Mechanistic basis of a key chiral checkpoint and functional insights

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D-aminoacyl-tRNA deacylases (DTDs) remove D-amino acids mischarged on tRNA and therefore are implicated in enforcing homochirality in proteins. The DTD-fold is also found as the editing module of threonyl-tRNA synthetase from archaea. We have shown using three distinct archaeal species that this domain does not use specific side chains neither for catalysis nor for substrate specificity. However, it differentially remodels the RNA-protein interface for both activities (1). We also elucidated the crucial 'chiral proofreading' mechanism of DTD by which D-amino acids are preventedfrom infiltrating the translational machinery (2). Recently, we showed that DTD's mechanistic design principle is based only on L-amino acid rejection and hence, besides acting on D-aminoacyl-tRNA, DTD also efficiently hydrolyses glycyl-tRNA(Gly). However, DTD's activity on glycyl-tRNA(Gly) is harmful for the cell as glycine is an essential constituent of proteins. *In vitro* and *in vivo* experiments indicate that elongation factor Tu (EF-Tu) protects glycyl-tRNA(Gly) from DTD, thereby preventing DTD-induced cellular toxicity (3). The study suggests that DTD levels need to be tightly controlled across systems to avoid such cross-reactivity. The ongoing work on DTD's ability to act on glycine and its functional consequences will be presented.

References:
1. Ahmad et al. Nature Communications (2015) ***6****:7552, 1-12.*
2. Ahmad, Routh et al. eLife (2013) ***2****:e0159, 1-18.*
3. Routh et al. PLOS Biology (2016) e1002465, 1-22.