IN BRIEF

TRANSCRIPTION

A novel termination pathway

The mechanisms involved in the processing of long non-coding RNAs (lncRNAs) are largely uncharacterized. Dhir *et al.* now find that transcription termination of lncRNA transcripts containing primary miRNAs (lnc-pri-miRNAs) — which encode 17.5% of human miRNAs — involves cleavage by the Microprocessor complex rather than the canonical cleavage and polyadenylation pathway. The Microprocessor complex, which comprises the double-stranded RNA-binding protein DGCR8 and the RNase III endonuclease Drosha, is known to process pri-miRNA-containing protein-coding transcripts to give rise to miRNAs. Here, the authors found that liver-specific lnc-pri-miR-122 is not polyadenylated but contains a cleavage site for Drosha at its 3′ end. Moreover, depletion of DGCR8 or Drosha led to readthrough transcription, indicative of a termination defect. Genome-wide chromatin RNA sequencing analyses in HeLa cells indicated that Microprocessor terminates transcription of most lnc-pri-miRNAs.

ORIGINAL RESEARCH PAPER Dhir, A. *et al.* Microprocessor mediates transcriptional termination in genes encoding long noncoding microRNAs. *Nature Struct. Mol. Biol.* http://dx.doi.org/10.1038/nsmb.2982 (2015)

STEM CELLS

Linking stemness to low DNA damage

The frequency of genomic mutations is much lower in embryonic stem cells (ES cells) than in somatic cells, but the mechanisms that contribute to genome stability in ES cells remain largely unknown. Xiong *et al.* now find that the zinc-finger protein Sall4, which is known to be important for the maintenance of stemness, is required for activating the ATM-dependent cellular responses to DNA double-stranded breaks (DSBs) in mouse ES cells. Autophosphorylation of ATM at Ser1987, a marker for ATM activation, was greatly reduced in *Sall4*$^{-/-}$ cells following the induction of DSBs. Moreover, phosphorylation of ATM target proteins was decreased and levels of DNA damage were increased, indicating that Sall4 is required for activation of the ATM-dependent repair pathway. The authors show that Sall4 is recruited to sites of DNA DSBs, through interactions with the chromatin remodelling factor Baf60a (a member of the SWI/SNF complex), where they stabilize the Mre11-Rad50-Nbs1 (MRN) complex that links DSBs to ATM signalling.

ORIGINAL RESEARCH PAPER Xiong, J. *et al.* Stemness factor Sall4 is required for DNA damage response in embryonic stem cells. *J. Cell Biol.* **208**, 513–520 (2015)

PROTEIN METABOLISM

Get3 hides transmembrane domains in its pocket

Tail-anchored (TA) membrane proteins are targeted to the endoplasmic reticulum (ER) post-translationally by the guided entry of TA proteins (GET) pathway; this involves the formation of a complex between the TA protein and the cytosolic factor Get3. During transit, the hydrophobic transmembrane domain (TMD) of TA proteins must be shielded from the cytosol until they are inserted into the ER lipid bilayer, but the exact underlying mechanisms are unclear. Structural studies by Mateja *et al.* now reveal that the cytosolic factor Get3 forms a homodimer with a hydrophobic pocket. They show that one TA protein is loaded onto the dimeric Get3 in a closed conformation, and that the TMDs binds to the hydrophobic groove spanning the dimer interface.

ORIGINAL RESEARCH PAPER Mateja, A. *et al.* Structure of the Get3 targeting factor in complex with its membrane protein cargo. *Science* 3**47**, 1152–1155 (2015)