

# Structural insights into eukaryotic ribosome-associated quality control (RQC)

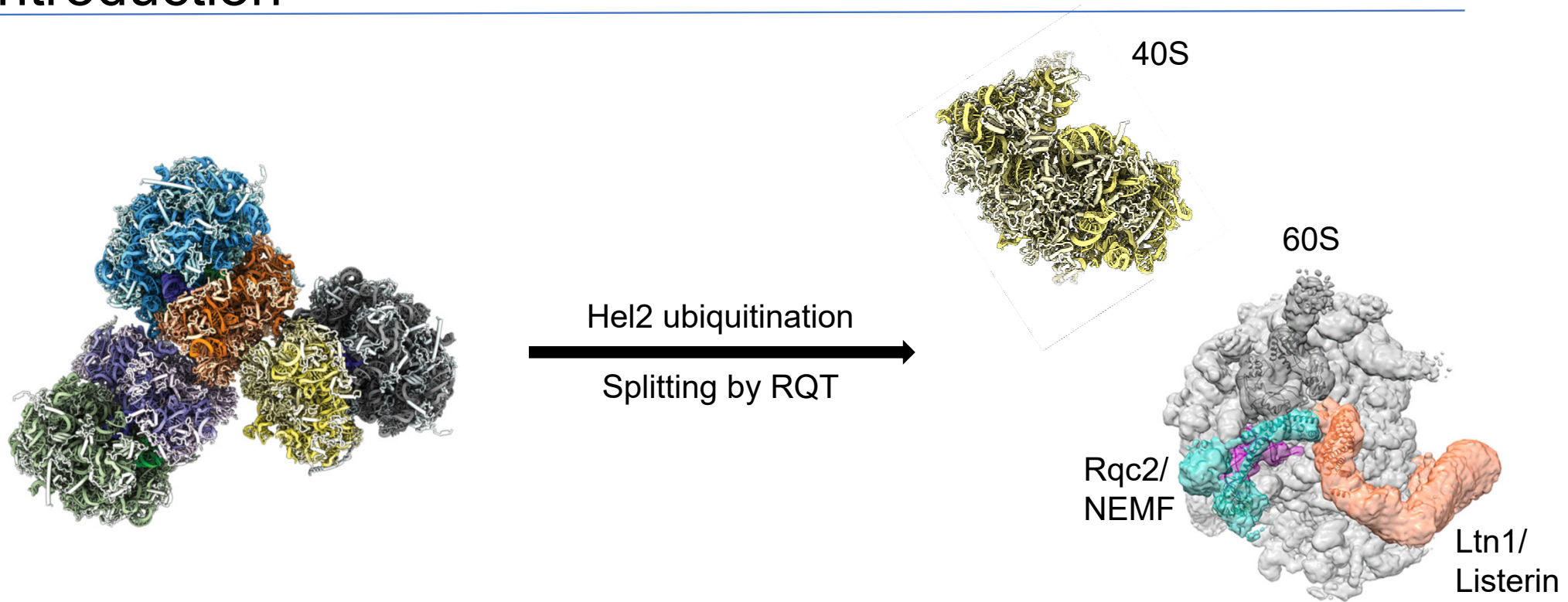
Petr Těšina



Gene Center  
Munich

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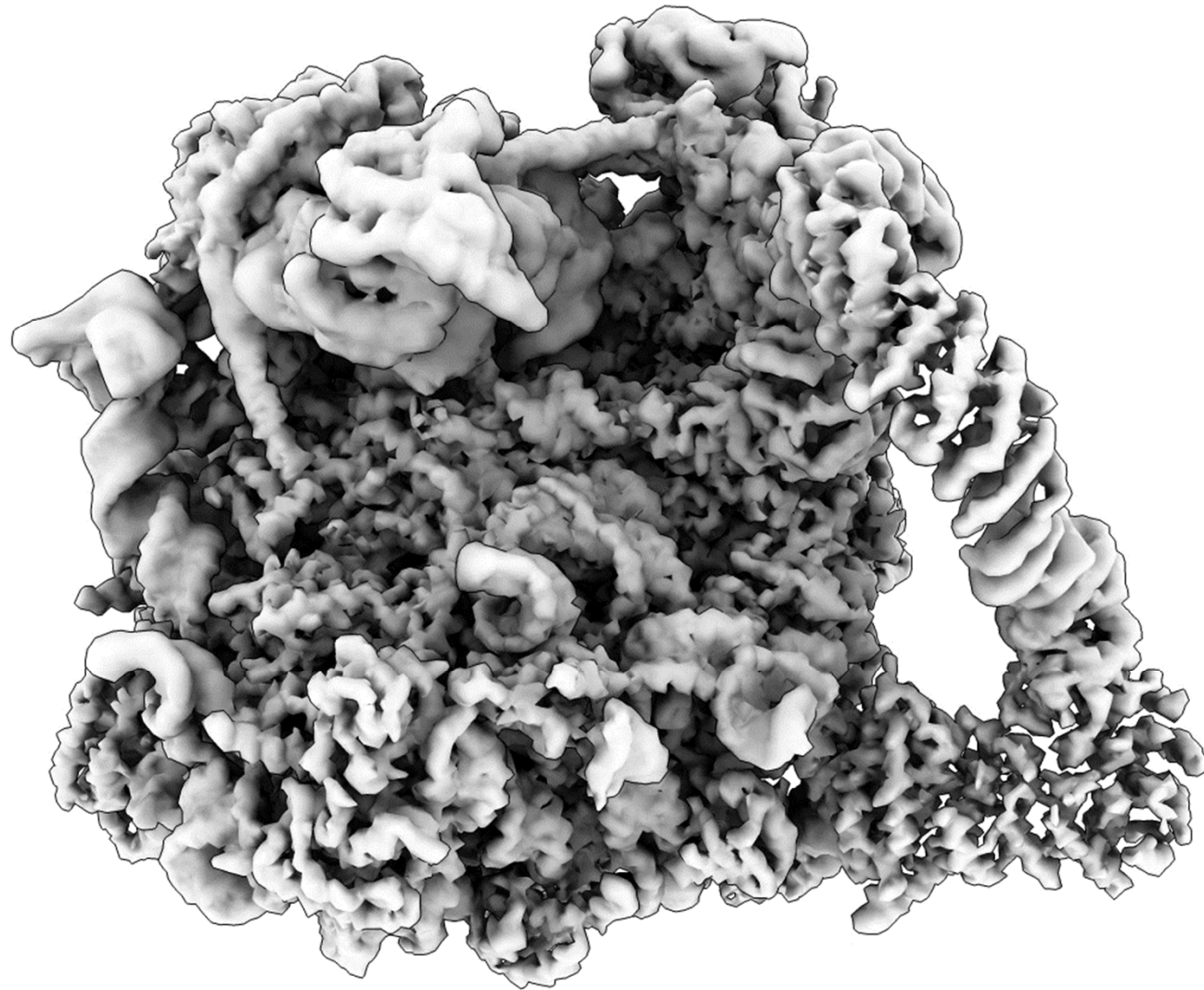
# Introduction



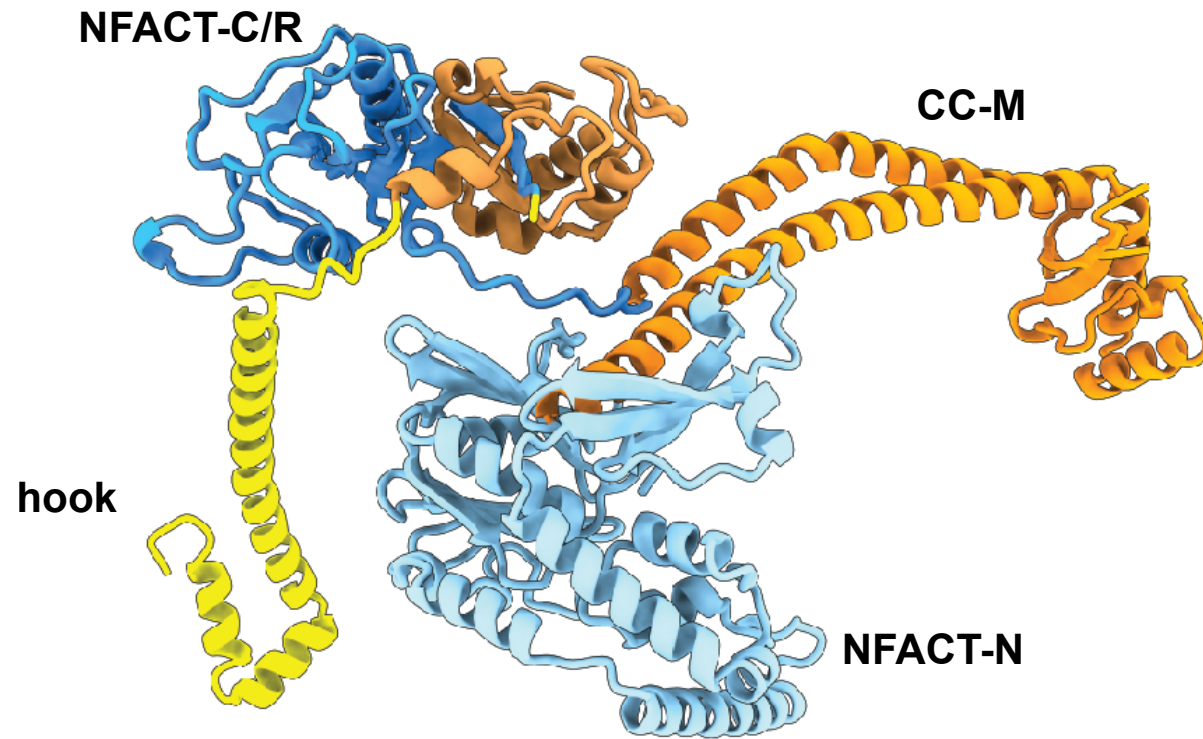
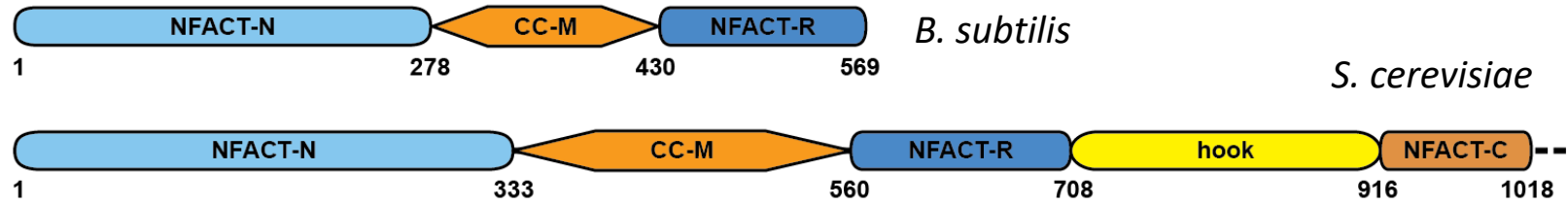
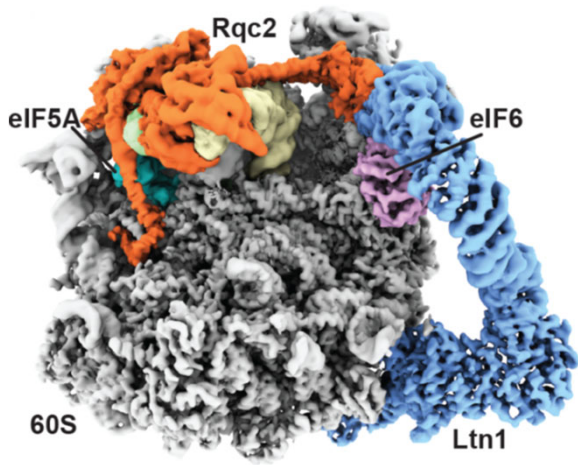
- RQC is conserved from bacteria to humans (CARboxy-Terminal tails)
- How does Rqc2 govern peptide elongation cycle without 40S and mRNA?

# Overview

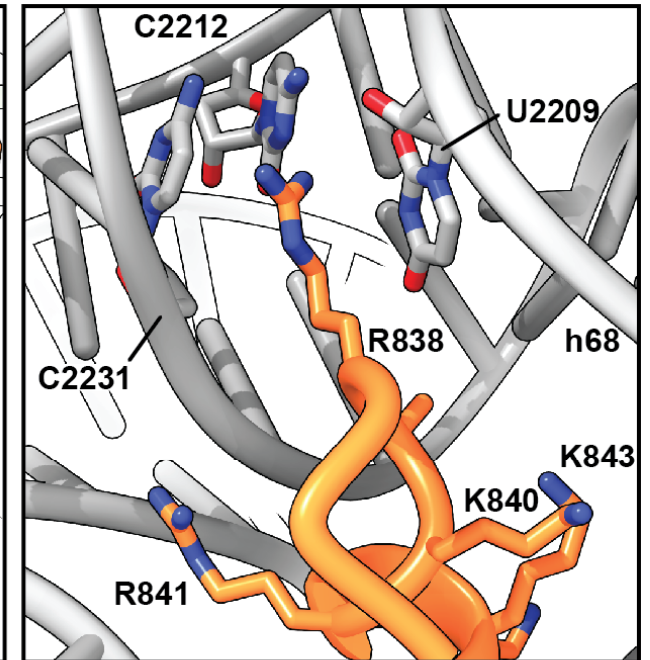
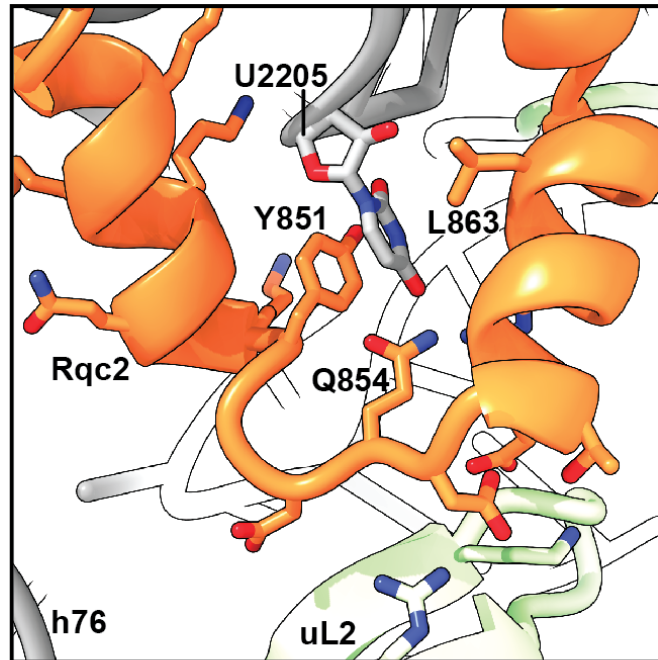
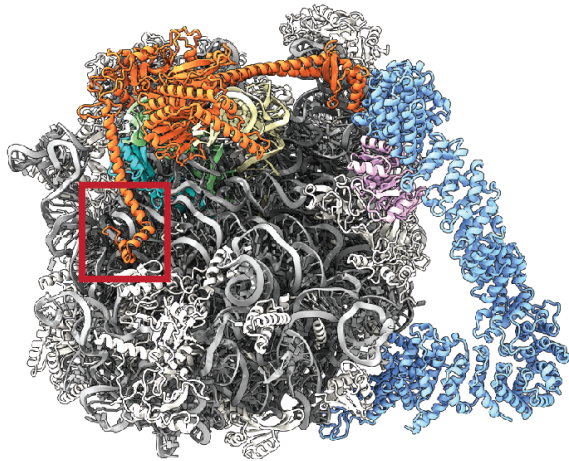
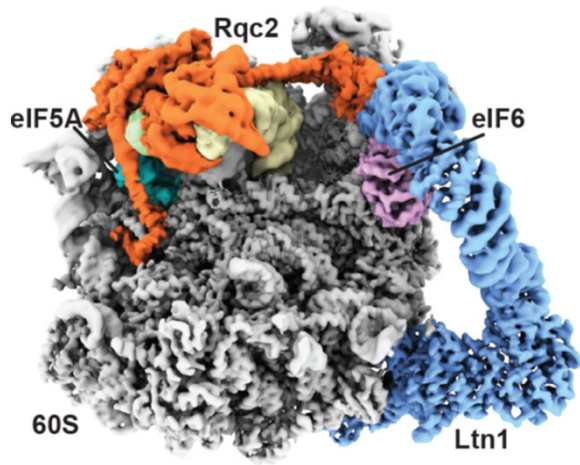
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# Rqc2

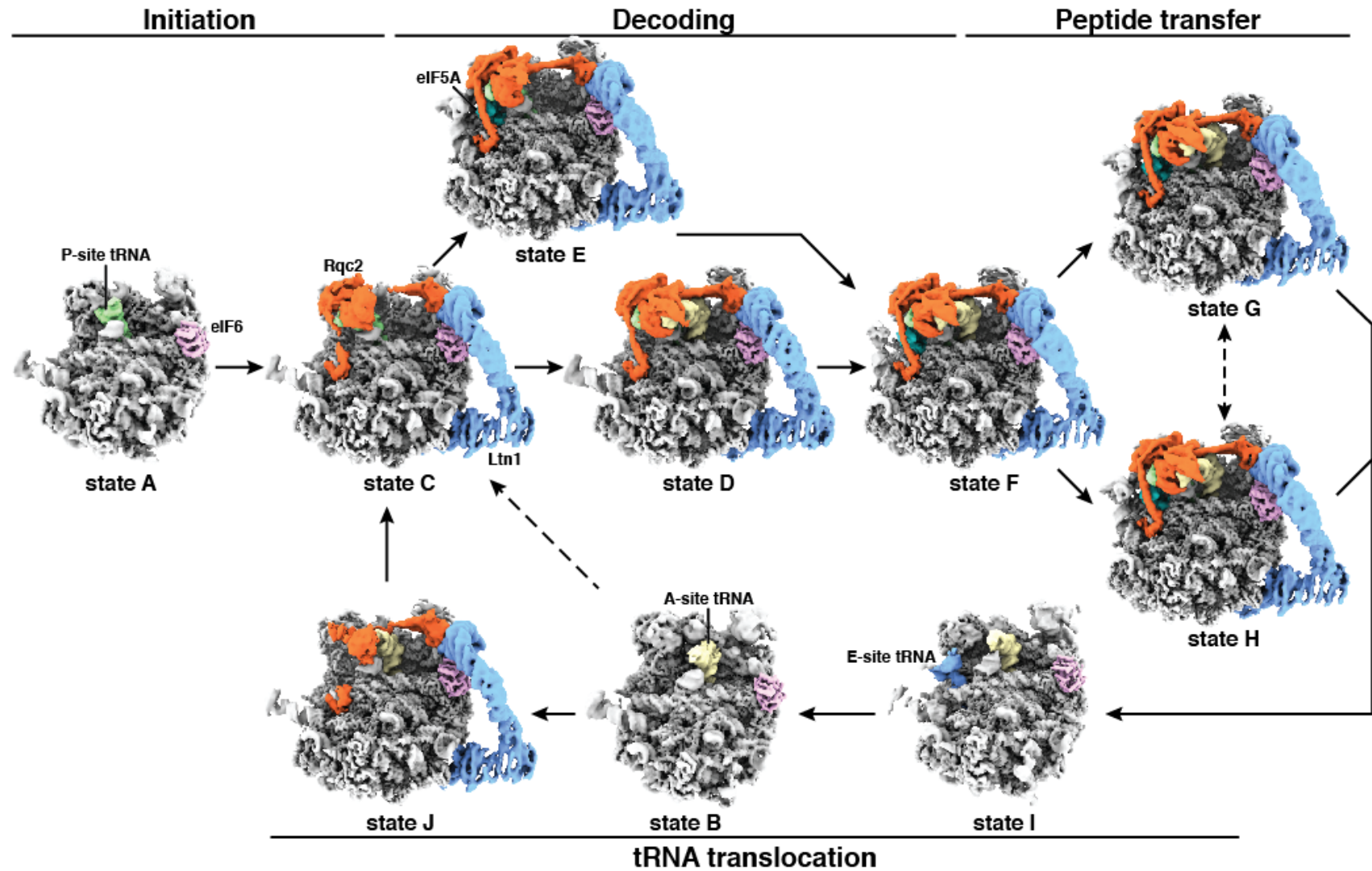


# Rqc2

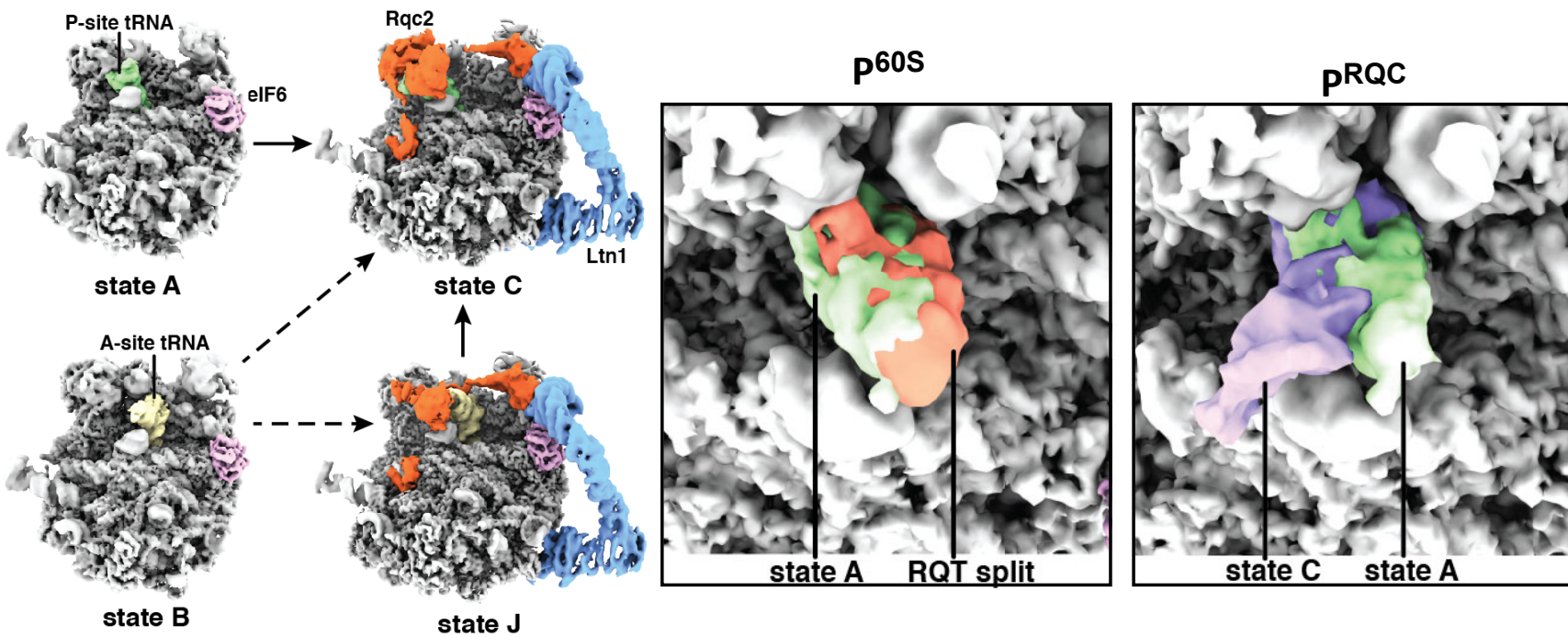


	R838	R851	Q854	L863
<i>S. cerevisiae</i>	VR	-GKRGKL	KKIQKKYADQ	DETERLLRLEALG
<i>H. sapiens</i>	KR	-GQKSKM	KMKMKEKYKDQ	DEEDRELIMKLLG
<i>M. musculus</i>	KR	-GQKSKM	KMKMKEKYKDQ	DEEDRELIMKLLA
<i>G. gallus</i>	KR	-GQKSKM	KMKMKEKYKDQ	DEEDRELIMKLLG
<i>X. tropicalis</i>	KR	-GQKSKL	KKIKEKYKDQ	DEEDRDLIMQLLG
<i>D. melanogaster</i>	KR	-GQKGL	KMKQKYKDQ	DEEREIRMMILK
<i>C. elegans</i>	KRRQRKEKL	-	-AKMKYKDQ	TDDDLLELHKELLK

# CAT tailing cycle

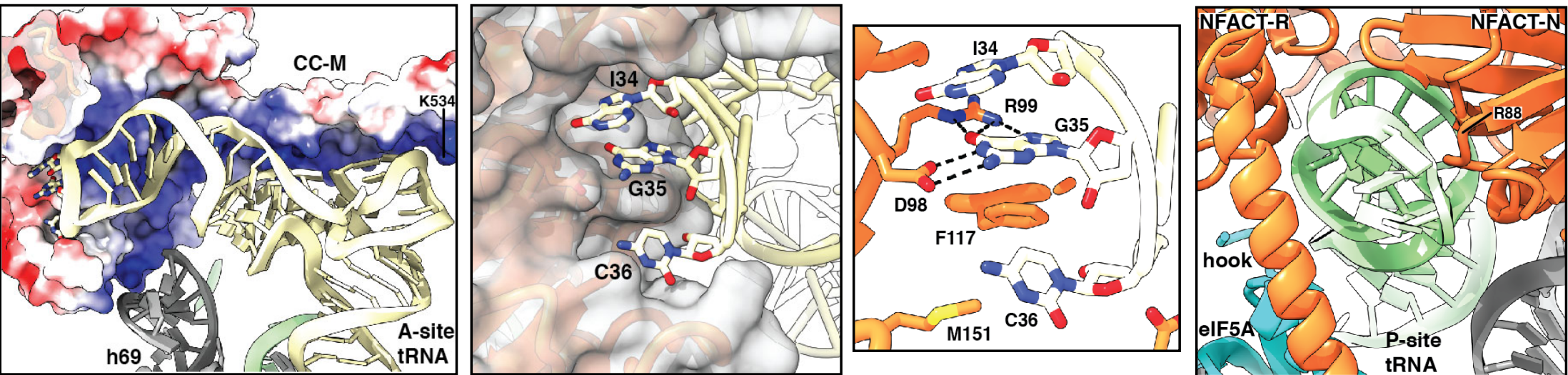


# Initiation



- The P<sup>60S</sup> conformation is the *bona fide* substrate and turns into P<sup>RQC</sup> conformation upon Rqc2 binding

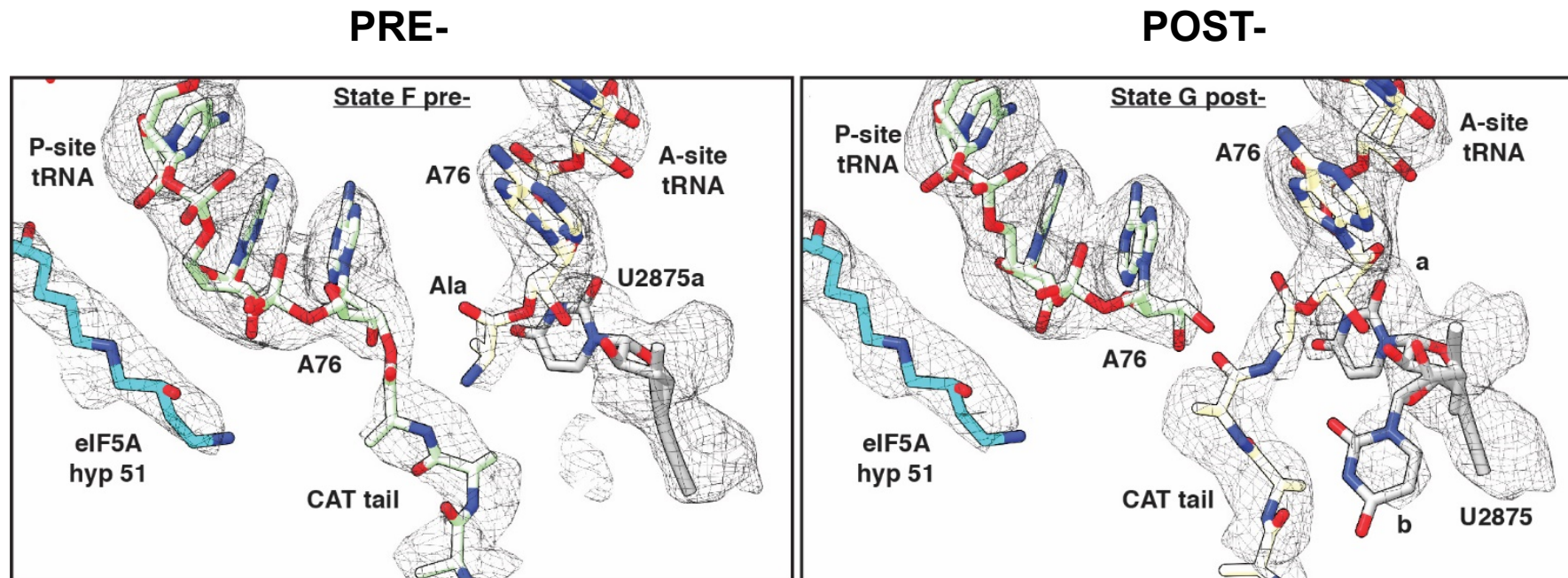
# Decoding



- Rqc2 structure selects for NGY anticodon, RCN in “codon language” - GCN = Ala; ACN = Thr
- No sequence specific interaction with P-site tRNA

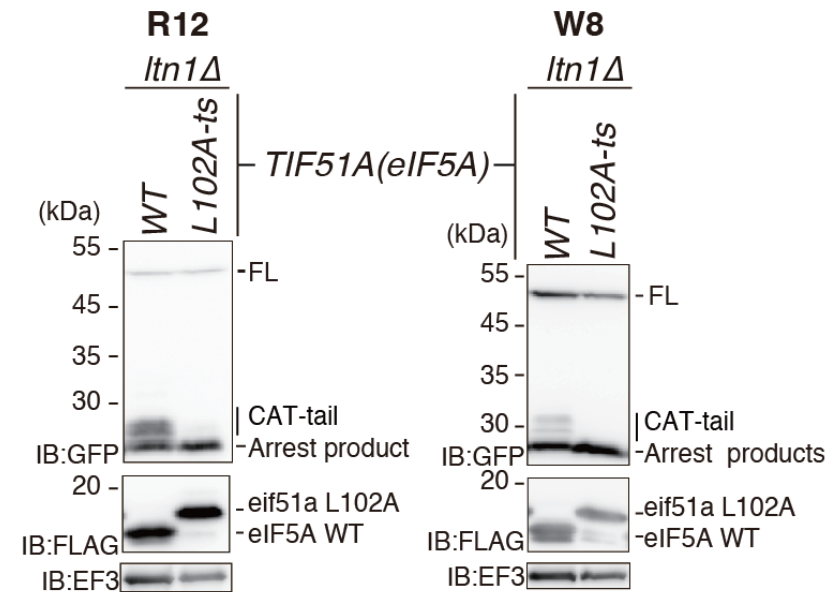
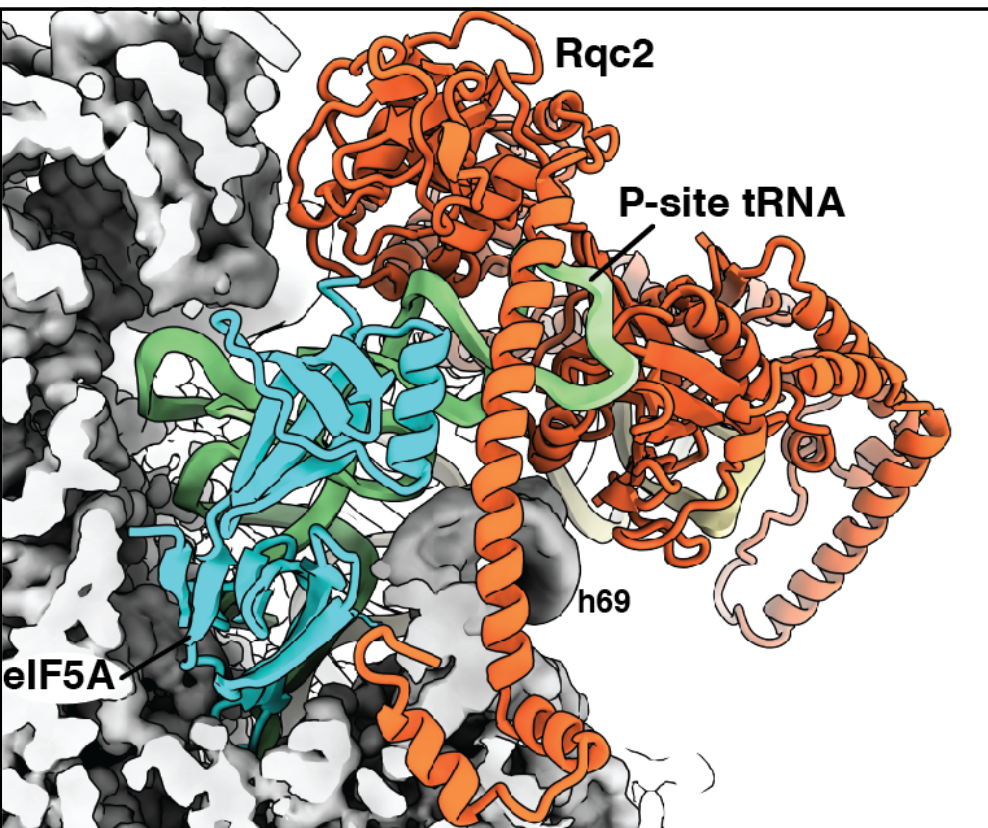


# Peptide transfer



- eIF5A present in all peptide transfer states

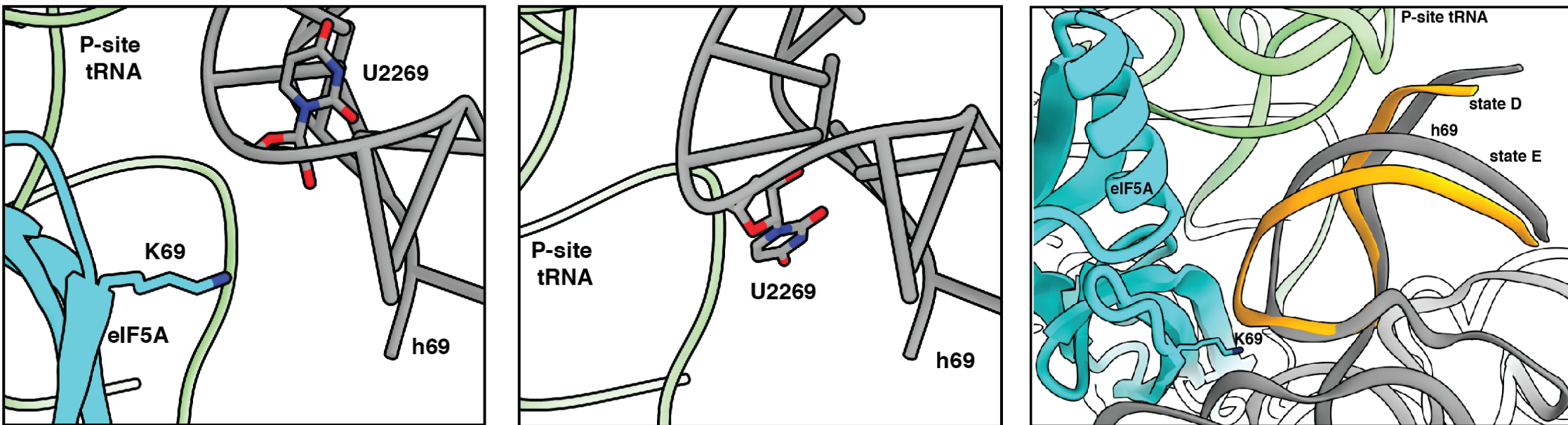
# eIF5A is a novel CAT tailing factor



- eIF5A is essential for CAT tailing

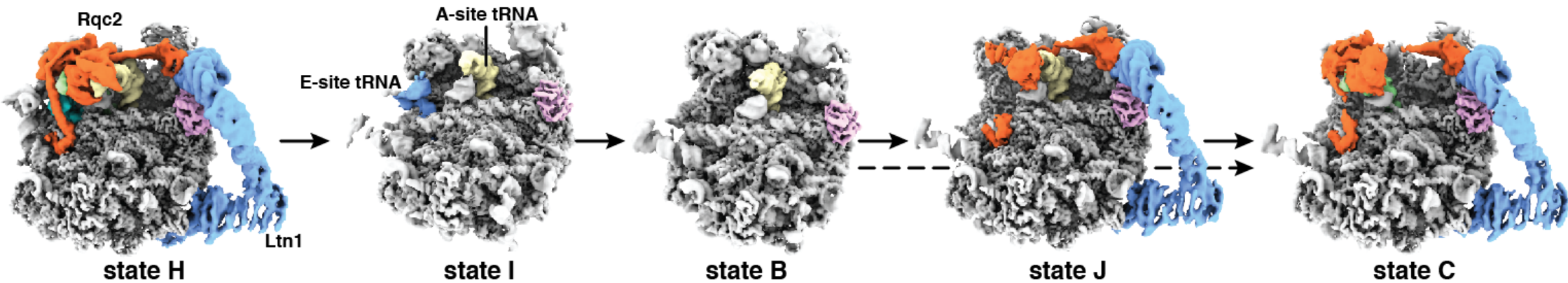
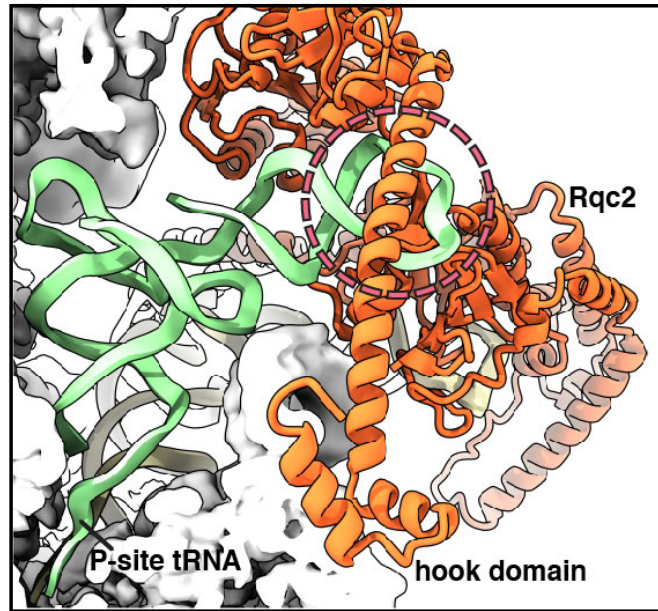
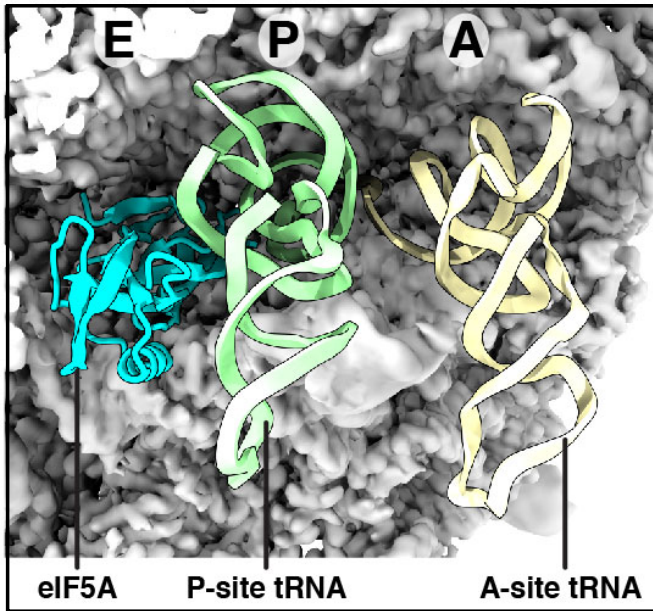
Data from the Inada laboratory

## eIF5A affects helix 69 of 25S rRNA



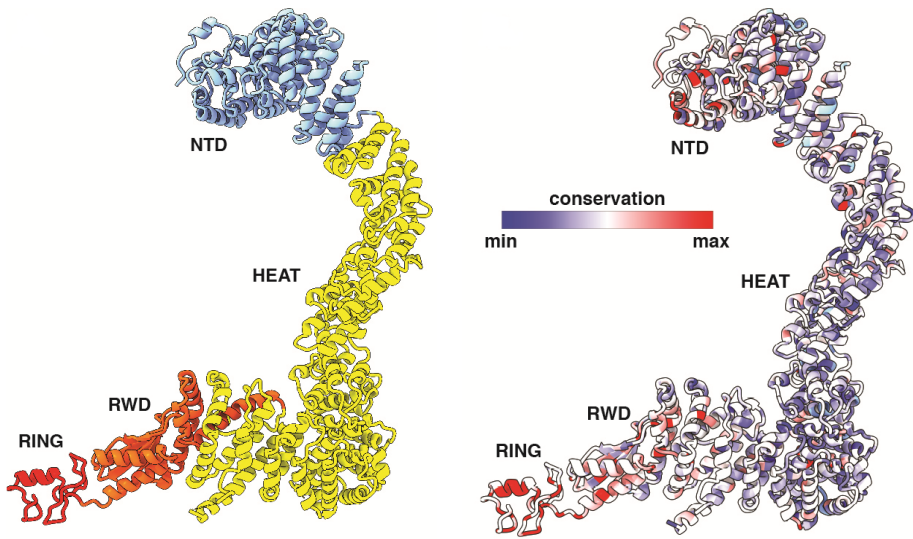
- eIF5A changes the conformation of helix 69
- Analogous function to RqcP (YabO)

# tRNA translocation faces two obstacles



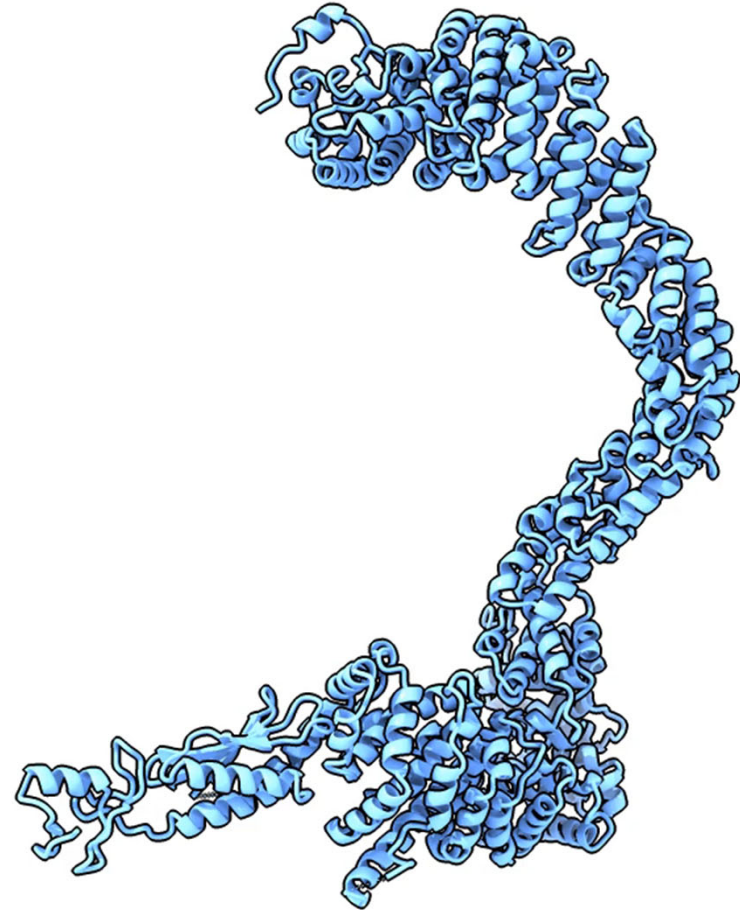
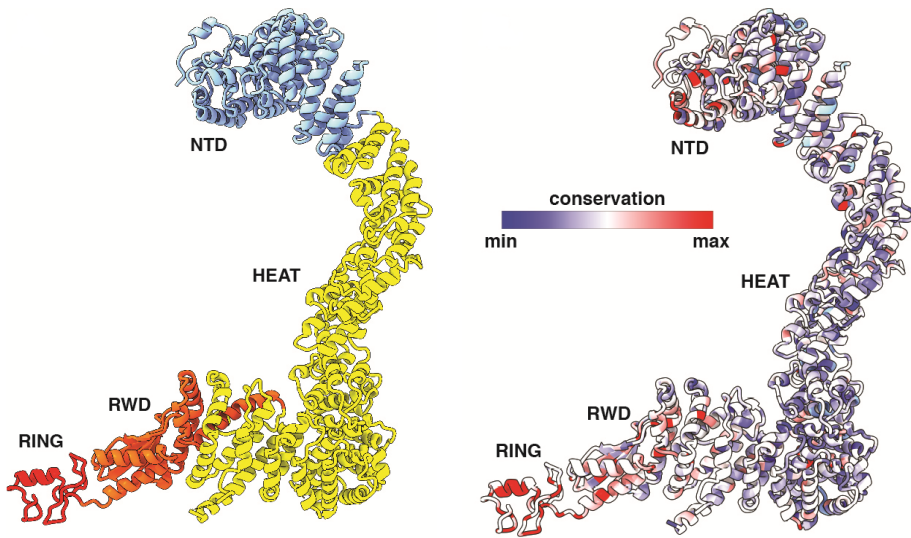
# Ltn1

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# Ltn1 dynamics

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# Conclusions

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- eIF5A is a novel factor in eukaryotic CAT tailing
- Rqc2 governs initiation, decoding specificity and peptide transfer
- Rqc2 undergoes conformational rearrangement to allow for tRNA translocation
- Ltn1 exerts a broad range of movement to ubiquitinate a variety of degradation targets

**Molecular Cell**

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## **Molecular basis of eIF5A-dependent CAT tailing in eukaryotic ribosome-associated quality control**

Petr Tesina,<sup>1,3,\*</sup> Shuhei Ebine,<sup>2,3</sup> Robert Buschauer,<sup>1,3</sup> Matthias Thoms,<sup>1</sup> Yoshitaka Matsuo,<sup>2</sup> Toshifumi Inada,<sup>2,\*</sup>  
and Roland Beckmann<sup>1,4,\*</sup>



@BeckmannLab

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## The Inada lab

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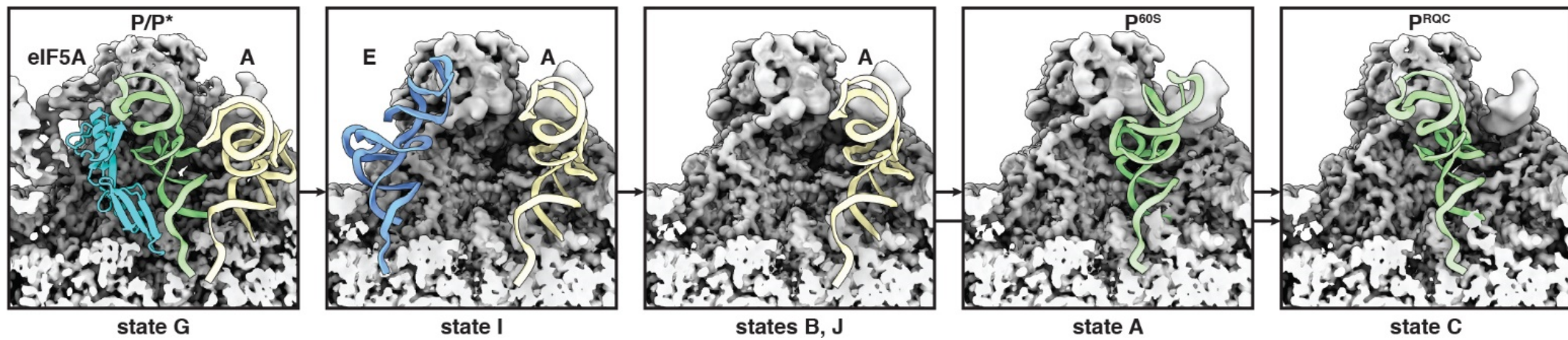


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