Cellular mechanic engineering

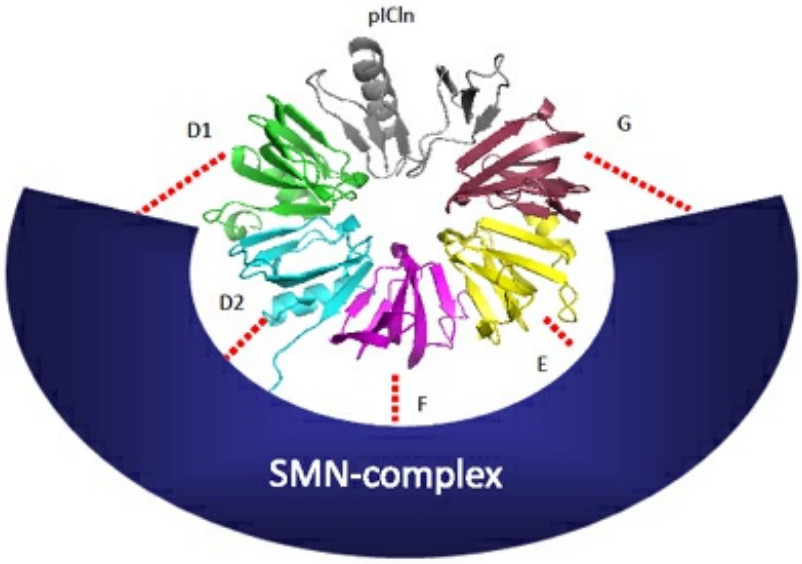
Cells are like factories, only smaller: Tiny machines assemble large proteins from very small molecules. But where do the machines come from? Researchers at the University of Würzburg have now found an answer to this question.

It has now become clear that cells are home to 'mechanical engineers' that assemble molecular machines. These molecular machines carry out numerous vital processes in the cell, one example being the correct translation of hereditary information (DNA) into proteins. Before this process was discovered, researchers believed that the molecular machines assembled spontaneously, as if driven by a ghost hand. If the cell's mechanical engineers are not working properly, malfunctions can result, potentially causing any of a number of illnesses. The researchers from Würzburg have already shown that the loss of motor neurones leads to spinal muscular atrophy. Utz Fischer's team at the University of Würzburg's Biocentre and Holger Stark at the Max Planck Institute of Biophysical Chemistry have recently published in the scientific journal Cell a guide to the proteins involved in the assembly of a specific RNA-protein complex. These proteins are referred to as assembly chaperones.

Assembly chaperones in the cell

Many of the processes that occur in our cells are driven by a number of different "machines", rather like the processes in a large factory. Since these machines are generally only a few millionths of a millimetre in diameter, they are referred to as molecular machines. Rather than metal or plastics, the cellular protein-assembly machines consist of proteins or nucleic acids (DNA and RNA) and are as complex as man-made machines.

This complexity and size is the reason why some researchers found it difficult to believe that such highly complex machines assembled spontaneously as had been suggested. "We have now been able to completely refute this assumption. Our investigations have shown that the cells work in a similar way to standard factory machinery. The small cellular constituents behave very much like real mechanical engineers," said Utz Fischer.



The researchers have shown that the chaperone pICln organises the assembly of the protein complex and that the SMN complex catalyses spliceosomal snRNP formation. (Figure: Ashwin Chari)

The proteins follow a detailed construction plan

Fischer and his team of researchers investigated the composition of RNA-protein complexes of the spliceosome. This is a very complex molecular machine that removes introns from a transcribed pre-mRNA. Fischer's team discovered a group of proteins that are involved in the assembly phase rather than in the actual translation process. "This caused us to suspect that these particular proteins contributed to the assembly of the protein complex," said Fischer who was surprised at how this was done. "The assembly process is like a very complicated puzzle that can only be completed if many different proteins (suppliers and assemblers) work together," explains Fischer. The assembly starts with the preparation of the proteins that need to be placed next to one another in the final RNA-protein complex. This job is done by a protein that supplies other proteins and oversees their temporal and spatial formation. Experts call these helpers "chaperones". The prefabricated proteins are then handed over to the actual assembler, the SMN complex. The SMN complex assembles the proteins and the RNA into a functional whole. "The assembly of the particles follows a predetermined plan, in which the suppliers and assemblers are constantly checking the quality," said Ashwin Chari, supervisor of the study.

Faulty machines result in severe diseases

If the assembly fails to produce a fully functional RNA-protein complex, diseases may result. This is what happens in the case of spinal muscular atrophy (SMA). In SMA patients, the helpers are unable to produce the required number of assembly machines, which results in a lack of important RNA-protein complexes. SMA is characterised by the loss of motor neurones in the spinal cord and brainstem, resulting in severe paralysis and death.

Literature:

Ashwin Chari, Monika M. Golas, Michael Klingenhäger, Nils Neuenkirchen, Bjoern Sander, Clemens Englbrecht, Albert Sickmann, Holger Stark, and Utz Fischer (2008), An Assembly Chaperone Collaborates with the SMN Complex to

Generate Spliceosomal SnRNP. Cell, DOI 10.1016/j.cell.2008.09.020

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