TRANSCRIPTOMICS

Revealing the extent of RNA editing

Mammalian RNAs can be edited by the conversion of adenosine to inosine, which is read as guanosine, but technological constraints have limited our view of the overall contribution of RNA editing to transcriptomic diversity. A new method now allows RNA editing sites to be identified genome-wide.

Identifying edited sites requires sequencing of both the genome and the transcriptome; this is very costly and has limited the number of potentially edited sites that have been profiled. Li and colleagues overcame this problem by using a targeted sequencing approach. They first identified 59,437 potentially edited sites from the non-repetitive portion of the human genome by comparing the reference genome sequence with all available human mRNA and EST sequences. The next step was to design probes that allow targeted, massively parallel amplification of these putative editing sites. The authors were able to design probes for just over 41,000 of the candidate sites.

Li and colleagues then took genomic DNA and cDNA from seven different tissues of one individual and used high-throughput sequencing to compare the genome with the transcriptome at the sites targeted by the probes. At high levels of stringency, the authors identified 239 sites that are likely to undergo RNA editing. Validation using PCR and Sanger sequencing and enrichment of the sites for features that are consistent with targets of adenosine deaminases acting on RNA (ADARs) — the enzymes responsible for RNA editing in mammals — suggest the reliability of the method.

As only 19 edited sites were previously known in humans, this study significantly expands our view of the extent to which adenosine to inosine editing affects the human transcriptome. The newly identified sites lie in both coding and non-coding regions, although there is, as might be expected, a bias away from editing that affects protein sequence. The targets of editing are enriched in functions related to the nervous system, consistent with previously identified targets and the fact that RNA editing is known to be essential for normal brain function. The method described in this paper will allow the identification of other edited sites in different tissues and individuals, and will facilitate the investigation of potential roles of RNA editing in human disease.

Louisa Flintoft

ORIGINAL RESEARCH PAPERS Li, J. B. *et al.* Genome-wide identification of human RNA editing sites by parallel DNA capturing and sequencing. *Science* **324**, 1210–1213 (2009)
FURTHER READING Wang, Z. *et al.* RNA-Seq: a revolutionary tool for transcriptomics. *Nature Rev. Genet.* **10**, 57–63 (2009)