Scientists observe single gene activity in living cells

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Researchers at Albert Einstein College of Medicine of Yeshiva University have for the first time observed the activity of a single gene in living cells. In an unprecedented study, published in the April 22 online edition of Science, Einstein scientists were able to follow, in real time, the process of gene transcription, which occurs when a gene converts its DNA information into molecules of messenger RNA (mRNA) that go on to make the protein coded by the gene.

Robert Singer, Ph.D., co-director of the Gruss Lipper Biophotonics Center at Einstein and professor and co-chair of anatomy and structural biology, is senior author of the paper. The study's lead author is Daniel Larson, Ph.D., previously a member of Dr. Singer's lab and now an investigator at the National Cancer Institute and head of the institute's Systems Biology of Gene Expression Section.

Using florescent proteins, the researchers were able to follow mRNA activity by inserting DNA sequences into a gene in live yeast cells. RNA made from these sequences bound a modified green fluorescent protein; expression of the entire gene resulted in mRNA molecules that were visible with fluorescent light. Gene transcription is a key step in synthesizing proteins, which govern the body's structure and function and underlie many diseases when present in mutated form or in aberrant amounts.

The study involved monitoring the activity of RNA polymerase—the enzyme that constructs mRNA molecules by linking single nucleotides

together into a molecular chain. The researchers were able to directly observe and measure the key steps involved in transcription: initiation (triggered when proteins called transcription factors bind to the promoter region of the gene), elongation (the progressive lengthening of mRNA as RNA polymerase adds more nucleotides to it) and termination (when mRNA breaks free from its DNA template, eventually migrating from the cell nucleus to the cytoplasm to serve as a blueprint for protein construction).

"The view of transcription in yeast that emerges from this study is that its initiation seems to be a random event that depends on the success of transcription factors searching through the yeast nucleus looking for a particular gene's promoter region," said Dr. Singer. "By contrast, once initiation occurs, RNA polymerase recruits individual nucleotides for the growing mRNA molecule in an efficient and predictable manner."

"Understanding how gene expression is regulated in a single-celled organism such as yeast is a first step in understanding the same processes in humans, which have a vastly larger and more complex genome," said Dr. Larson. "But fundamentally, the same molecular laws governing transcription factors will still apply."

More information: The *Science* paper is entitled "Real time observation of transcription initiation and elongation on an endogenous gene."

Provided by Albert Einstein College of Medicine