

Slight differences: New insights into the regulation of disease-associated genes

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Researchers of the Max Delbrück Center for Molecular Medicine (MDC) in the Helmholtz Association, in collaboration with the National Heart Research Institute Singapore (NHRIS), have gained new insights into the regulation of disease-associated genes. They used a new technique that enables them to observe gene regulation at the level of protein production. They could thus capture more individual gene regulations than with traditional methods that only capture gene expression and transcription.

When a gene is read, its blueprint for proteins encoded in the language of DNA is transcribed in the cell nucleus into RNA. "At this level, many but by far not all of the individual differences in gene regulation can be identified," said Professor Norbert Hübner, senior author of the publication and head of the research group Genetics and Genomics of Cardiovascular Diseases at the MDC. Together with Sebastian Schafer (MDC, NHRIS) and Eleonora Adami (MDC), as well as researchers from several research institutions in Berlin, the Netherlands, England and the Czech Republic, they investigated [gene regulation](#) on the next level, translation. It takes place outside the [cell nucleus](#), in the cell plasma. During translation, the RNA sequence is translated into [amino acid sequences](#) and assembled into proteins in the protein factories of the cell, the ribosomes.

First, the researchers searched the entire genome of two strains of rats,—one strain had high blood pressure, the other strain not—and specifically investigated [genes](#) of the heart and liver tissue. Then they

used a [new technique](#) called ribosome profiling, abbreviated ribo-seq, which enables them to determine what proportion of the transcriptome is actively translated into proteins. The result: They observed almost double the number of differentially expressed heart and liver genes in translation as in transcription. Next, they compared these data with the corresponding human genes in genome-wide association studies. This comparison revealed that a large number of heart and liver genes in humans are regulated primarily during translation. The researchers are confident that capturing interindividual differences in the translated genome will lead to new insights into the genes and regulatory pathways underlying disease.

More information: Translational regulation shapes the molecular landscape of complex disease phenotypes, *Nature Communications*, [DOI: 10.1038/ncomms8200](#)

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