The genetic code, elucidated in the 1960s through the work of Nirenberg, Ochoa, Khorana and their coworkers, provides a set of molecular instructions for translating nucleic acids into proteins. Codons are assigned to amino acids through high-fidelity charging of transfer RNAs, and through accurate base-pairing between charged tRNAs and messenger RNA. Over the last decade, cells have been outfitted with modified translational machinery that enables the participation of an expanded set of amino acids in protein synthesis. These developments have stimulated a unified view of the chemistry of natural and synthetic macromolecules, and provided a basis for powerful new approaches to protein design, protein evolution, biological imaging, and proteome-wide analysis of cellular processes.

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