

D-chiral specificity of archaeal and cyanobacterial D-aminoacyl-tRNA deacylases

Mohd Mazeed¹, Raghvendra Singh¹, Santosh Kumar Kuncha¹, Satya Brata Routh¹, Shobha P. Kruparani¹, Rajan Sankaranarayanan¹

¹Centre For Cellular And Molecular Biology, Hyderabad, India
E-mail: mazeedmohd@ccmb.res.in

Biological macromolecular world is homochiral. D-aminoacyl-tRNA deacylase (DTD) plays an important role in maintaining homochirality of proteins by removing mistakenly attached D-amino acids from tRNAs [1]. In nature, three distinct DTDs exist, namely DTD1, DTD2 and DTD3. DTD1 is present in bacteria and eukaryotes, but absent in most archaea and cyanobacteria. DTD function is carried out by DTD2 in archaea and by DTD3 in cyanobacteria. Additionally, DTD2 is also reported in several plants. Interestingly, DTD1, DTD2 and DTD3 perform similar function without sharing any sequence similarity and structural homology among each other. Surprisingly, DTD2 shares structural similarity with a peptidyl-tRNA hydrolase, which is an essential enzyme. We have solved the first crystal structure of DTD3 at 1.68 Å, which is a structural homolog of DNase TatD. Strikingly, the positions of active site elements are also conserved between DTD3 and TatD. Active site of DTD1 has a fundamental design flaw by being porous to the smallest and achiral amino acid glycine, making it incapable of discriminating between glycine and D-amino acids, leads to glycine "misediting paradox" [2,3]. Biochemical analysis of DTD2 and DTD3 revealed absolute D-chiral specificity, which does not cross-react with even the smallest and achiral glycine. Attempts are underway to understand this mechanism of absolute D-chiral configuration specificity of DTD2 and DTD3. Remarkably, the role of 2'-OH of A76 of tRNA is indispensable for catalysis in all the three DTDs.

[1] Calendar, R. & Berg, P. (1967). J. Mol. Biol. 26:39-54.

[2] Ahmad, S., Routh, S. B. et al. (2013). Elife, 2:e01519, 1-18.

[3] Routh, S. B. et al. (2016). PLoS Biol. 14:e1002465, 1-22.

Keywords: [homochirality](#), [D-aminoacyl-tRNA deacylase](#), [peptidyl-tRNA hydrolase](#)