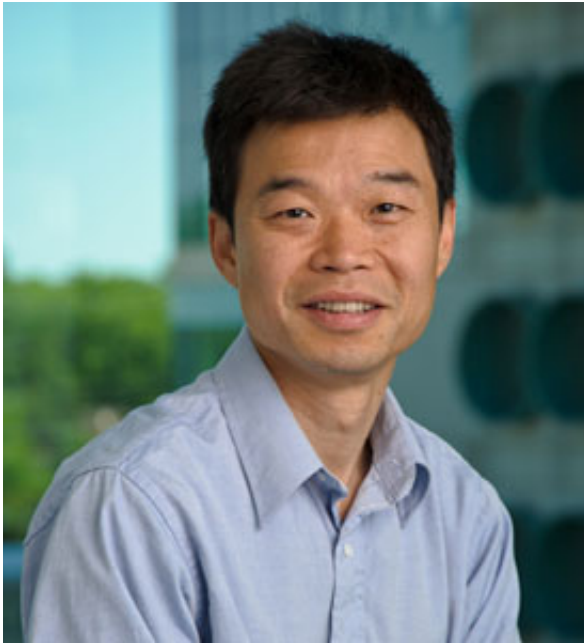


Physiologists uncover a new code at the heart of biology

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Dr. Yi Liu. Credit: UT Southwestern

UT Southwestern physiologists trying to understand the genetic code have found a previously unknown code that helps explain which protein should be created to form a particular type of cell.

The human body is made up of tens of trillions of cells. Each cell contains thousands of proteins, which determine how the cell should form and what functions it needs to perform. Proteins, in turn, are made up of hundreds of amino acids. The blueprint for each [protein](#) is

specified by genetic codons, which are triplets of nucleotides that can make 20 different types of amino acids. The way in which amino acids are linked together then determines which proteins are eventually produced, and in turn, what functions the cell will have.

What researchers found was that not only does the sequence of the amino acids matter, but so does the speed of the process in which the amino acids are put together into a functional protein.

"Our results uncovered a new 'code' within the genetic code. We feel this is quite important, as the finding uncovers an important regulatory process that impacts all biology," said [Dr. Yi Liu](#), Professor of Physiology.

It was long known that almost every amino acid can be encoded by multiple synonymous codons and that every organism, from humans to fungi, has a preference for certain codons. The researchers found that more frequently used codons – the "preferred codons" – speed up the process of producing an [amino acid chain](#), while less frequently produced codons slow the process. The use of either preferred or non-preferred codons is like having speed signs on the protein production highway: some segments need to be made fast and others slow.

"The genetic code of nucleic acids is central to life, as it specifies the [amino acid sequences](#) of proteins," said Dr. Liu, the Louise W. Kahn Scholar in Biomedical Research. "By influencing the speed with which a protein is assembled from amino acid building blocks, the use of "fast" and "slow" codons can affect protein folding, which is the process that allows a protein to form the right shape to perform a specific function. This speed control mechanism makes sure that proteins are assembled and folded properly in different cells. Therefore, the genetic code not only specifies the sequence of amino acids but also the shape of the protein."

The researchers found that proteins with identical amino acid sequences can have different functions if they are assembled at different speeds. This can have important implications for identifying human disease-causing mutations because this study indicates that a mutation does not have to change amino acid identity to cause a disease. In fact, most mutations in human DNA do not result in amino acid change.

"Therefore, our study indicates that the new "code" ? the speed limit of assembly ? within the [genetic code](#) can dictate the ultimate function of a given protein," said Dr. Liu.

The findings appear as the cover story of the journal *Molecular Cell*, one of the top molecular biology, biophysics, and biochemistry journals.

The latest findings extend prior research published by Dr. Liu and colleagues in *Nature* in 2013 that broke new ground by demonstrating that synonymous codons of a circadian clock protein are not the same in making functional proteins, despite the fact that they encode the same [amino acids](#). Genes can adapt to different environmental changes by choosing the most optimal codon, which is counterintuitive to natural selection.

Dr. Liu and his team are able to study these systems using a type of bread mold fungus called *Neurospora crassa*. The use of the mold allows for easy manipulation of its genes and codons in the laboratory that are more difficult to do in animals. Dr. Liu's lab is also trying to unravel the secrets of chronobiology and the molecular mechanisms that underlie an organism's daily biological clock, called the circadian clock. Biological clocks have been described in almost all organisms ranging in complexity from single cell organisms to mammals, and to function in the control of daily rhythms such as sleep-wake and activity cycles, body temperature cycles, endocrine functions, and gene expression.

Provided by UT Southwestern Medical Center

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