UC SANTA BARBARA

THE Current

January 2, 2025
Harrison Tasoff

It’s all about expression

Our brain is arguably the organ that most distinguishes humans from other primates. Its exceptional size, complexity and capabilities far exceed those of any other species on Earth. Yet humans share upwards of 95% of our genome with chimpanzees, our closest living relatives.

UC Santa Barbara professor Soojin Yi, in the Department of Ecology, Evolution, and Marine Biology, her doctoral student Dennis Joshy and collaborator Gabriel Santepere, at Hospital del Mar Medical Research Institute in Barcelona, aimed to determine how genes in different types of brain cells have evolved compared to those in chimpanzees. They found that, while our genes code for almost all the same proteins as other apes, many of our genes are much more productive than those of other primates. Their results, published in the Proceedings of the National Academy of Sciences, highlight the role of gene expression in the evolution and function of the human brain.

Interpreting nature’s blueprints

Each gene tells a cell to make a specific molecule, but this isn’t performed by the DNA itself. Instead, the information is relayed to cellular machinery by a molecule called messenger RNA. Researchers measure gene expression by observing the amount of mRNA a specific gene produces.

As scientists began to understand the role of the genome as life’s blueprint, they thought perhaps the human genome could explain our unique traits. But a thorough

comparison with chimpanzees in 2005 revealed we share 99% percent of our genes (though scientists have since revised this number). This confirmed earlier studies based on small numbers of genes that had suggested there was only a small difference between the human and chimpanzee genome.

Now biologists suspect that gene expression may underlie these differences. Consider a monarch butterfly. The adult has the same genome as when it was a caterpillar. The incredible differences between the two life stages all come down to gene expression. Turning on and off different genes, or having them code for more or less mRNA, can drastically alter an organism’s traits.

Getting a clearer picture

Previous research has found differences in gene expression between humans and chimpanzees, and that human cells tend to have higher gene expression, but the picture was blurry. The brain is made up of many varieties of cells. Traditionally, scientists organized brain cells into two major types: neurons and glial cells. Neurons carry electrochemical signals, a bit like the copper wiring in a building. Glial cells perform most of the other functions, such as insulating the wires, supporting the structure and clearing out debris.

Until recently, scientists could only study bulk tissue samples composed of many different types of cells. But within the past decade, it’s become possible to assay cell nuclei one at a time. This allows researchers to distinguish between cell types, and often even subtypes.

Yi, Joshy and Santepere used datasets generated from a device with a very narrow channel to separate each nucleus into its own chamber in an array. Then they grouped the cells by type before performing statistical analysis.

The team measured gene expression by observing the amount of mRNA a specific gene produced in humans, chimpanzees and macaques. An upregulated gene produces more mRNA in a given species compared to the others, while a downregulated gene produces less. Comparing chimpanzees and humans to macaques enabled the researchers to tell when differences between the two apes were due to changes in chimpanzees, changes in humans, or both.

The authors recorded differences in the expression of about 5-10% of the 25,000 genes in the study. In general, human cells had more upregulated genes compared to chimpanzees. This is a much larger percentage than researchers found when they couldn't break down the analysis by cell type. And the percentage grew to 12-15% when the authors began to consider cell subtypes.

"Now we can see that individual cell types have their own evolutionary path, becoming really specialized," Yi said.

Not just neurons

The intricacy of our neural pathways is unrivaled in the animal kingdom, however Yi suspects that our unique intellect isn't a result of this on its own. Human glial cells account for more than half of the cells in our brains, a much larger percentage than in even chimpanzees.

Among glial cells, oligodendrocytes showed the greatest differences in gene expression. These cells create the insulation that coats neurons, enabling their electrical signals to travel much more quickly and efficiently. In a collaborative study published the previous year, the team observed that humans have a higher ratio of precursor versus mature oligodendrocytes compared with chimpanzees. Yi suspects this may relate to the amazing neural plasticity and slow development of human brains.

"The increased complexity of our neural network probably didn't evolve alone," Yi said. "It could not come to existence unless all these other cell types also evolved and enabled the expansion of the neuron diversity, the number of neurons and the complexity of the networks."

This study only considered cells from a few regions of the brain; however, the cells in one area of the brain may differ from their counterparts in other areas. Yi plans to study the mechanisms behind differences in gene expression and how genes map to different traits.

She also plans to trace differential gene expression even earlier in our evolutionary history by incorporating baselines from even more distantly related animals. And she's interested in studying genomic differences between us and other archaic humans, like Neanderthals and Denisovans.

Evolution is about more than merely changing genes. “Differential gene expression is really how human brains evolved,” Yi said.

Media Contact
Harrison Tasoff
Science Writer
(805) 893-7220
harrisontasoff@ucsb.edu

About UC Santa Barbara

The University of California, Santa Barbara is a leading research institution that also provides a comprehensive liberal arts learning experience. Our academic community of faculty, students, and staff is characterized by a culture of interdisciplinary collaboration that is responsive to the needs of our multicultural and global society. All of this takes place within a living and learning environment like no other, as we draw inspiration from the beauty and resources of our extraordinary location at the edge of the Pacific Ocean.