

## WHAT MADE US HUMANS?

*In search of fastest-evolved regions of the human genome (Human Ancestor Quickly Evolved Regions, HAQERs).*

What are the genetic basis of human uniqueness? The search obviously began with the search for human-specific genes. Genome sequencing of the great apes has revealed, however, that chimpanzees and humans are very similar in this respect. As a result, HAQER's research focused on differences in regulatory regions. The search became much more complex when the ENCODE project revealed that regulatory domains are widespread in the genome.

[Mangan et al.](#)<sup>1</sup>, in a paper on Cell, reported the development of a multiple *in vivo* single cell enhancer assay able to reveal rapid sequence divergence in HAQERs leading to human specific enhancers in the developing cerebral cortex development. They found evidence of both positive selection and high local mutation rates in HAQERs, once thought to be mutually exclusive, and pointed to an episodic burst of directional positive selection prior to the human-Neanderthal split. They also comment that this high mutation rate is a trade-off between rapid evolution and neurodevelopmental disease.

Trade-off can be considered a general rule in biology. A recent article in [Science](#)<sup>2</sup> provided yet another example of a trade-off. B cells express the mutator enzyme activation-induced deaminase (AID), generating double-strand breaks (DSB) at Ig genes through the processing of AID-induced mismatches by DNA repair pathways. In this way a large range of antibodies can be produced. These DSBs, however, can affect proto-oncogenes, especially MYC and BCL6, leading to cancers such as Burkitt's lymphoma and diffuse large B-cell lymphoma.

- 1- [https://www.cell.com/cell/retrieve/pii/S0092867422013587? returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867422013587%3Fshowall%3Dtrue](https://www.cell.com/cell/retrieve/pii/S0092867422013587?returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867422013587%3Fshowall%3Dtrue)
- 2- <https://www.science.org/doi/10.1126/science.abj5502>