In the news

UNEXPECTED MISMATCHES, BUT DOGMA INTACT

A debate has been stirred by a report from Vivian Cheung's laboratory published in *Science* (19 May 2011; doi:10.1126/science.1207018). The authors demonstrated unprecedented mismatches between RNA sequences and the DNA that encodes them, as identified by next-generation sequencing. The frequency of these mismatches (>10,000 exonic sites in the human genome) and the diversity of base changes seem far beyond our current understanding of RNA editing.

A discussion has ensued questioning whether next-generation sequencing and mapping are sufficiently accurate to detect such mismatches (*The Scientist*, 19 May 2011). However, technical artefacts cannot explain all of the mismatches, as the authors validated a subset by Sanger sequencing and by mass spectrometry of the resultant variant proteins.

Most of the debate tackles a cornerstone of molecular biology. In one commentary (*Nature News*, 19 May 2011), it is argued that these results violate the 'central dogma', because DNA is not faithfully transcribed into RNA. However, in his classic 1970 paper (*Nature* **227**, 561–563), Francis Crick frames the central dogma merely in terms of the direction of information transfer, and he acknowledges that the dogma says "in particular nothing about errors". Cheung agrees, telling us "we do not claim to find 'loopholes' in the central dogma. If our results violate the dogma then so would other findings including epigenetic changes, which no one would claim."

If widespread confirmation of this RNA and protein variation is forthcoming, key potential areas for future research include deciphering the molecular mechanisms responsible for this variation and determining whether it could influence human disease in ways that are invisible to current DNA-based analyses.

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