tRNA synthetases

The second genetic code
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Figure 11.3

Cytosine
(2-oxy-4-amino pyrimidine)

Uracil
(2-oxy-4-oxy pyrimidine)
Adenine (6-amino purine)

Guanine (2-amino-6-oxy purine)
Ribothymidine (T)  Pseudouridine (ψ)  Dihydouridine (D)
Aminoacyl-tRNA

- tRNA “charged” with amino acid
- Carries out codon recognition through anticodon loop
- Delivers amino acid to ribosomes
- Amino acid has no role in codon recognition
\[
\text{HS-CH}_2-\text{C-CO} \quad \text{tRNA}^{\text{Cys}} \quad + \quad \text{Ni(H)}_x
\]

Cys-tRNA^{\text{Cys}} \quad \text{Raney nickel}

\[
\downarrow
\]

\[
\text{H-CH}_2-\text{C-CO} \quad \text{tRNA}^{\text{Cys}} \quad + \quad \text{H}_2\text{S} \quad + \quad \text{Ni}
\]

Ala-tRNA^{\text{Cys}}
The adapter molecule-tRNA synthetase

- Over 20 tRNAs each with its own amino acid tRNA synthetase (aaRS)
- Esterification reaction binds amino acid and cognate tRNA
- Synthetase reaction
  - Activates amino acid for peptide bond formation
  - Bridges the info gap between amino acids and codons
Garrett & Grisham: Biochemistry, 2/e
Figure 32.5

(a)

\[ R\text{--H--C--C}^- + \text{tRNA}^R \xrightarrow{\text{Mg}^{2+}} \text{Aminoacyl-tRNA} \]

(b)

\[ \text{R--H--C--C}^- + \text{ATP} \xrightarrow{\text{PP}} \text{Enzyme-bound aminoacyl-adenylate} \]
tRNA synthetases

- All synthetases have two major domains
- More ancient domain has catalytic site for binding minihelix portion of the tRNA
  - Divided into two classes
- Second domain for interacts with anticodon in most cases
  - More recent in evolutionary time
Two classes of aa-tRNA synthetases

- **Class I** (2’ esterification) are monomeric
  - Arg, cys, gln, glu, ile, leu, met, trp, tyr, val
- **Class II** (3’ esterification) are always oligomeric (usually homodimeric)
  - Ala, asn, asp, gly, his, lys, phe, pro, ser, thr
tRNA recognition

- Sequence elements in each tRNA are recognized by its specific synthetase including
  - 1) One or more of 3 bases in acceptor stem
  - 2) Base at position 73 “Discriminator base”
  - 3) In many, at least one anticodon base
**Alanyl-tRNA$^{\text{Ala}}$ synthtase (alaRS)**

- Single, non-canonical base pair G3:U70 in the acceptor stem defines the recognition
- All tRNA$^{\text{Ala}}$s have this base pair
- If this base pair is altered, recognition does not occur
- 24-base microhelix analog is also correctly aminoacylated by alanyl-tRNA$^{\text{Ala}}$ synthtase
Second genetic code

- Sequence and structures of RNA oligos that mimic the acceptor stem and confer specific aminoacylations constitute an operational RNA code for amino acids.
- Such as code may have predated the genetic code.