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How One Gene Can Produce Two Proteins

Max Planck Scientists Discovered a New Mechanism to Produce Two Proteins from a Single Gene

Small proteins of the ubiquitin family work as molecular switches and control many cellular functions. Scientists at the Max Planck Institute of Biochemistry (MPIB) in Martinsried near Munich, Germany, now discovered that the protein Hub1 of this protein family has a big effect on the synthesis of proteins: Hub1 influences the way how cells translate the information that is encoded in the genes. It even allows that one gene provides the information for two proteins and thus leads to more proteins than there are genes. This mechanism could also affect the protein repertoire of humans and hence will possibly have numerous implications for health and disease. (*Nature*, May 25, 2011)

Each cell possesses a large number of proteins, which steer all life functions. Each protein takes on special tasks, but these can be altered through protein modifications. Particularly fascinating cases are modifications in which the proteins are modified by chemical attachment of small proteins that belong to the ubiquitin family. Ubiquitin, which was discovered in the 1970ies, is known to work as a label for degradation: proteins marked with ubiquitin are specifically recognized by the cellular shredder, the proteasome.

In the laboratory of Stefan Jentsch at the MPIB scientists identified and studied Hub1, an unusual member of the ubiquitin family. Although Hub1 has a similar structure, it functions completely different to ubiquitin and other members of this protein family. Shравan Kumar Mishra, a postdoc in the laboratory, found that Hub1 binds tightly, but not chemically linked, to the highly conserved protein Snu66. This protein is part of a cellular machine, the spliceosome, which, by a process known as "splicing", cuts out segments of messenger RNAs (mRNAs) and pastes the remaining parts together. As mRNA molecules transport the genetic information that is stored in the genes of the chromosomes to cellular machines (ribosomes) that translate the information into proteins, splicing can significantly alter the repertoire of proteins in cells. Mishra and colleagues now discovered that binding of Hub1 to Snu66 changes the properties of this machine in a dramatic way: in the presence of Hub1 it can act on RNAs that are otherwise not spliced. In a few cases, Hub1-modified spliceosomes can even generate two different mRNAs from one single gene. In this process, which is called "alternative splicing", one gene thus provides the information for two different proteins.



The Hub1-mediated mechanism that the Jentsch team identified may be the oldest evolved mechanism that leads to more proteins than there are genes. Mishra and co-workers found out that the mechanism they identified is conserved from single-cellular organisms like yeast to humans. As the newly discovered mechanism is expected to influence the production of a large range of proteins also in humans, the new findings will have numerous implications for human cells in health and disease.

Original Publication:

Mishra *et al.* (2011): Role of the ubiquitin-like protein Hub1 in splice-site usage and alternative splicing. *Nature*, May 25, 2011.

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