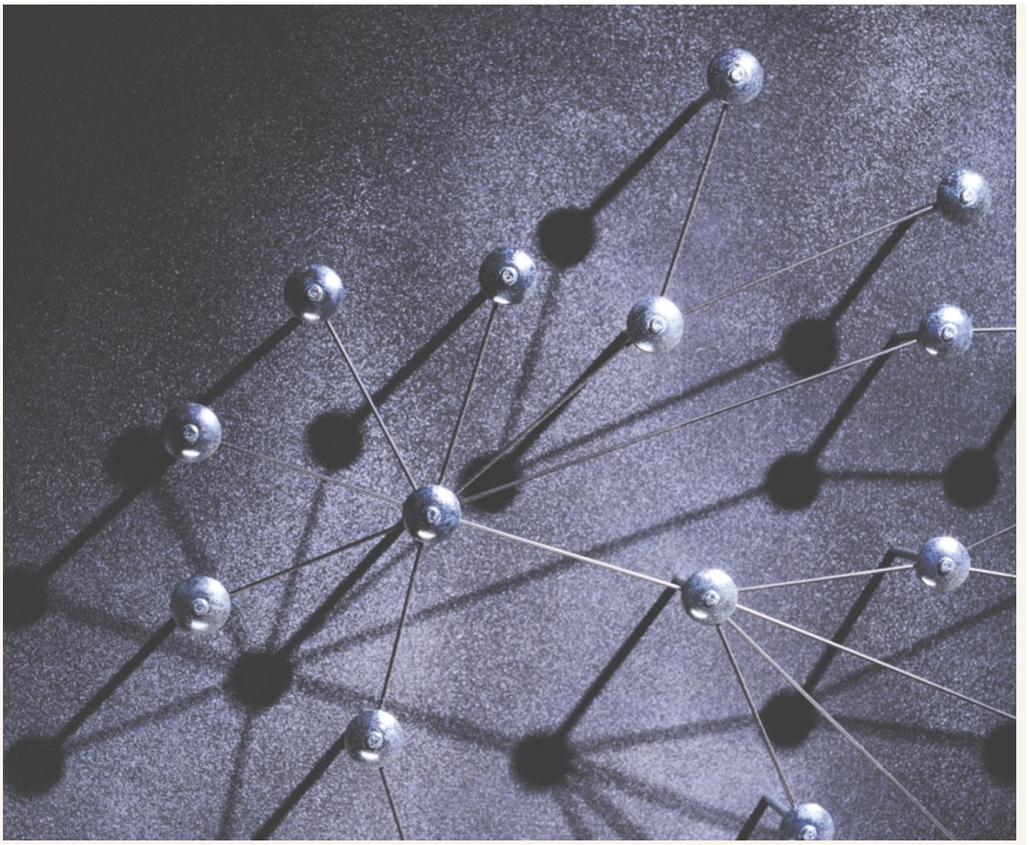

TECHNOLOGY

Expanding life's repertoire

Living organisms have had to adapt to diverse and extreme habitats, and yet all of them use the same repertoire of 20 amino acids. New proteins have evolved by generating novel combinations of amino acids, sometimes through amino-acid modification but never by incorporating non-standard amino acids. Two groups, reporting in *Science,* explore the possibilities of expanding the amino-acid set of a living organism. By generating bacteria that incorporate non-standard amino acids into their proteins, these studies promise to create proteins with new chemical and structural properties *in vivo*.

The specificity of amino-acid incorporation into a protein is achieved in two main steps. First, a tRNA molecule is loaded with a correct amino acid by a specific aminoacyl tRNA synthetase (aaRS), and second, the correct tRNA–amino-acid pair binds to its cognate mRNA codon by complementary base pairing. The crucial step in amino-acid specificity is the loading of the amino acid onto the tRNA, which is why both groups focused on this process.

The approach of Döring *et al.* relies on the fact that certain aaRSs, as well as being able to discriminate between amino acids at the tRNA-loading stage, also have an editing function, which replaces any wrongly loaded amino acids. The authors take advantage of the fact that under wild-type conditions, $tRNA^{Val}$ can be charged with several chemically similar amino acids, which are then edited out before protein synthesis. After random mutagenesis, Döring *et al.* recovered mutations in the editing subunit of aaRS that incorrectly charge $tRNA^{Val}$ with cysteine. Moreover, when amino acids similar to cysteine (such as L-aminobutyrate or L-threonine) were provided in the growth medium, they were incorporated into the proteins of this mutant strain in response to valine codons.

Wang *et al.* set about expanding the genetic code of *Escherichia coli* by introducing a modified form of both the $tRNA^{Tyr}$ and the tyrosyl-tRNA synthetase from the archaebacterium *Methanococcus jannaschii* into it. The anticodon of this $tRNA^{Tyr}$ was modified so that it recognized an *E. coli* nonsense codon; and a mutagenized version of the tyrosyl-tRNA synthetase was used that binds *O*-methyl-L-tyrosine (instead of tyrosine) to $tRNA^{Tyr}$. The new synthetase does not recognize endogenous *E. coli* tRNAs and attaches only this unnatural amino acid to the foreign tRNA.

Such engineered organisms could be used to study proteins and their cellular functions, and have important implications for biotechnology. For example, incorporating non-standard amino acids into proteins might in some cases result in structural changes and new catalytic properties. The work of Döring *et al.* also raises interesting issues of how the restriction of the genetic code has evolved, in particular the crucial role of the aaRS editing function.

Magdalena Skipper

References and links

ORIGINAL RESEARCH PAPERS Döring V. *et al.* Enlarging the amino acid set of *Escherichia coli* by infiltration of the valine coding pathway. *Science* **292**, 501–504 (2001) | Wang, L. *et al.* Expanding the genetic code of *Escherichia coli*. *Science* **292**, 498–500 (2001)

FURTHER READING Böck, A. Invading the genetic code. *Science* **292**, 453 (2001)

WEB SITES Philippe Marliére's lab | Paul Schimmel's lab | Peter Schultz's lab

IN THE NEWS

Sweet genes?
Two studies, published last month in *Nature Genetics* and *Nature Neuroscience* report:
"The gene behind the most seductive of taste receptors — sweetness — has been at last identified."
The New Scientist, UK

Not surprisingly, the studies generated much media interest:
"Can't resist that daily dose of chocolate? Piling on the pounds with puddings? Fear not, you are not suffering from a weak will; you can now blame it on your genes."
***The Times*, UK**

It might explain why you take "three lumps of sugar in [your] coffee, as opposed to one lump or two."
The New York Times, US

The good news is that this research could
"Pave the way for a new generation of designer diet foods and even drugs to encourage healthy eating."
***The Times*, UK**

And, for those who can't resist a snack …
"Decreasing the activity of this gene may enable people to control their urges to overindulge in sweets."
The New York Times, US

Having a sweet tooth also makes evolutionary sense.
"Sweet things are high in carbohydrates with a high nutritional value. [Discerning]… bitterness also stops you from eating unripe fruit or many poisonous plants."
***The Times*, UK**

Commenting on the nature of the difference between the receptor in two strains of mouse:
" 'It seems fitting that the presence or absence of a sugar chain on a sweet taste receptor should determine sensitivity and preference for sweetness in life.' "
BBC News Online

Tanita Casci