

# **Engineering the genetic code: state of the art, problems, solutions and future prospects**

*Nediljko Budisa, Berlin Institute of Technology/TU Berlin, Germany*

The expansion of the genetic code offers the best possible platform for the transfer of numerous chemical reactions and processes from the chemical synthetic laboratory into the biochemistry of living cells. The incorporation of biologically occurring or chemically synthesized non-canonical amino acids (ncAAs) in recombinant proteins and even proteomes works efficiently via reprogrammed protein translation. Orthogonal pairs consisting of aminoacyl-tRNA synthetase and its cognate tRNA proved to be general tool for the assignment of certain codons of the genetic code with a maximum degree of chemical liberty. However, orthogonal pairs should also be designed to serve as generalist tools so that ncAAs-mediated protein engineering will not only be relevant for single recombinant proteins, but also feasible throughout the entire cellular proteome.

In the near future, I anticipate ground-breaking works on various systems with the codons in the genetic code emancipated and liberated from the current chemical function. In addition, the use of genome remodeling will enable stable and valuable ncAAs additions to the entire proteome of a cell. As the whole research area moves towards maturity, more and more approaches will contribute to solve industrially relevant bio-production problems, including advanced peptide and protein production. Moreover, the genetic code engineering is just first step of the long way in search for reliable methodologies to design and deploy artificial biodiversity while preserving the old natural world.