Peoples' Democratic Republic of Algeria
Ministry of Higher Education and Scientific Research
University of Abou Bakr Belkaid Tlemcen

FACULTY OF NATURAL AND LIFE SCIENCES AND EARTH AND UNIVERSE
DEPARTMENT OF BIOLOGY

MOLECULAR BIOLOGY 3RD YEAR LICENSE COURSE TITLE: SCIENTIFIC ENGLISH

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TD Chap 03

Exercise 01:

Summarize the Article

THE DNA REGIONS IN OUR BRAIN THAT CONTRIBUTE TO MAKE US HUMAN

Date:
December 16, 2020
Source:
Swiss Institute of Bioinformatics

Gene expression, not gene sequence

To explain what sets human apart from their ape relatives, researchers have long hypothesized that it is not so much the DNA sequence, but rather the regulation of the genes (i.e. when, where and how strongly the gene is expressed), that plays the key role. However, precisely pinpointing the regulatory elements which act as 'gene dimmers' and are positively selected is a challenging task that has thus far defeated researchers (see box).

Marc Robinson-Rechavi, Group Leader at SIB and study co-author says: "To be able to answer such tantalizing questions, one has to be able identify the parts in the genome that have been under so called 'positive' selection [see box]. The answer is of great interest in addressing evolutionary questions, but also, ultimately, could help biomedical research as it offers a mechanistic view of how genes function."

A high proportion of the regulatory elements in the human brain have been positively selected

Researchers at SIB and the University of Lausanne have developed a new method which has enabled them to identify a large set of gene regulatory regions in the brain, selected throughout human evolution. Jialin Liu, Postdoctoral researcher and lead author of the study explains: "We show for the first time that the human brain has experienced a particularly high level of positive selection, as compared to the stomach or heart for instance. This is exciting, because we now have a way to identify genomic regions that might have contributed to the evolution of our cognitive abilities!"

To reach their conclusions, the two researchers combined machine learning models with experimental data on how strongly proteins involved in gene regulation bind to their regulatory sequences in different tissues, and then performed evolutionary comparisons between human, chimpanzee and gorilla. "We now know which are the positively selected regions controlling gene expression in the human brain. And the more we learn about the genes they are controlling, the more complete our understanding of cognition and evolution, and the more scope there will be to act on that understanding," concludes Marc Robinson-Rechavi.

Positive selection: a hint of the functional relevance of a mutation

Most random genetic mutations neither benefit nor harm an organism: they accumulate at a steady rate that reflects the amount of time that has passed since two living species had a common ancestor. In contrast, an acceleration in that rate in a particular part of the genome can reflect a positive selection for a mutation that helps an organism to survive and reproduce, which makes the mutation more likely to be passed on to future generations. Gene regulatory elements are often only a few nucleotides long, which makes estimating their acceleration rate particularly difficult from a statistical point of view.

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Story Source:

Materials provided by **Swiss Institute of Bioinformatics**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Jialin Liu, Marc Robinson-Rechavi. **Robust inference of positive selection on regulatory sequences in the human brain**. *Science Advances*, 2020; 6 (48): eabc9863 DOI: 10.1126/sciadv.abc9863

Exercise 02:

Summarize the Article

RECENT HIGHLIGHTS IN MOLECULAR BIOLOGY AND EVOLUTION

Source:

Molecular Biology and Evolution (Oxford University Press)

Human females, unlike males, have two copies of the X chromosome. This double dose of the X chromosome presents an interesting genetic conundrum, namely what happens to the genes on this extra chromosome? If all of the genes were to be expressed then females would have twice the dose of the genes' products compared with males.

To compensate for this extra set of genes in females, a process called X-Chromosome Inactivation switches off one entire X chromosome and its complement of genes, shriveling it up like a raisin so that the genes can't be expressed.

However, this process is not perfect, and some genes are able to escape this 'silencing'. These escaping genes are of interest as in about one in a thousand births of girls where the newborn inherits a further copy of the X chromosome, making them XXX rather than simply XX. The very high level of expression of the genes that have escaped X-chromosome inactivation can have serious consequences including growth abnormalities and mental impairment.

Professor Laurence Hurst, from the University of Bath's Department of Biology & Biochemistry, in collaboration with colleagues from Shanghai Institute for Biological Sciences, in China, has carried out a unique study which has built on previous understanding in this area. Unlike previous research that compared X-chromosome inactivation between mice and humans, this study looked within the human species at two different groups, Europeans and Yorubans from Africa, with interesting results.

The study found that 114 genes on the X chromosome had escaped X-chromosome inactivation, including 76 that had not been previously identified.

Professor Hurst said: "The genes we have identified are located in areas of the X chromosome where we expected to find escaping genes. We have now found that there are also great variations between the two populations we studied, and between individuals within these populations. This level of variation matches what we see in women with three X chromosomes -- some appear normal but some are profoundly affected."

In some individuals, up to 80 genes were shown to escape. The genes that were most variable in escape were also shown to be the fastest evolving. Previous research has found that escaping genes undergo stronger purification selection -- the process of selective removal of genes that are deleterious or harmful, but the current evidence didn't confirm this.

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The work has implications for understanding genetic diseases. Professor Hurst commented that "importantly, our research could tie in the sorts of genes that escape X-chromosome inactivation with the symptoms of having too many X chromosomes, in that the genes we found were commonly those previously associated with mental impairment, the most common symptom of XXX syndrome.

"We have found 22 genes of interest that both escape X inactivation and that are associated with mental functioning. We hope that this research will enable the pinpointing of exactly which of these genes are associated with XXX syndrome and in turn, in the future, to better management of the condition."

Story Source:

Materials provided by **Molecular Biology and Evolution (Oxford University Press)**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Y. Zhang, A. C. Morales, M. Jiang, Y. Zhu, L. Hu, A. O. Urrutia, X. Kong, L. D. Hurst. **Genes that escape X-inactivation in humans have high intraspecific variability in expression, are associated with mental impairment but are not slow evolving.**. *Molecular Biology and Evolution*, 2013; DOI: 10.1093/molbev/mst148