The ancient essential process of ribosomal protein synthesis requires twenty sets of aminoacyl-tRNAs (aa-tRNAs), one for each canonical amino acid. Since Crick proposed his adaptor hypothesis (1) it was commonly accepted that all organisms possess twenty aaRSs, each enzyme specific for attaching one amino acid to tRNA. It is now clear that aa-tRNA formation is more varied, as the biosynthetic routes to Asn-tRNA, Gln-tRNA, Lys-tRNA, Cys-tRNA and Sec-tRNA vary greatly in nature (2). Asn-tRNA and Gln-tRNA can be formed by two redundant mechanisms, direct acylation or pre-translational amino acid modification by amidation; the routes to these aa-tRNAs differ not only in the three domains of life (3) but also vary among organelles (4). These transamidation enzymes (5) appear to have evolved by recruitment of amino acid metabolizing enzymes. The aminoacylation of pyrrolysine, the 22nd cotranslationally inserted amino acid, is catalyzed by an aaRS solely specific for a modified amino acid (6). An analogous enzyme forms O-phosphoseryl-tRNA$_{Cys}$ (7), the required intermediate in Cys-tRNA formation in methanogenic archaea (7). Based on similar enzymology, O-phosphoseryl-tRNA$_{Sec}$ is the precursor for synthesis in archaea and eukaryotes of selenocysteine, the 21st cotranslationally inserted amino acid (8,9).

2. Sheppard K et al. (2008) From one amino acid to another: tRNA-dependent amino acid biosynthesis. Nucl Acids Res. 36, 1813.