Scientists make fundamental discovery about how gene expression functions in bacteria

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Researchers from NYU Langone Medical Center have discovered and characterized a general mechanism that controls transcription elongation in bacteria. The mechanism, described in the April 23 issue of *Science,* relies on physical cooperation between a moving ribosome and RNA polymerase (RNAP) that allows for a precise adjustment of the transcriptional yield in response to translational needs. The study could lead to the development of new ways to interfere with bacterial gene expression and serve as a new target for antimicrobial therapy.

"The finding that the active ribosome controls the rate of transcription at every protein-coding gene and under various growth conditions was quite unexpected - and the results are far reaching," says Evgeny Nudler, PhD, the Julie Wilson Anderson Professor of Biochemistry at NYU Langone Medical Center and lead author of the study. "It appears that the ribosome not just moves behind RNAP while translating the nascent transcript, but it is actually able to 'push' the paused or arrested RNAP molecules forward, thereby accelerating RNAP speed and also helping RNAP to traverse road blocks imposed by DNA binding proteins."

In the study, Nudler and colleagues demonstrate that the rate of transcription elongation perfectly matches the rate of translation under various growth conditions. They also show that the transcription rate depends on codon usage, or the frequency of rare codons which modulates the speed of a ribosome. Finally, the authors illustrate that it is the speed of the ribosome that determines the speed of RNAP -- whereby the acceleration or deceleration of a ribosome by chemical or

genetic manipulation leads to corresponding changes in RNAP speed.

Transcription and translation are the two principle events in the pathway of converting the genetic code into proteins. The data shows that these two events are tightly coupled, and cannot proceed efficiently without each other. Thus, uncoupling these processes, by breaking the proposed physical linkage between RNA and polymerase and the ribosome, could be a new way to disrupt bacterial gene expression and serve as a new target for antimicrobial therapy.

The implications of the study are important because it could lead to the development of novel ways to disrupt gene expression and the creation of new antimicrobial therapies. Not only does this cooperation mechanism save energy by limiting any excessive transcripts that cannot be translated in a timely manner, but it also prevents premature transcription termination by Rho factor, ensuring continuous coupling between transcription and translation. Thus, bacteria rely on macromolecule trafficking and cooperation, a fundamentally novel mechanism, to finely control expression of each individual gene in response to nutrient availability and growth phase.

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