REWRITING THE GENETIC CODE

CRISPR-Cas9 has allowed the manipulation of genomic DNA fragments. The 2020 Nobel Prize to Doudna and Charpentier underscored its importance. This technology is usually used to modify some bases of the genomic DNA, and much of the debate has focused on applications in humans.

There are other fields of application of CRISPR and related technologies where the manipulation of the genetic material is incredibly more profound. A striking example is reported by Ostrov et al. in Science 372, 1057-1062, 2021 in *Escherichia coli* (commented on by Jewel and Chatterjee, same issue).

Earlier, in 2016, authors of an article in Science (353, 819-822, 2016) designed, and partially generated, an *E. coli* in which a few appropriate triplet codons were replaced, using CRISPR-Cas9, by synonymous codons. The corresponding tRNAs were deleted. There were no substantial consequences for the bacterium, but the infecting phages were not able to synthesize their proteins due to the absence of some tRNAs. The *E. coli* had become immune to phages!

The authors of the paper by Ostrov et al. have gone further. They have created an *E. coli* in which some codons were forged to encode three non-canonical amino acids. In this way they ensured phage immunity and the potential to produce a range of novel proteins.