Expression analysis of medium-length RNA in the human, chimpanzee, macaque and mouse brains

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Changes in expression of transcripts have been suggested to play an essential role in evolution of the human phenotype[1]. Indeed recent studies examining differences in expression of messenger RNA (mRNA) and short regulatory RNA – microRNA (miRNA) – between the human brain and brains of non-human primates identified a number of human-specific changes potentially driving phenotypic specialization of our species.

Here, we assessed expression of ncRNA with specific size distribution – between 100 and 200 nt – in the prefrontal cortex (PFC) of humans, chimpanzees, rhesus macaques and mice using high-throughput RNA sequencing (RNA-seq). This fraction primarily includes snRNA and snoRNA. PFC is one of the fast evolving regions of the mammalian neocortex and was implicated in a number of cognitive processes particularly enhanced in humans such as executive planning.

We identified differentially expressed ncRNA genes and show that small ncRNA expression evolves rapidly across species, with more changes found on the human than

on the chimpanzee evolutionary lineages.

One of the striking examples showing human-specific expression change is SNORA29 gene, which appears to be “shunted down” in human PFC, while being expressed in other primates and mice. Indeed in situ hybridization shows SNORA29 localized in neuron nuclei of macaque PFC, but is not detectable in human PFC tissue.

Our sequencing protocol provided reads from 5’ ends of unsonicated RNA. Aligned on the genome the reads form easily identifiable stacks at transcription starts. We took advantage of it and predicted novel ncRNA. For that a specific procedure was designed and trained on a set of annotated human snoRNAs. It performed better than a PeakPredictor program developed to predict peaks in ChIP-seq data yielding 85 novel ncRNA predictions in human.

1. King and Wilson (1975) Evolution at two levels in humans and chimpanzees, *Science,* **188** (4184): 107-116