Study shows how modification of mRNA controls cellular protein synthesis

August 25 2023

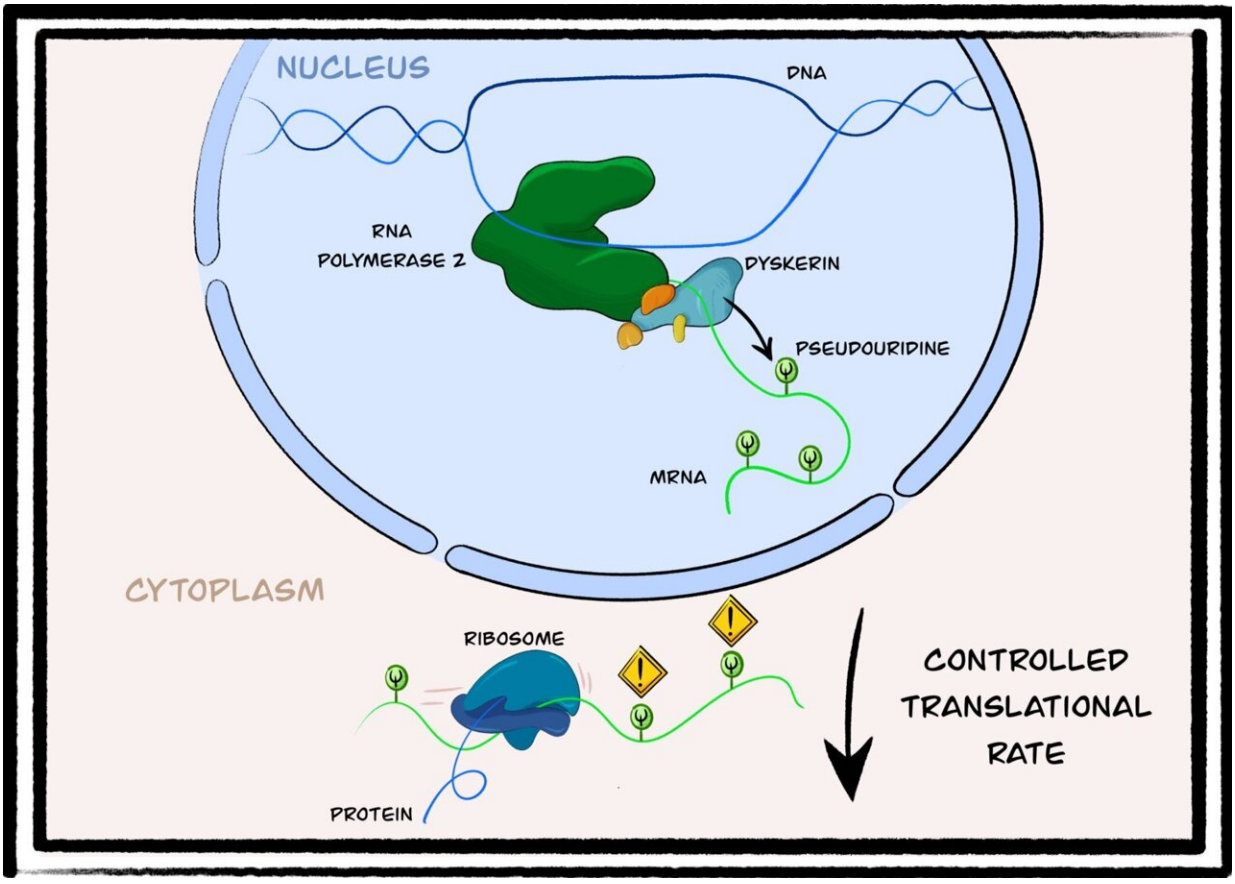

Illustration of mRNA pseudouridylation by dyskerin and its influence on protein synthesis. Credit: *Science Advances* (2023). DOI: 10.1126/sciadv.adg1805

RNA has a central role in the cell's protein production. New research

shows that RNA can be changed through various chemical modifications, the function of which is unknown to most. The study was carried out by researchers within Department of Cell and Molecular Biology and Department of Biosciences and Nutrition and published in the journal *Science Advances*.

"Our findings show that already from the production of an mRNA (during transcription), the cell can put on chemical modifications that can control how that mRNA is translated into protein," says Chiara Pederiva, postdoc at the Department of Cell and Molecular Biology, Karolinska Institutet and the study's first author.

"Our findings reveal that an RNA modification called pseudouridylation controls how quickly mRNA is translated into protein. We show which enzyme performs this modification (dyskerin), when it occurs in the cell (already during transcription) and what happens if this modification does not occur (abnormal protein production).

"Finally, we have discovered that pseudouridylation of mRNA is lost in patients with dyskeratosis congenita, a disease associated with increased risk of cancer risk and premature aging and which is caused by mutations in the enzyme dyskerin. This opens the possibility that problems in RNA pseudouridylation contributes to development of this disease," says Davide Trevisan, Ph.D. student at the Department of Biosciences and Nutrition, Karolinska Institutet and the study's shared first author.

This provides important information about one of the cell's most central processes—protein production—and how the cell can control protein production in the cytoplasm right from the transcription of mRNA, which takes place in the cell nucleus. The findings also show a connection to a genetic disease.

The importance of RNA modifications for cellular processes and disease development is a research field in its infancy. These new findings raise the knowledge to a new level and can help in the development of new therapies.

The study was performed with combination of high-throughput sequencing, cell biological and biochemical techniques. "We now want to investigate the scope of this mechanism in detail and use information to design new treatments against dyskeratosis congenita and cancer," says Marianne Farnebo the study's senior author.

More information: Chiara Pederiva et al, Control of protein synthesis through mRNA pseudouridylation by dyskerin, *Science Advances* (2023). DOI: 10.1126/sciadv.adg1805

Provided by Karolinska Institutet