Auxin holds things together

Auxins are phytohormones that are involved in plant growth regulation in response to various environmental and developmental cues. Recent data show that a signaling cascade involving the ubiquitin ligase SCF^{TIR1}, which targets the proteolysis of the Aux/IAA family of transcriptional repressors, requires auxin binding by TIR1, an F-box protein. The degradation of Aux/IAAs, which requires a highly conserved degron peptide for SCF^{TIR1} recognition, leads to the activation of the auxin response factor family of transcription factors. Zheng and colleagues have now determined the crystal structures of complexes formed between TIR1-ASK1, auxin and the Aux/IAA degron peptide, which suggest how auxin promotes degradation of Aux/IAAs. The leucine-rich–repeat domain of TIR1 forms a highly curved solenoid in the shape of a closed horseshoe. Three long loops located on the same face of the protein contribute to formation of a promiscuous binding site that can accommodate different auxin compounds. The structures reveal that auxin helps to create the binding site for the Aux/IAA degron peptide, extending a protein-interaction surface that makes intimate hydrophobic contacts with a conserved central motif in the degron. This explains the weak affinity between SCF^{TIR1} and Aux/IAAs observed in the absence of auxin. Because an increasing number of human diseases have been linked to defects in ubiquitin ligase–target interactions, the authors suggest that this mode of promoting ligase-substrate interactions can potentially be used to rectify disease states and may provide a new approach for drug therapies. (*Nature* **446**, 640–645, 2007) *MM*

Fidelity affects σ^S stability

Sigma factors are required for the initiation of transcription by bacterial RNA polymerase. In *Escherichia coli*, σ^S controls the activity of genes involved in the general stress response. The amount of σ^S in the cell is controlled at multiple levels, by transcription, translation and post-translational events. The latter are particularly important: under normal growth conditions, σ^S is delivered by the adaptor protein SprE/RssB to the ClpXP protease, which rapidly degrades it. Under stress conditions, σ^S is stabilized by mechanisms that are not fully understood. Now Nyström and colleagues have uncovered a novel regulator of σ^S stability: ribosome translational fidelity. Glucose and amino acid starvation are known to increase translation errors by ribosomes. By directly altering ribosomal accuracy with mutations or drugs, the authors show an inverse relationship between translational fidelity and the level and stability of σ^S during carbon stress. This effect requires SprE and ClpXP, as well as oxidative conditions. The authors also demonstrate that ClpP is a limiting factor for the control of σ^S levels, and they propose a model where the decrease in translational fidelity under carbon starvation leads to the accumulation of aberrant proteins, which are more prone to oxidative modifications. The oxidized abnormal proteins are substrates for ClpP protease complexes, so their high levels can titrate ClpP away from its interaction with σ^S, which is thus stabilized. This work adds a new signal into the known network of events controlling σ^S and provides insight on how bacteria sense and respond to stress. (*Genes Dev.* **21**, 862–874, 2007) *IC*

Research Highlights written by Inês Chen, Sabbi Lall and Michelle Montoya.

Unwinding miRNA processing

MicroRNAs (miRNAs) are small RNAs involved in post-transcriptional repression of target mRNAs. They are initially expressed as primary transcripts (pri-miRNAs) and are processed into hairpin precursors by the Drosha complex, which consists of multiple components, including the DEAD-box RNA helicases p68 and p72. Kato and colleagues have now analyzed the function of these helicases in mice. Gene knockouts indicated that lack of p68 or p72 was lethal during the embryonic or neonatal stage, respectively. In addition, cell proliferation was impaired and cell death increased in embryonic fibroblasts derived from p72-knockout mice. A subset of miRNAs were present at decreased levels in the p72-deficient cells, but corresponding pri-miRNA levels were normal, indicating defective processing rather than expression. Decreased miRNA levels can be rescued by wild-type p72, but not by a p72 mutant expected to lack ATPase activity. The involvement of the helicases in pri-miRNA processing was confirmed using *in vitro* processing assays with purified Drosha complex, with processing inhibited by antibodies to p68, p72 or Drosha itself. Using RNA–ChIP, the authors found that two pri-miRNAs affected by the p72 mutants, pri-miR-214 and pri-miR-16, copurify with Drosha, an association lost in p72-mutant cells or upon p68 knockdown by RNA interference. The data indicate a role for these DEAD-box helicases in pri-miRNA processing, though the mechanism by which they act in the complex, and why processing of particular miRNAs is affected in the mutants, are avenues for further exploration. (*Nat. Cell Biol.*, advance online publication 15 April 2007, doi:10.1038/ncb1577) *SL*

Surrogate pairing

B-cell receptors (BCRs) are composed of heavy and light chains, but during B-cell maturation, the gene encoding the heavy chain undergoes rearrangement before the light chain. The rearranged heavy chain forms a pre-BCR by pairing with the surrogate light chain (SLC), which is formed by two invariant proteins, λ5 and VpreB. Not all rearranged heavy chains are able to pair with the SLC to form the pre-BCR, an event required for clonal expansion. Garcia and colleagues provide new insight into the pairing of heavy chain and SLC in the pre-BCR by solving the structure of a monomeric Fab-like complex, containing the antigen-specific region of human heavy chain in complex with VpreB and truncated λ5. The SLC occupies the same position as the LC in mature BCR. Examining the region of the pre-BCR analogous to the antigen-binding site (CDR3), the authors found that the loop of the heavy chain is in a more extended conformation and makes more contacts with the SLC than it does with the LC in BCR. Such interactions might select for specific heavy chains, thereby influencing antibody repertoire. BCR signaling requires receptor oligomerization induced by antigen binding. In contrast, the pre-BCR was found to bind antigen poorly, but dimers could be observed by electron microscopy. In addition, full-length SLC components promoted ligand-independent dimerization of the pre-BCR Fab-like complex in solution. Thus, on the surface of a maturing B cell, dimerization between the Fab-like regions from different pre-BCR molecules may lead to receptor clustering and signal activation. These findings show that SLC contributes to B-cell development by selecting heavy chains and promoting pre-BCR signaling. (*Science* **316**, 291–294, 2007) *IC*