Scientists identify genes activated during learning and memory

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Researchers have long recognized that for learning and memory to take place, certain genes must be activated to alter neuron activity inside the brain. Disruptions in normal gene expression within these neurons can lead to alarming consequences, such as seizures and epilepsy. But identifying and cataloging all the genes involved in learning is a daunting task. In the March 13 issue of *BMC Neuroscience*, Carnegie Mellon University scientists show how an innovative computational approach can provide a rapid way to identify the likely members of this long sought-after set of genes.

"The work could ultimately lead to the development of drugs to treat neurological disorders," said Alison Barth, assistant professor of biological sciences and a member of the Center for the Neural Basis of Cognition (CNBC). "We also expect this work to provide a valuable platform for any investigator to understand how neurons change at the molecular level during learning and the formation of memory."

As an animal learns and remembers, specific neurons inside its brain are activated. The molecular changes associated with learning alter a neuron's function — a process called plasticity. For many years, neuroscientists have known that two factors, CREB and zif268, activate genes involved in neuronal plasticity and learning. CREB and zif268 are transcription factors, binding to a cluster of chemical bases represented in the genetic code as letters. Once bound, they regulate genes that, in turn, dictate the assembly of other proteins that alter a neuron during memory and learning.

The Carnegie Mellon team created a step-by-step set of instructions for a computer to search the letters of code that make up the human genome to find just those genes activated by CREB and zif268. They specifically searched almost 20,000 genes to find those that CREB and zif268 bind to. This work, conducted by Carnegie Mellon undergraduate Andreas Pfenning and supervised by Assistant Professor of Biological Sciences Russell Schwartz, was also performed on our distant mammalian relative, the mouse.

The computer program found hundreds of instances of genes that bind with either CREB or zif268 — and sometimes both — in human and mouse genomes. A huge proportion of these genes had never been previously identified as CREB or zif268 targets.

"Finding a gene that appears to be activated in both the mouse and human strongly suggests that the gene is involved in memory and learning," said Schwartz. "Genes that behave similarly in distantly related animals are more likely to have an important function that has been retained over the course of evolution."

The Carnegie Mellon team has made its findings available and searchable via an open source/online journal. Previous studies on genes associated with neural plasticity have not focused on a complete set of genes, nor has the work been searchable, according to Barth. But now, their online database of the plasticity transcriptome includes the gene name, symbol and reference number — data that are not usually all collected and made freely available.

"By using standard nomenclature and multiple identifiers, we've made this a robust set of data for future research studies," Schwartz added.

Source: Carnegie Mellon University