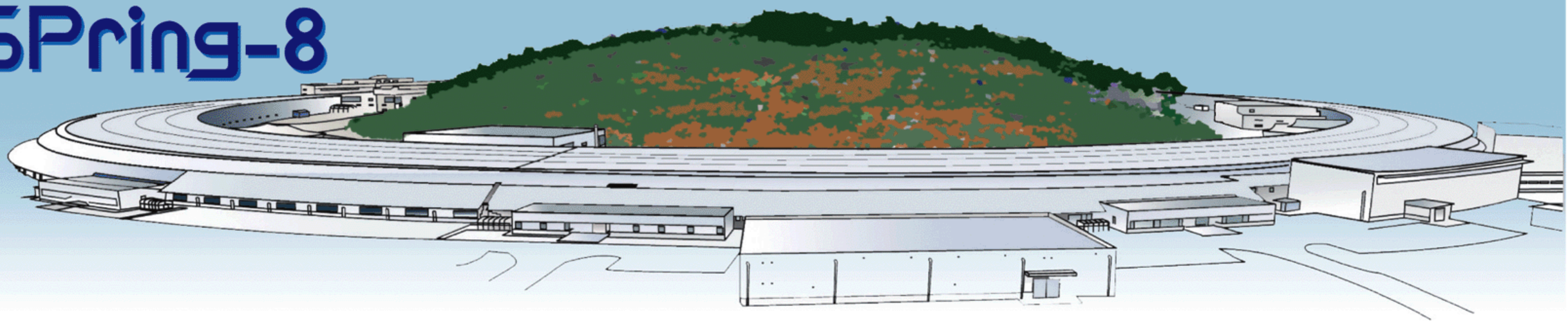
SPring-8



Structure and Function of a Protein Mimicking Transfer RNA

Translation elongation factor P, a transfer RNA-like L-shaped protein, accepts an amino acid in a reaction similar to that of transfer RNA

A joint research team, consisting of scientists from RIKEN and The University of Tokyo, successfully solved the crystal structure of a complex of translation elongation factor P (EF-P), a tRNA-like L-shaped protein playing an indispensable role in the translation of genetic information, with an aminoacyl-tRNA synthetase (aaRS)-related protein, GenX, with unclarified functions, using X-rays at SPring-8. The team also discovered that GenX ligates EF-P with the amino acid lysine. These results show, for the first time in the world, that the shape and the reaction of EF-P are both very similar to those of tRNA. In addition, the transfer of the lysine moiety from GenX to EF-P was indispensable for the proliferation of eubacteria, such as *Escherichia coli*. This discovery was achieved by a research team consisting of Shigeyuki Yokoyama, Director of the Systems and Structural Biology Center, RIKEN (also a professor at The University of Tokyo), Tatsuo Yanagisawa, a research scientist, and Tomomi Sumida, a postdoctoral researcher at RIKEN.

To properly synthesize the proteins encoded by the genetic information of living organisms, the cognate amino acids and tRNAs must be selected according to the genetic code for the accurate amino acid polymerization. This process is called translation; various proteins, such as aaRSs and translation factors, are involved in this process. Thus far, the research team has determined that the shape of the EF-P involved in translation initiation is similar to that of tRNA. In the present study, the team successfully crystallized the complex of EF-P and GenX (a protein with unknown functions that is distantly related to an aaRS) and clarified its steric structure, which is very similar to that of the tRNA-aaRS complex. Based on this finding, they elucidated that EF-P accepts an amino acid from GenX, in a reaction similar to that of tRNA. This is the first discovery of the striking similarities in both the structure and reaction between a nucleic acid and a protein, although they are completely different molecules. This phenomenon seems to be analogous to convergent evolution, in which different living organisms acquire similar shapes and living behaviors through evolution. Furthermore, transfer of the lysine moiety from GenX to EF-P was indispensable for the proliferation of *E. coli*. GenX exists only in eubacterial species, such as *E. coli* and *Salmonella*, and not in eukaryotic organisms, such as humans. Therefore, GenX is a promising target for developing new antimicrobial agents for pathogenic bacteria and antimicrobial-agent-resistant bacteria, without adverse side effects.

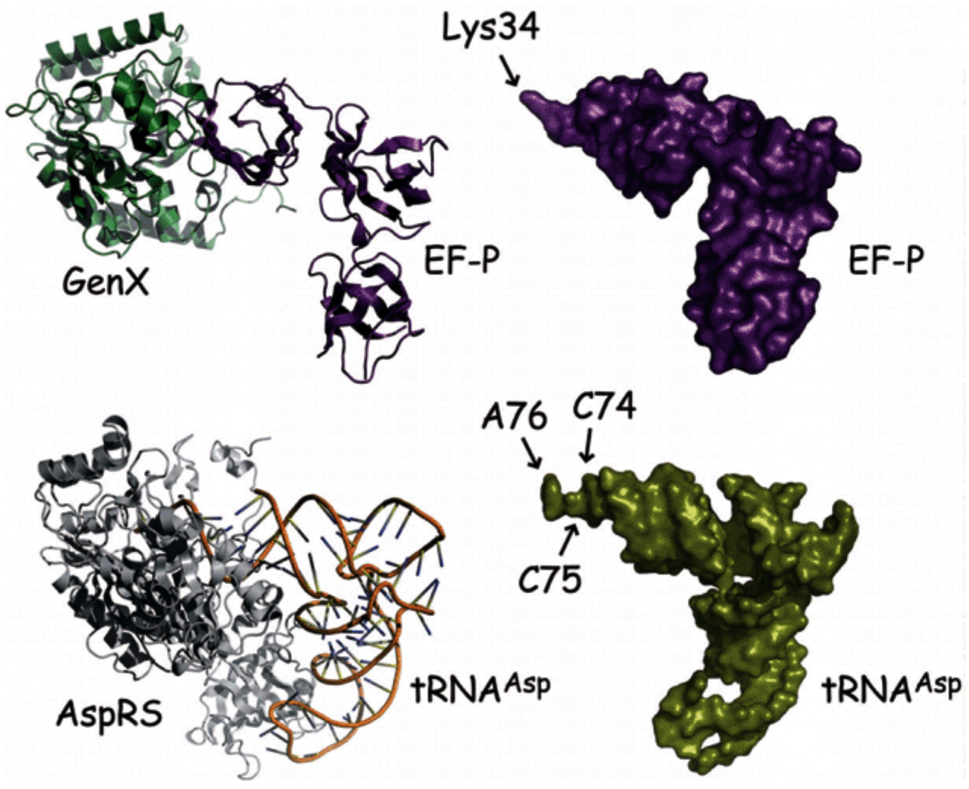


Figure: Structural comparison between the EF-P-GenX complex and a tRNA-aaRS complex

A complex of aspartic acid tRNA and aspartyl-tRNA synthetase ($tRNA^{Asp}$-AspRS) is shown, as an example of a tRNA-aaRS complex. The structures of the EF-P-GenX complex (upper left) and the tRNA-aaRS complex (lower left) are very similar. The Lys34 of EF-P corresponds to the CCA terminus (A76) where an amino acid binds to tRNA.

Reference: *Nature Structural & Molecular Biology* **17**, 1136-1143 (2010)