Investigating the role of transposable elements in human brain evolution

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Abstract

The human brain is the largest and most complex of all primates, having increased about 3-fold in size compared to that of our closest living relative, the chimpanzee. Little is known about non-human primate brain development as non-human primate tissue is not readily available at early developmental time points. Yet, it is essential to analyse non-human primate models to identify and understand molecular features unique to the human brain and its function. As only few changes occurred in protein-coding genes, significant differences must be present in other parts of the genome.
Transposable elements (TEs) comprise at least 50% of most primate genomes. They can contribute to genome evolution as they carry regulatory sequences and have been found to serve, for example, as enhancers and alternative promoters. Moreover, TEs are insertional mutagens leading to genetic disease. Therefore, they are silenced by repressive histone marks and DNA methylation. Interestingly, methylation can spread and impact adjacent regions making TEs noteworthy candidates for methylome evolution. However, due to their challenging analysis and lack of non-human primate material, the role of TEs in primate brain development and human brain evolution has not been investigated thoroughly.
Here, we exploit human, chimpanzee and rhesus macaque induced pluripotent stem cells and cerebral organoids as a model for primate brain development. We employ bulk and single-nuclei RNA-seq as well as Oxford Nanopore Technologies long-read whole genome DNA sequencing to investigate differential TE and gene methylation along with expression during neural differentiation in human and non-human primates. Using this multi-omics approach, we aim to identify species-specific TE loci important for brain development and evolution.

Keywords: human brain evolution, primate brain development, methylation

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