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Structure Watch

SIGNAL PEPTIDE RECOGNITION

Most secretory and membrane proteins contain a signal peptide, which is recognized by the signal recognition particle (SRP) when newly synthesized polypeptide chains emerge from the ribosome. The signal peptide targets the SRP–ribosome nascent chain (RNC) complex to protein-translocating channels in the endoplasmic reticulum membrane in eukaryotes and in the plasma membrane in bacteria. Bacterial SRPs consist of 4.5S RNA and Ffh, which comprises an amino-terminal (N) domain, a GTPase (G) domain and a carboxy-terminal Met-rich (M) domain. The signal peptide was proposed to bind to the M domain, but a SRP structure with bound signal peptide has been lacking. Janda *et al.* produced a fusion protein of bacterial Ffh and a signal peptide connected by a flexible linker. The fusion protein oligomerizes in solution through the interaction between Ffh and signal peptides of different polypeptide chains. The X-ray structure of a dimeric complex was then determined. The signal peptide binds to a groove formed between α-helices of the M domain, and residues in the hydrophobic region of the signal peptide interact with hydrophobic residues in the groove. Furthermore, binding of the SRP to the RNC complex causes a large movement of the N and G domains with respect to the M domain. However, binding of signal peptide to the M domain alone is insufficient to induce this large rearrangement, and the linker between the N and G domains and the M domain is thought to couple signal peptide binding and ribosome binding.

ORIGINAL RESEARCH PAPER Janda, C. Y. *et al.* Recognition of a signal peptide by the signal recognition particle. *Nature* 4 Apr 2010 (doi:10.1038/nature08870)

CELL–CELL INTERACTIONS

p120 catenin mediates cell–cell adhesion by interacting with the conserved juxtamembrane domain (JMD) of cadherins. Uncoupling of the p120 catenin–JMD interaction or a reduction in p120 catenin levels increases cadherin internalization through an endocytic diLeu (LL) motif; the association of p120 catenin with JMD is proposed to sterically hinder the endocytic machinery from associating with cadherin. The authors determined the crystal structure of p120 catenin isoform 4A in complex with the JMD core region of epithelial cadherin (E-cadherin). JMD electrostatically and hydrophobically interacts with p120 catenin armadillo repeats 1–5. Structure-based mutagenesis studies in epithelial and neuronal cells showed that single-residue mutations in the JMD-binding site of p120 catenin are sufficient to uncouple p120 catenin from E-cadherin and neuronal cadherin, respectively. NMR studies identified dynamic and static binding interfaces between p120 catenin and JMD; the static binding site is mainly responsible for the specific interaction between p120 catenin and E-cadherin, whereas the dynamic binding site protects the LL motif from the endocytic machinery.

ORIGINAL RESEARCH PAPER Ishiyama, N. *et al.* Dynamic and static interactions between p120 and E-cadherin regulate the stability of cell–cell adhesion. *Cell* **141**, 117–128 (2010)