

From gene to protein: Gene expression quantification offers new insights

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How do genes control us? This fundamental question of life still remains elusive despite decades of research. Genes are blueprints for proteins, but it is the proteins that actually carry out vital functions in the body for maintaining life. Diseases such as cancer are not only characterized by altered genes, but also by disturbed protein production. But how is protein production controlled?

Researchers of the Max Delbrück Center for Molecular Medicine (MDC) Berlin-Buch of the Helmholtz Association, Germany, have now comprehensively quantified gene expression (the activation of a gene for [protein production](#)) for the first time. According to their latest findings, control mainly occurs in the cytoplasm of the cell and not in the 'high-security tract' of the [cell nucleus](#). The results also highlight where [gene expression](#) can get out of control. The research was enabled by the close collaboration of a team led by the biologists Bjorn Schwanhauser and Matthias Selbach, the biomathematician Jana Wolf (all MDC) and the biotechnologist Wei Chen of the Berlin Institute for Medical Systems Biology (BIMSB) of the MDC.

Proteins are the major building blocks of life. "They control virtually all biological processes ranging from heartbeat and oxygen transport up to and including thinking," Matthias Selbach explained. The blueprint for proteins is stored in the genes in the cell nucleus. The [messenger RNA](#) (mRNA) formed in the cell nucleus (transcription) brings a copy of the blueprint to the [protein](#) factories of the cell in the cytoplasm, to the ribosomes. There the information of the mRNAs is used for protein

production (translation). The fundamental question was which of the two processes, i.e. transcription or translation, plays the dominant role in regulating [cellular protein](#) levels.

The starting point of the MDC researchers was to measure the turnover of cellular mRNAs and proteins and mRNA and [protein levels](#). They used high-throughput technologies such as quantitative [mass spectrometry](#) and the latest sequencing techniques, which are available close by at the MDC / BIMS. In total, they quantified proteins and mRNAs for more than 5,000 genes. By means of mathematical modeling, the researchers drew conclusions from the collected data about the control of protein levels. Intriguingly, they observed that cellular protein levels mainly depend on translation of mRNAs in the protein factories of the cytoplasm. "The [ribosomes](#) ultimately determine protein abundance. Some mRNAs are translated into only one protein per hour, others are translated 200 times," Matthias Selbach said.

Cells work in an energy-efficient way

Furthermore, the researchers found that cells use their resources very efficiently. Most mRNAs and proteins of abundantly expressed housekeeping genes (these genes maintain the normal operations of the body) are very stable. In this way the cell saves valuable energy, because protein production consumes many resources. In contrast, proteins responsible for rapid signaling processes are typically unstable. Cells can therefore quickly adapt to changes in their surroundings. This may also explain why the decisive control step takes place in the cytoplasm and not in the nucleus. Since it constitutes the last step in the production chain, this allows cells to respond dynamically to their environment.

The researchers hope their results will also be relevant for diseases. "So far, this is purely basic research," Matthias Selbach stressed. "But we also know that the production of proteins is disturbed in many diseases,

for example cancer." Very little is known about where the process gets out of control. Until now, researchers focused almost exclusively on the nucleus to find answers to this question. The new findings, however, show that the protein factories in the cytoplasm are of great significance. Perhaps this is where the key to understanding diseases can be found.

More information: Global quantification of mammalian gene expression control , *Nature* [doi:10.1038/nature10098](https://doi.org/10.1038/nature10098)

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