatic genes is enhanced through PROX1 binding to p300 and preferentially recruiting it to PROX1-target genes.

ORIGINAL ARTICLE Wong, B. W. *et al.* The role of fatty acid β -oxidation in lymphangiogenesis. *Nature* <u>http://dx.doi.org/10.1038/nature21028</u> (2016)

TRANSLATION

Ubiquitylation mediates quality control

Terminally stalled ribosomes can initiate degradation of nascent polypeptides and the dissociation of ribosome subunits, a process known as ribosome-associated quality control (RQC). Using a reporter that quantitatively measures ribosome terminal stalling, Juszkiewicz and Hegde found that most ribosomes in human cells stalled when they encountered an array of 21 AAA Lys codons (AAA₂₁) and that degradation of the 'arrested' nascent polypeptides was mediated by RQC. Depletion of the putative ubiquitin E3 ligase ZNF598 abolished terminal stalling at the AAA₂₁ region. Moreover, ZNF598-mediated ubiquitylation of several ribosomal proteins, primarily 40S ribosomal protein S10, was necessary for RQC activation. Because translation of only poly(A) sequences that are longer than endogenous sequences can effectively trigger RQC, this mechanism could be tuned to prevent translation of the poly(A) tail.

ORIGINAL ARTICLE Juszkiewicz, S. & Hegde, R. S. Initiation of quality control during poly(A) translation requires site-specific ribosome ubiquitination. *Mol. Cell* <u>http://dx.doi.org/10.1016/j.molcel.2016.11.039</u> (2017)