tRNA-dependent Cysteine biosynthesis in ancient life requires a unique complex

Nature Communications **8**,1521(2017)

Aminoacylation of tRNA is the key step in translation, where aminoacyl-tRNA synthetases (aaRSs) ligate the cognate amino acid to the specific tRNA. Generally, there are 20 kinds of amino acids in cells, and accordingly 20 kinds of aaRSs each responsible for one specific amino acid. For example, CysRS ligates cysteine to $tRNA^{Cys}$ to produce $Cys\text{-}tRNA^{Cys}$, which is delivered to ribosome, and decodes the triplet code for cysteine. aaRSs are so crucial for the creature life that they are almost invariable or highly conserved throughout the evolution. Therefore, it was surprising when the whole genome sequencing of methanogens showed the absence of CysRS, and enzymes responsible for cysteine biosynthesis in this ancient life. Later on, a two enzymes involved indirect pathway was discovered, where the first enzyme, SepRS, attaches a phosphoserine(Sep) to $tRNA^{Cys}$, and then the second enzyme, SepCysS, converts the $Sep\text{-}tRNA^{Cys}$ to $Cys\text{-}tRNA^{Cys}$. This indirect pathway not only provides the $Cys\text{-}tRNA^{Cys}$ for protein synthesis, it also paves a way for *ab initio* biosynthesis of cysteine to satisfy the cellular requirement. A decade passed since the discovery, however, the mechanism how the two enzymes work together was still ambiguous.

In our recent research, we found a scaffold protein, SepCysE, is required to bridge SepRS and SepCysS to form a stable ternary complex, named transsulfursome. SepCysE is essential for tRNA binding and transfer between two active sites. The combination of crystallography analysis, SEC-SAXS, TEM, together with biochemical evidences, showed the dynamic architecture of transsulfursome mediated by the flexible structure of SepCysE (Figure 1), and provided snapshots of tRNA on transsulfursome in each step of the process (Figure 2). The results help to have a clear image how the indirect pathway works. Furthermore, the stable architecture of transsulfursome makes it advantageous in thermophile and may explain why the methanogens preserve this indirect pathway, and another possibility could be, as cysteine is highly reactive especially in high temperature,

transsulfursome could to some extent protect cysteine, and probably produce it in an energy-saving way.

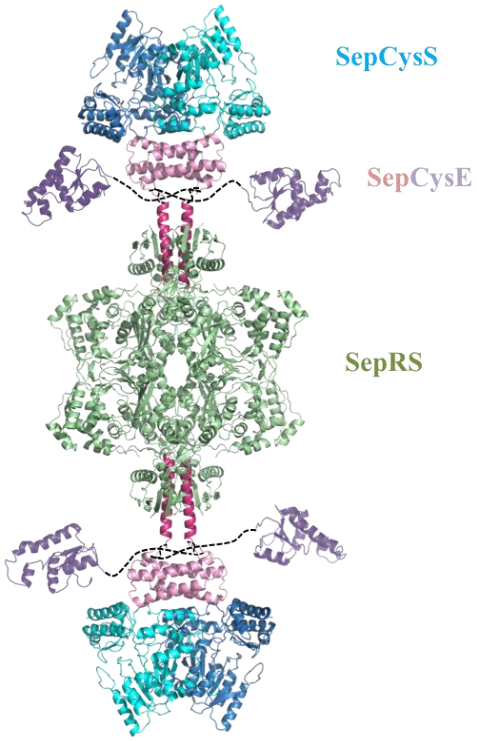

Figure 1. The architecture of transsulfursome

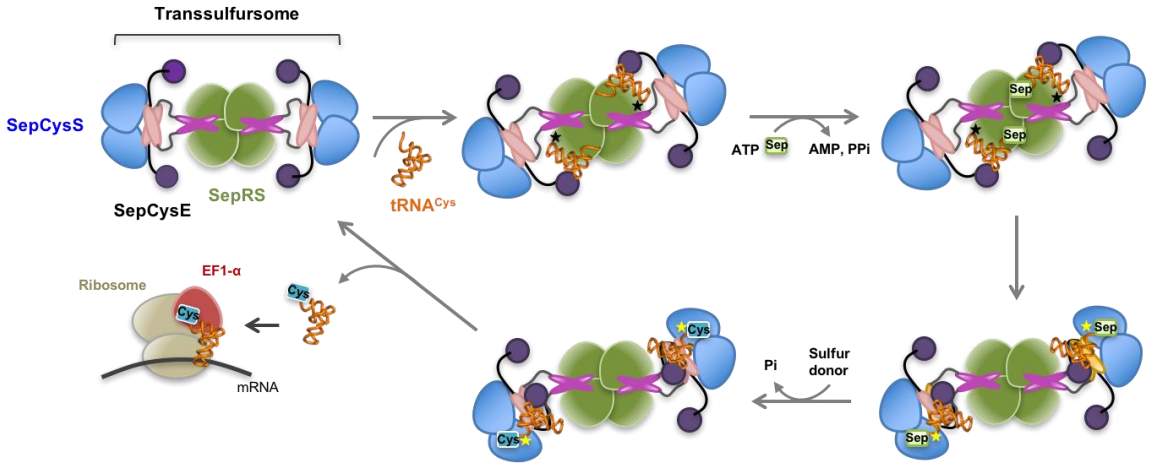

Figure 2. The scheme of indirect pathway for cysteine incorporation into peptides.