Scientists examine variations in a cell's protein factory

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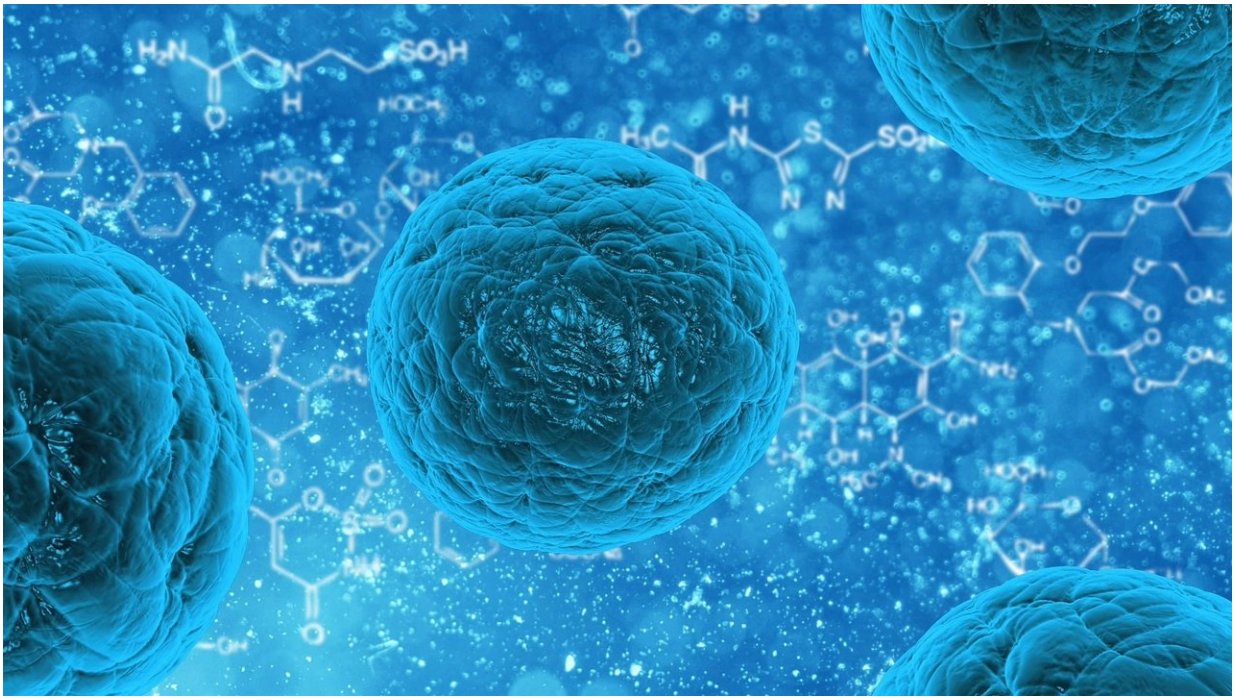

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You can think of a cell in your body like a miniature factory, creating a final product called proteins, which carry out various tasks and functions. In this cellular factory, genes control the series of sequential steps needed to create proteins, much like an assembly line moving a product along to completion. This process is known as gene expression.

Even when two cells are genetically identical and in the same environment, the amount of each protein they express can be very different. This variability—or noise—has been shown to play a role in viral infection, antibiotic resistance, and drug resistance in cancer cells.

A group of scientists led by Leor S. Weinberger, Ph.D., the William and Ute Bowes Distinguished Professor and director of the Center for Cell Circuitry at the Gladstone Institutes, are studying the factors within a cell that can influence noise.

"We are trying to determine whether differences in one step along the assembly line influences the final amount of proteins produced more than other steps," said Weinberger, who is also a professor of pharmaceutical chemistry at UC San Francisco.

Using a combination of computational and experimental methods, the team examined how a variety of cells produce different proteins, and measured noise for each step along the production process. They discovered that for 85 percent of genes, the noise magnitude is higher in the last step as compared to the first step.

"When thinking about gene expression, we used to be unsure how each step contributed to the final outcome," said Maike Hansen, Ph.D., postdoctoral scholar in Weinberger's laboratory and first author of the new study. "But we discovered that one step works very differently than we thought. It's as if you always thought the production process was very streamlined, but then realized it's actually much noisier."

Their findings, published in the scientific journal *Cell Systems*, indicate that the scientific community may have been misinterpreting an important step in gene expression for a long time. This could impact work by synthetic and systems biologists, as well as cell biologists.

The group's next step will be to investigate what mechanisms the cells employ to control noise.

"We've discovered an important step that increases cell-to-cell differences. These differences contribute to difficulties in treating various diseases." said Weinberger. "Once we understand the mechanisms involved, we can start to exploit them for therapeutic targets."

The paper "Cytoplasmic amplification of transcriptional noise generates substantial cell-to-cell variability" was published by *Cell Systems* on September 19, 2018

More information: Cytoplasmic Amplification of Transcriptional Noise Generates Substantial Cell-to-Cell Variability, *Cell Systems* (2018). www.cell.com/cell-systems/full … 2405-4712(18)30317-X , doi.org/10.1016/j.cels.2018.08.002

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