Difference in gene switching discovered in different parts of brain

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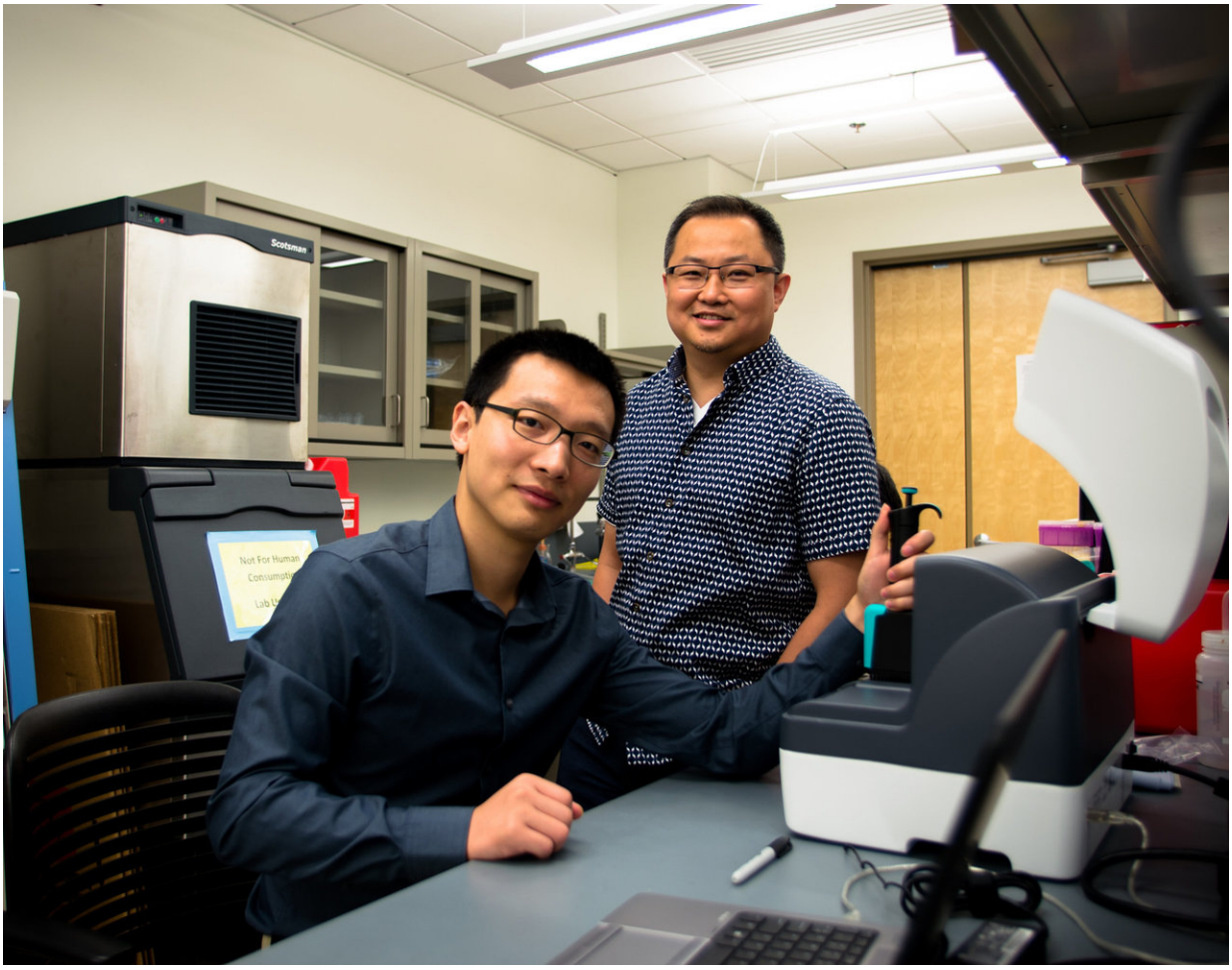

Sai Ma, former Virginia Tech biomedical engineering Ph.D. student, and Chang Lu, the Fred W. Bull professor of Chemical Engineering at Virginia Tech. Credit: Virginia Tech

It is understood that different parts of brain have drastically different functions. However, how these different functions are sustained and regulated at the molecular level has been elusive.

In a study published in *Science Advances*, Chang Lu and his team found significant difference in the molecular machinery that turns on and off gene expression between cerebellum and prefrontal cortex of a mouse brain. Their results provide clues to the molecular apparatus that is involved in conscious thinking in brains.

"Prefrontal cortex, at the frontal part of the brain, is generally considered the center for decision making and planning, while cerebellum, at the back of the skull, is responsible for motor control," said Lu, the Fred W. Bull professor of Chemical Engineering at Virginia Tech.

The goal of the study was to gain fundamental understanding at the molecular level on how different brain functions are linked with the molecular biology. Cells in different parts of brain have the same DNA sequence, or genome, but their epigenomes can be different. The study of how epigenomic biology differs in these two parts of brain provides the basis for deciphering the biology of thinking, identifying drug targets and designing drugs to treat mental illnesses.

Lu and researchers profiled one category of epigenomic changes called histone modification. Histones are the proteins that are involved in chromosomes. It is known that their changes track the changes in gene activities.

"We chose to study the epigenomes of the same type of brain cells in cerebellum and prefrontal cortex. Epigenome is the molecular machinery for switching genes on and off," said Lu. "They are much more variable and dynamic than the genome sequence."

A method called SurfaceChIP-seq was created to be compatible with mapping the epigenome using a tiny quantity of brain cells. The sensitivity of the method was critical for examining various types of histone modifications in brain cell types such as neurons and glia.

The team found some histone marks had patterns that were very specific to the brain region while the others looked very similar across the board. Also discovered were numerous functional elements in the epigenomes that were different across cerebellum and prefrontal cortex. One feature that stood out was that the so-called "super enhancers" discovered in the neurons were very unique to the brain region.

"I would summarize that the variable histone marks probably play bigger roles in shaping the different functions and activities in the two brain regions," said Lu "Eighty percent of the super enhancers in neurons of prefrontal cortex were not present in the neurons from cerebellum."

More information: "Low-input and multiplexed microfluidic assay reveals epigenomic variation across cerebellum and prefrontal cortex" *Science Advances* (2018). advances.sciencemag.org/content/4/4/eaar8187

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