UMassAmherst

Crystal Structure and Functions of EF-TU

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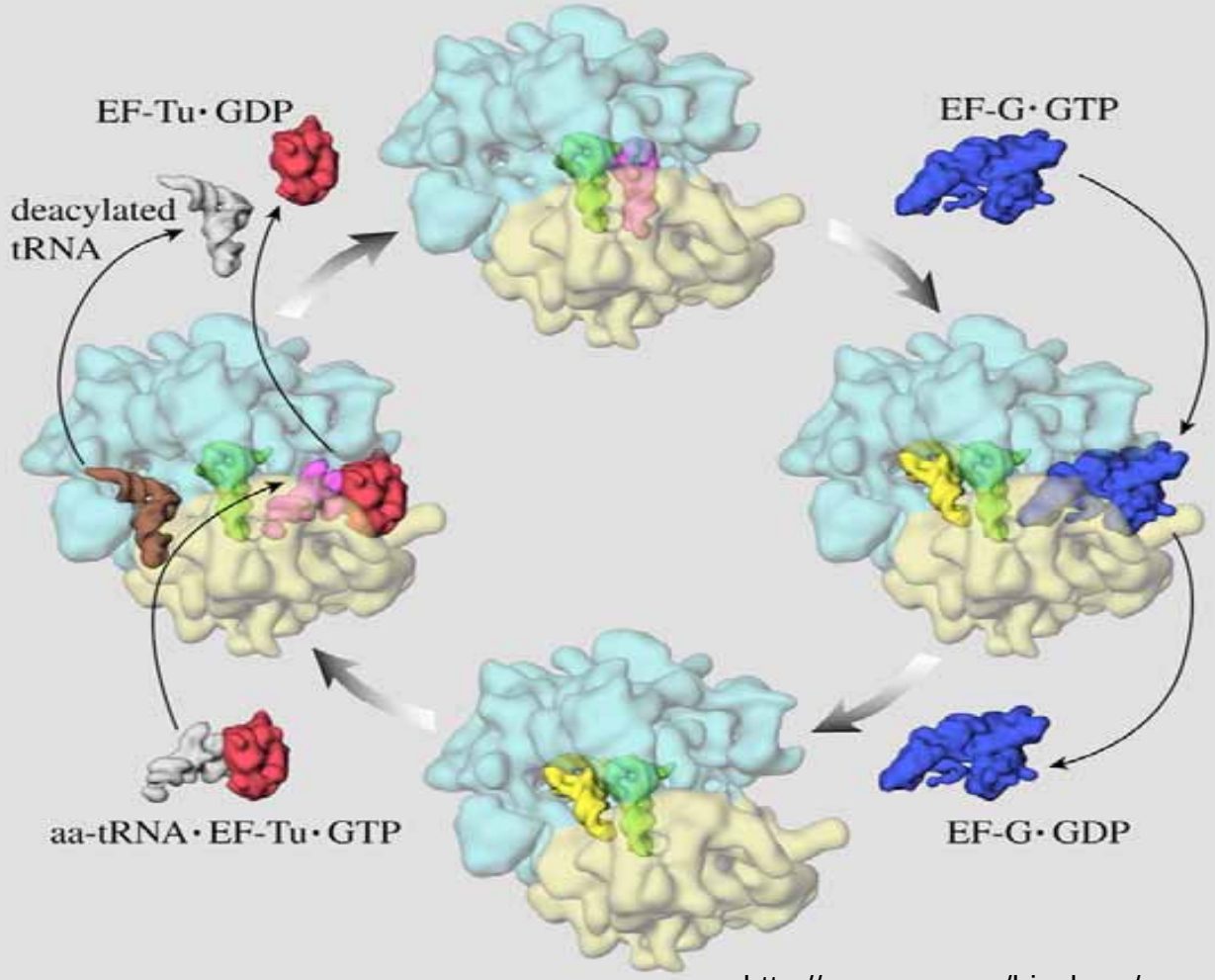
EF-TU and its functions :

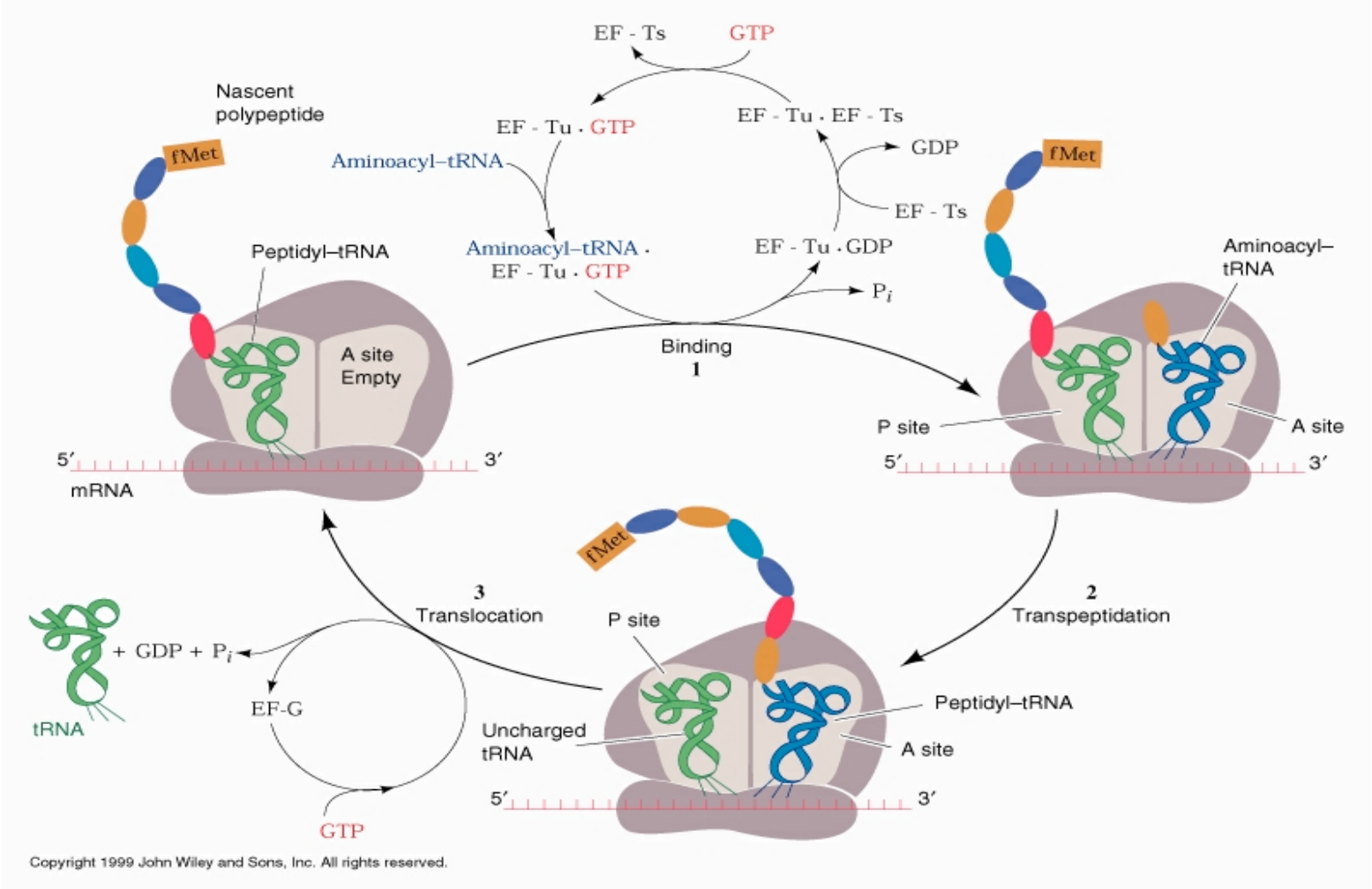
- EF-TU is a GTPase enzyme
- Facilitates the binding of aa t-RNA within a stable ternary complex
- Promotes ternary complex binding to the A site of ribosome
- Catalyze the translocation of the synthesized protein chain
- Chaperone properties (EF-TU-GDP complex is more active than EF-TU-GTP)
- Protection against thermal denaturation and stress
- Involved in signal transmission

Elongation of protein synthises:

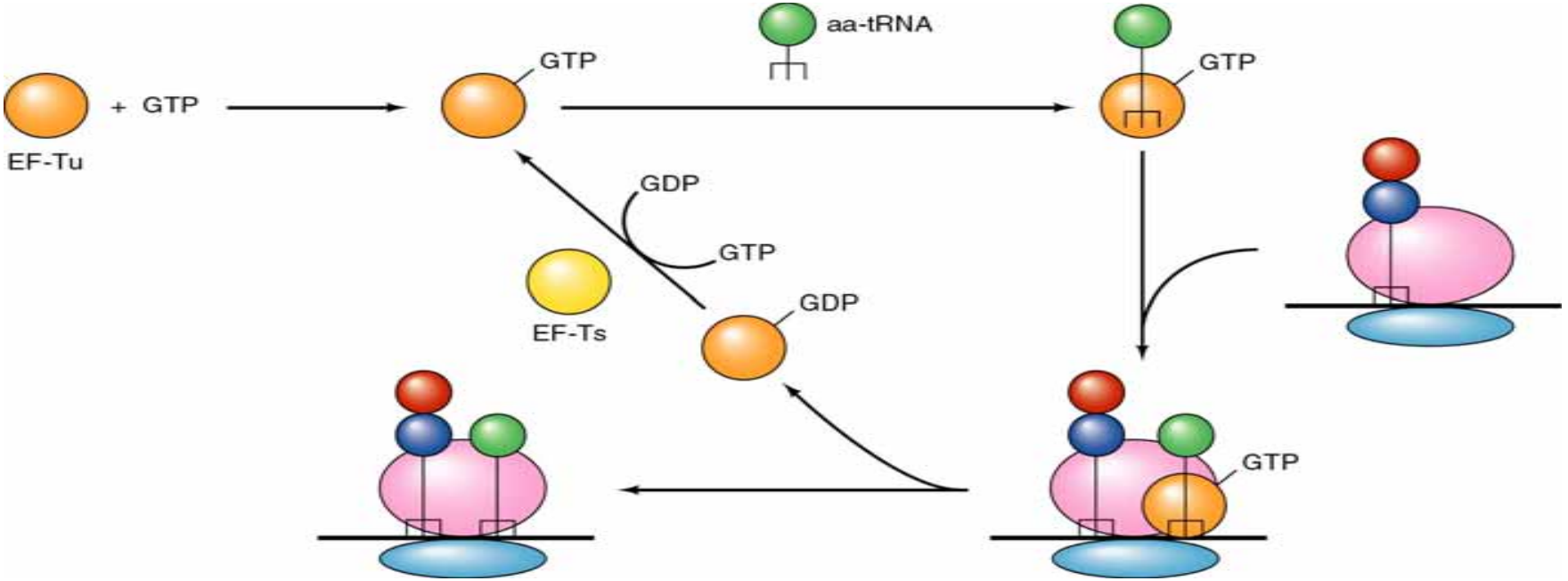


http://www.mun.ca/biochem/courses/3107/images/protsyn

Elongation of protein synthesis:



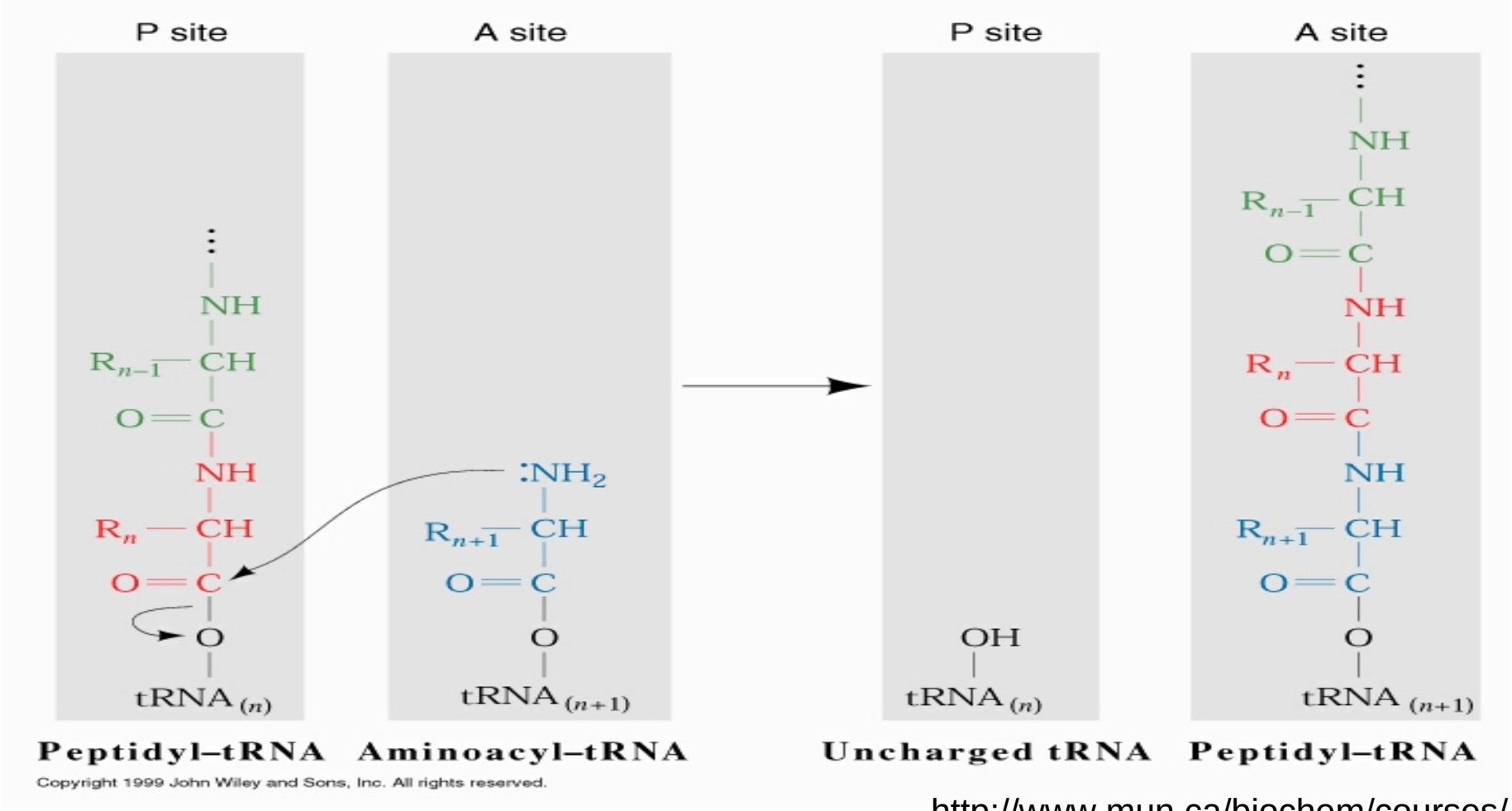
The Cycle of EF-TU:



SUBSTRATE BINDING: AMINOACYL-tRNA BINDS TO THE RIBOSOMAL A SITE IN A TERNARY COMPLEX WITH EF-Tu AND GTP

WEAVER: FIG. 18.14

The Chemistry:



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Elongation (Eukaryotes and Prokaryotes):

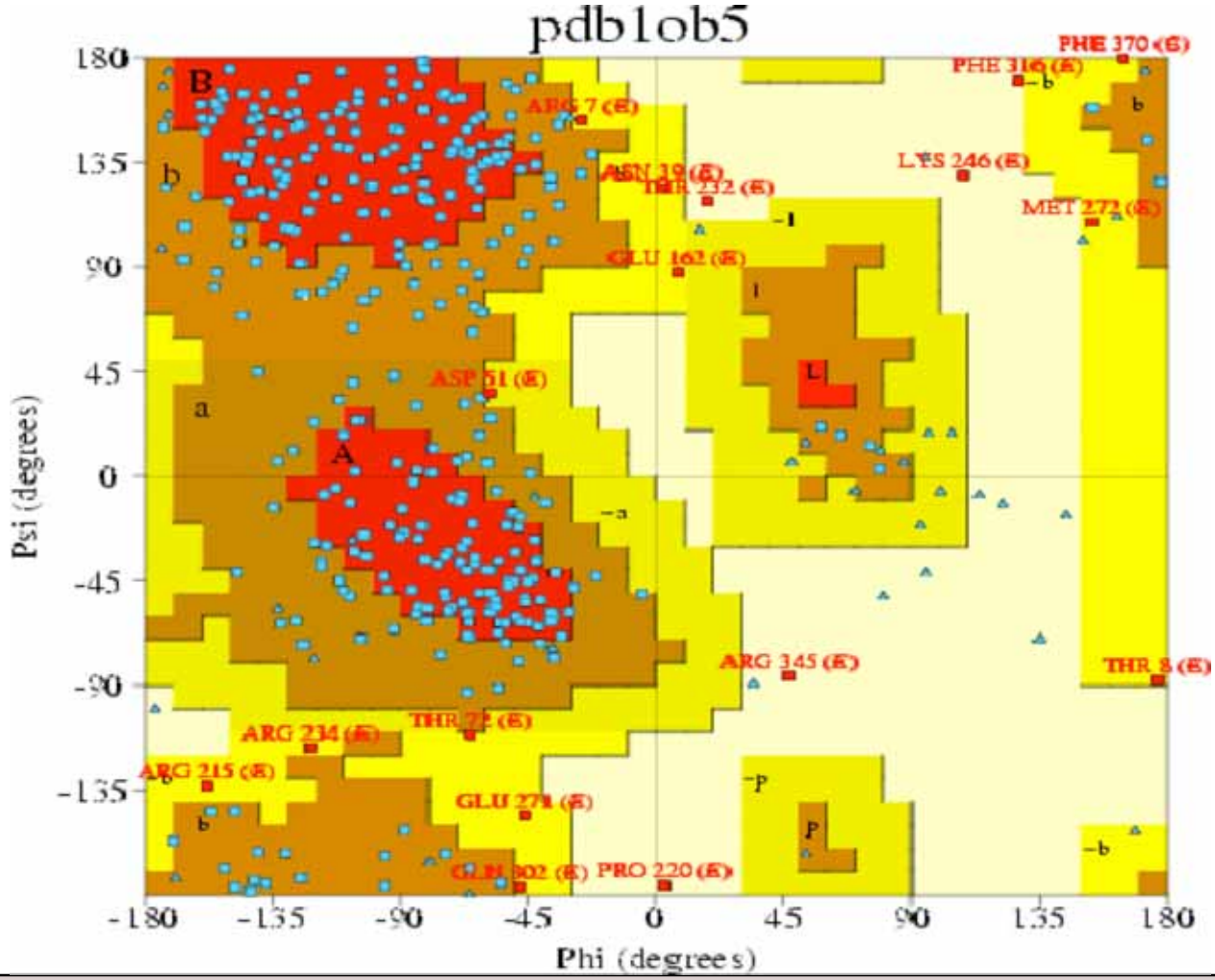
in Eukaryotes. exactly the same as in prokaryotes, protein names have been changed. The process is highly conserved.

Prokaryotes	Eukaryotes	Function
1) EF-Tu	eEF-1a	deliver tRNA to ribosome
2) EF-Ts	eEF-1bg	recharge the EF with GTP
3) EF-G	eEF-2	move ribosome down one space

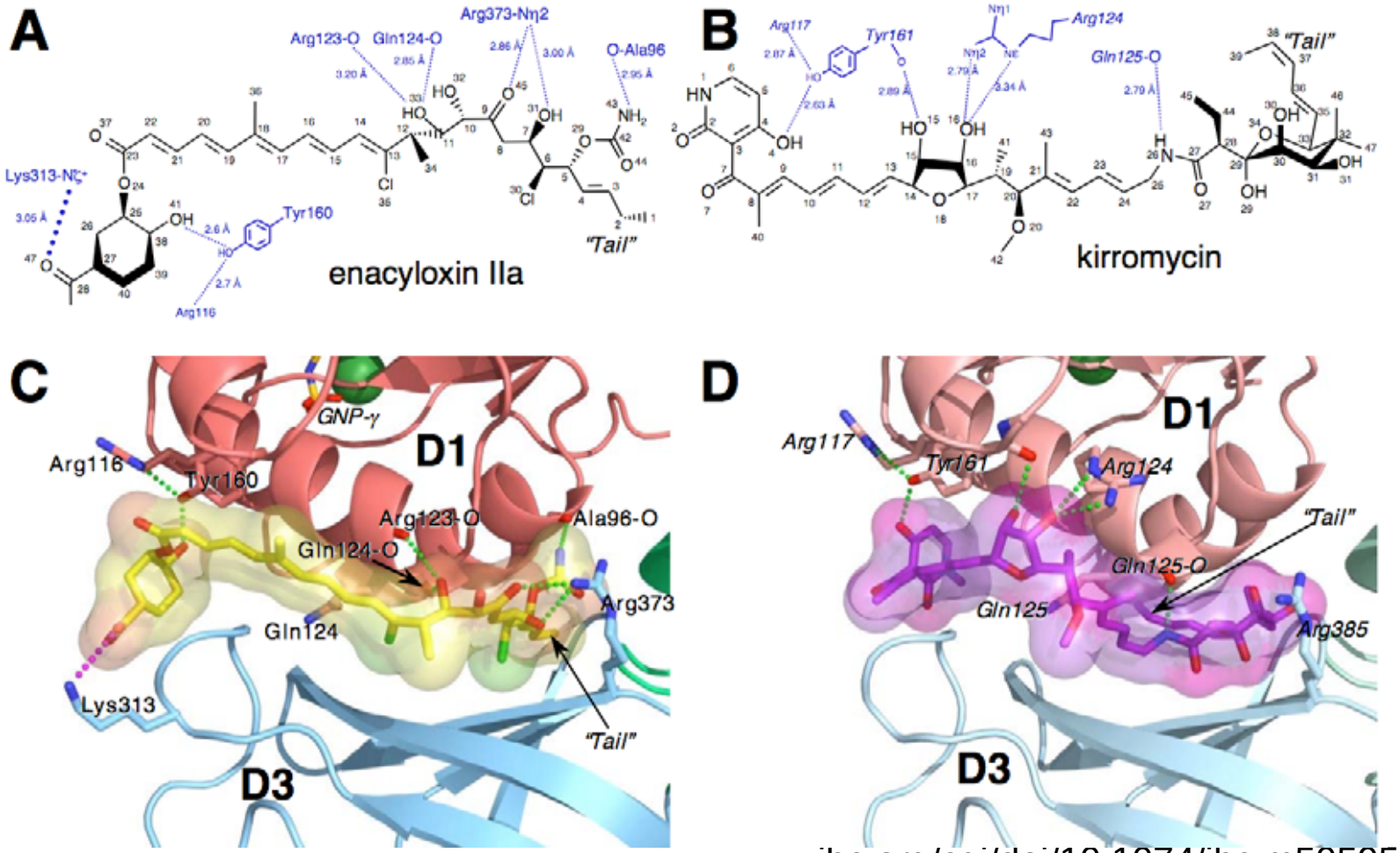
Structural Quality of EF-TU:

- Header : Hydrolase
- Source : Thermus aquaticus
- Resolution : 3.1 A
- Residue : 1449
- Chain : A,B,C,D,E,F
- R factor : 0.284
- Free R factor : 0.296
- B factor : 68.3
- Occupancy : 1.00
- Water molecule : 198

Ramachandran Plot:

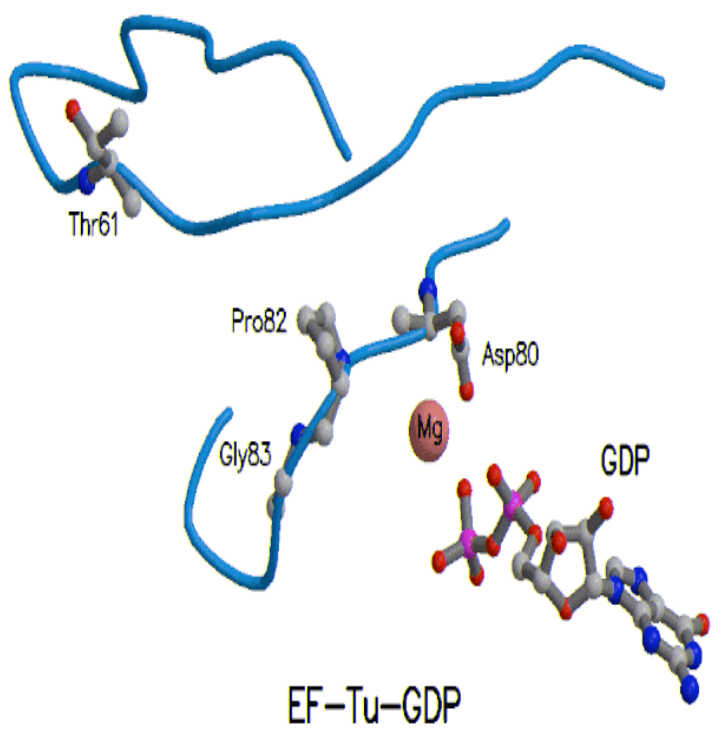


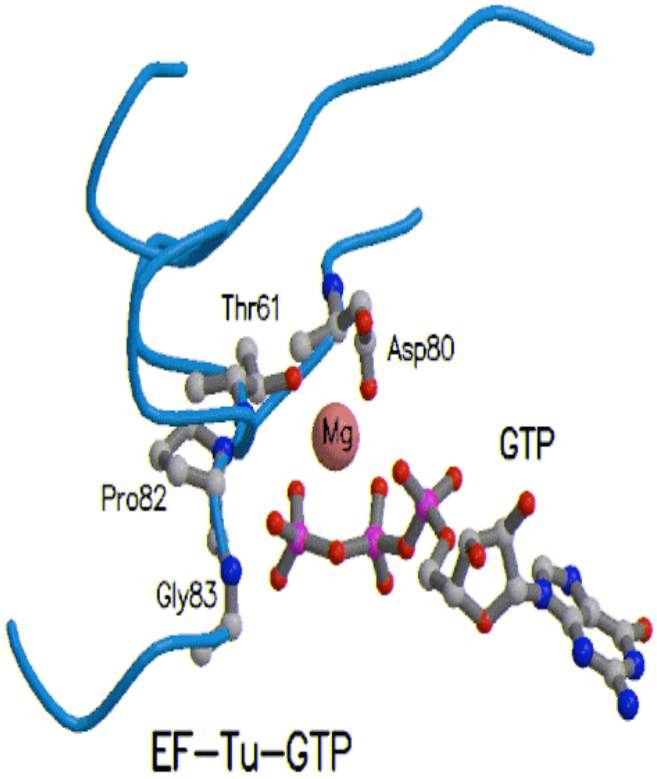
Comparison of Ena and Kir binding with EF-TU:



www.jbc.org/cgi/doi/10.1074/jbc.m505951200

Comparison of GDP and GTP binding region of EF-TU:





Conclusion:

- Antibiotics binding site share marked similarties
- Lower binding affinity of enacycloxin IIa
- New approach for a structure guided antibiotic design ("Head" moiety of enacycloxin with "Tail" moiety of kirromycin)
- Binding efficiency of an antibiotic can reduce the onset of resistance by microorganism

References:

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