MedicalXpress

A master switch that plays a key role in energy metabolism and human brain evolution

January 26 2016

Credit: public domain

Scientists have long used comparative animal studies to better understand the nuances of human evolution, from making diverse body plans to the emergence of entirely powerful and unique features structures, including the human brain.

Now, in a new study appearing in the advanced online edition of

Molecular Biology and Evolution, corresponding authors Katja Nowick and Robert Querfurth et al. have explored the global gene regulator GABPa to better understand its influence as a master switch. Their work honed in on human specific DNA regions potentially contributing to human evolution in key functions including cell energy, division and death, and diseases ranging from brain disorders to diabetes.

Many of the GABPa gene regulatory sites were found to be significantly enriched at genes important for brain, central nervous system and spinal cord functions that are unique to humans, an area ripe for future research, and GABPa deficits linked to Alzheimer's and Parkinson diseases, breast cancer, and autism.

GABPa exerts its profound genomic influence by a tandem repeat of four highly conserved DNA letters. The GGAA consensus motif is found to control genes in all primates, mice, dogs and cows, underscoring its importance in these animals. By performing ChIP-Seq experiments in a human cell line, the group found that GABPa exercises its influence across the genome at 11,619 putative GABPa binding sites representing nearly 4,000 genes.

Through a tour de force sequence comparison of the human GABPa bindingsites with similar sequences from 34 mammals, they identified 224 GABPa binding sites unique to humans. Comparing chimpanzee, macaque and human cell lines and mutating the GGAA sequence to more ancestral states to determine how these changes affected GABPa function, they further narrowed down their function. For instance, when the human GABPa binding sites were introduced into primate cells, gene expression was increased up to 5 times in 17 out of 18 cases, indicating that a recent human mutation in GABPa resulted in higher gene expression and forces behind the evolution of novel, uniquely human functions.

"Mutations that cause changes in the regulation of gene activities are one of the major factors in shaping species during evolution," said corresponding author Katja Nowick. "Our study demonstrates how, out of the millions of DNA regions, in which we differ from other apes, we can sift out those that, in response to a specific regulatory protein, cause gene activity changes in human cells. In this set, we find genes involved in brain and breast development and also in diseases like Alzheimer's and Parkinson's."

Provided by Oxford University Press

Citation: A master switch that plays a key role in energy metabolism and human brain evolution (2016, January 26) retrieved 10 April 2024 from https://medicalxpress.com/news/2016-01-master-key-role-energy-metabolism.html