IN BRIEF

PROTEIN DEGRADATION

A new player in ERAD

Misfolded proteins transiting through the secretory pathway are translocated from the endoplasmic reticulum (ER) to the cytosol, where they are degraded via ER-associated degradation (ERAD). In *Saccharomyces cerevisiae*, this involves polyubiquitylation by the ER membrane-associated E3 ligases Hrd1 and Doa10, although loss of both proteins does not completely block degradation. This study reveals that the cytoplasmic E3 ligase Ubr1 is also involved in ERAD. Ubr1 ubiquitylated Ste6* (a truncated version of pheromone mating type A transporter), promoting its proteasomal degradation, in the absence of both Hrd1 and Doa10, or under heat shock or ethanol treatment. The chaperone Ssa1 and the AAA+ ATPase Cdc48 were required for this process. Notably, Ubr1 was integral for the ubiquitylation of CTCF (a human protein that is completely degraded by ERAD when expressed in yeast) under standard growth conditions and in the presence of Hrd1 and Doa10.

ORIGINAL RESEARCH PAPER Stolz, A. *et al.* Previously unknown role for the ubiquitin ligase Ubr1 in endoplasmic reticulum-associated protein degradation. *Proc. Natl Acad. Sci. USA* http://dx.doi.org/10.1073/pnas.1304928110 (2013)

RNA DECAY

mRNAs get together

Staufen 1-mediated mRNA decay (SMD) is known to regulate the levels of transcripts involved in several cellular processes. SMD is triggered following binding of Staufen 1 to Staufen 1-binding sites (SBSs), which can form intramolecularly within an mRNA or through binding between an Alu element at the 3′ untranslated region (UTR) of an mRNA and a partially complementary Alu element of a long non-coding RNA. Here, the authors show that two mRNAs can also base-pair through their partially complementary 3′ UTR Alu elements, forming SBSs in the process. The mRNAs are then targeted for SMD, provided that they are translated and that the termination codon is sufficiently upstream of the SBS. Such SMD has functionally important consequences in cell migration and invasion.

ORIGINAL RESEARCH PAPER Gong, C., Tang, Y. & Maquat, L. E. mRNA–mRNA duplexes that autoelicit Staufen1-mediated mRNA decay. *Nature Struct. Mol. Biol.* http://dx.doi.org/10.1038/nsmb.2664 (2013)

PROTEIN STABILITY

Getting into the membrane

Integral membrane proteins are synthesized in the endoplasmic reticulum (ER), where they are co-translationally incorporated into the membrane. This depends on hydrophobic sequences, which stop further transfer into the ER lumen. However, many multipass transmembrane proteins have regions of low hydrophobicity. Here, the authors use αβ T cell receptor (αβTCR; which crosses the secretory pathway only when correctly assembled) as a model to determine the quality control mechanisms underlying this process. They found that unassembled α-chains, which have a transmembrane domain of low hydrophobicity, enter the ER lumen fully. Here, this domain is recognized by BiP (binding immunoglobulin protein), a chaperone of the ER quality control machinery, which initiates α-chain degradation. However, association with the CD3 co-receptor subunits CD3δ and CD3ε allows integration of the α-chains into the ER membrane and stabilizes them for subsequent assembly into the complete αβTCR–CD3 complex.

ORIGINAL RESEARCH PAPER Feige, M. J. & Hendershot, L. M. Quality control of integral membrane proteins by assembly-dependent membrane integration. *Mol. Cell* **51**, 297–309 (2013)