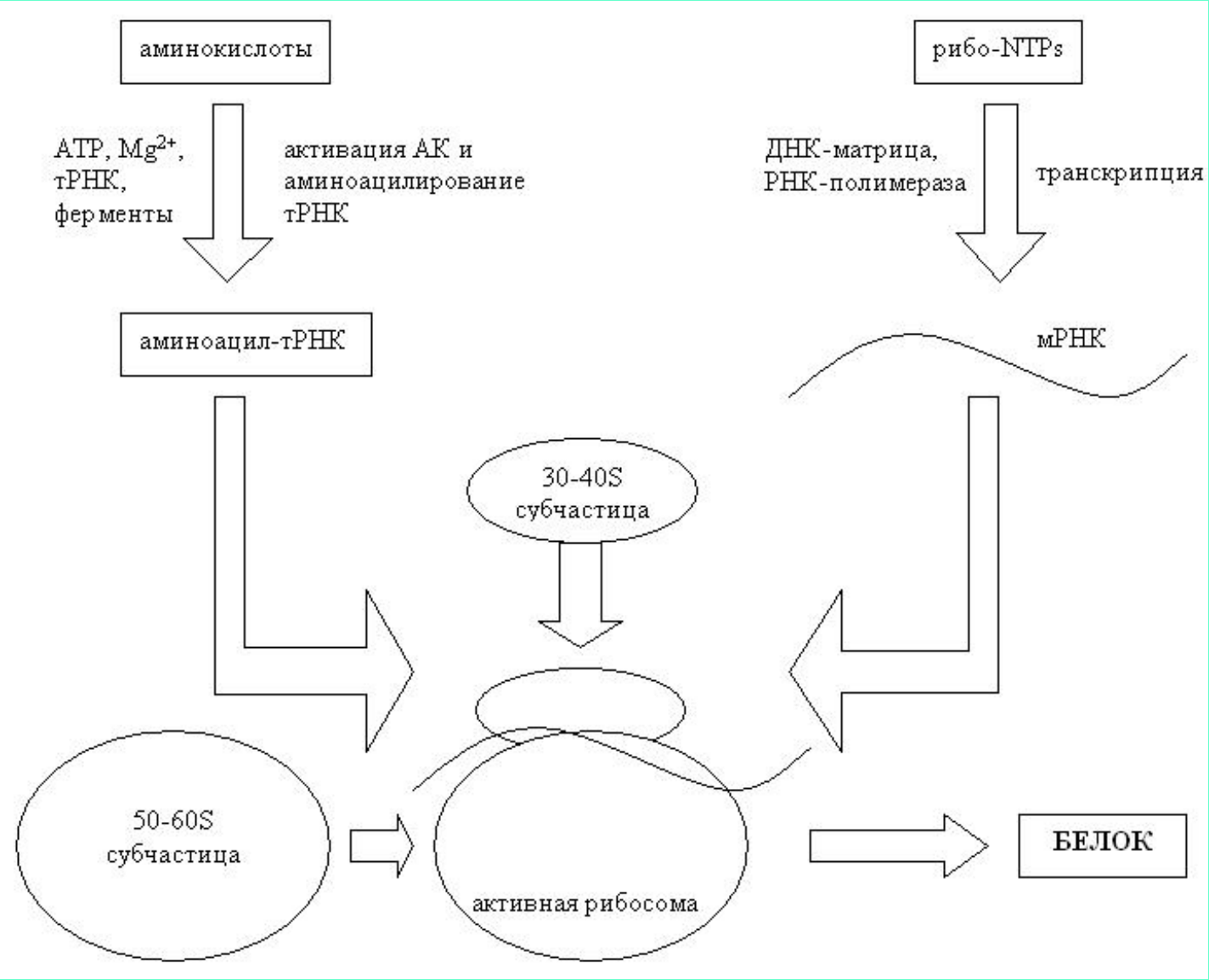
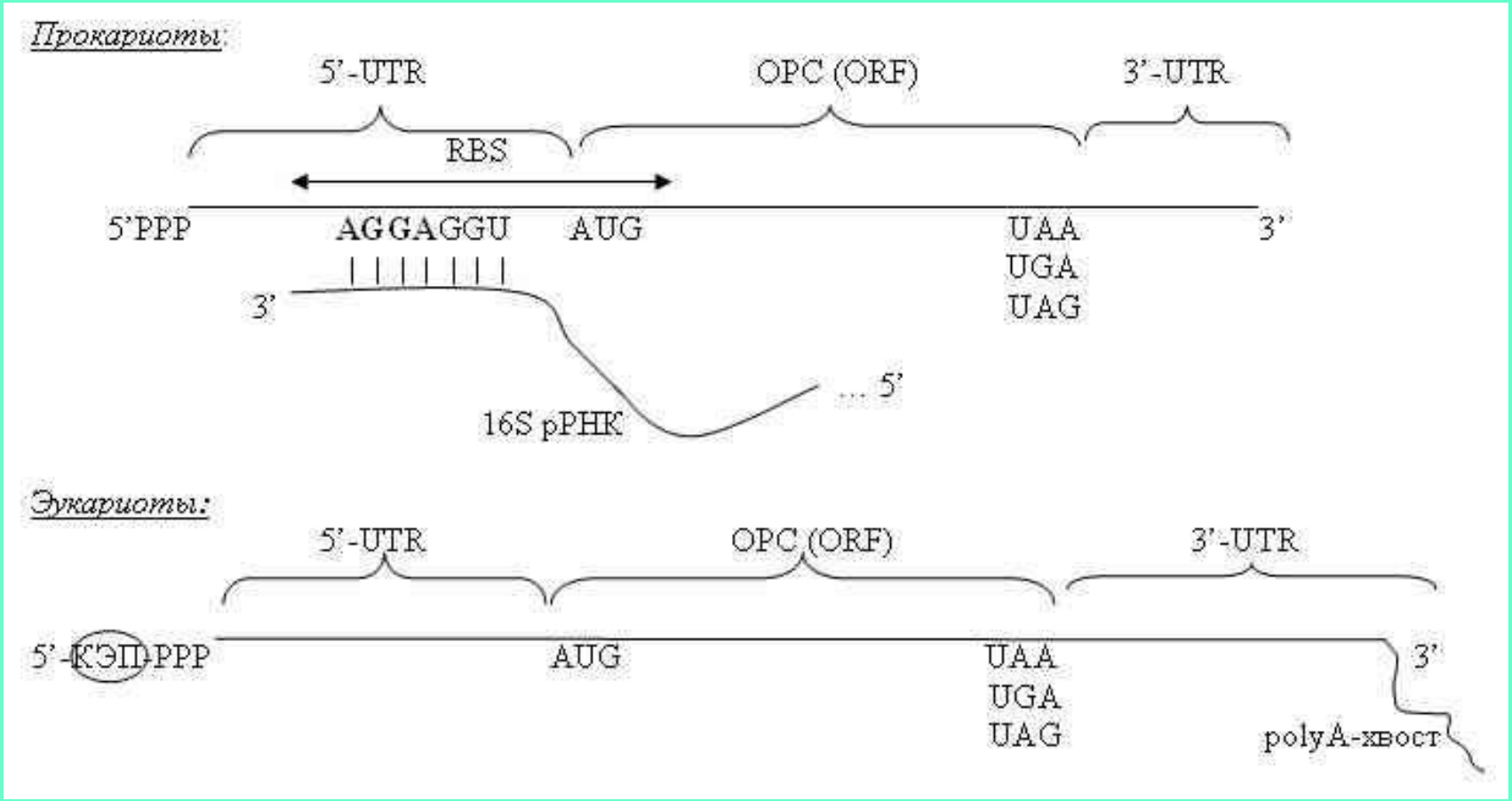
Трансляция – биосинтез белка на рибосоме

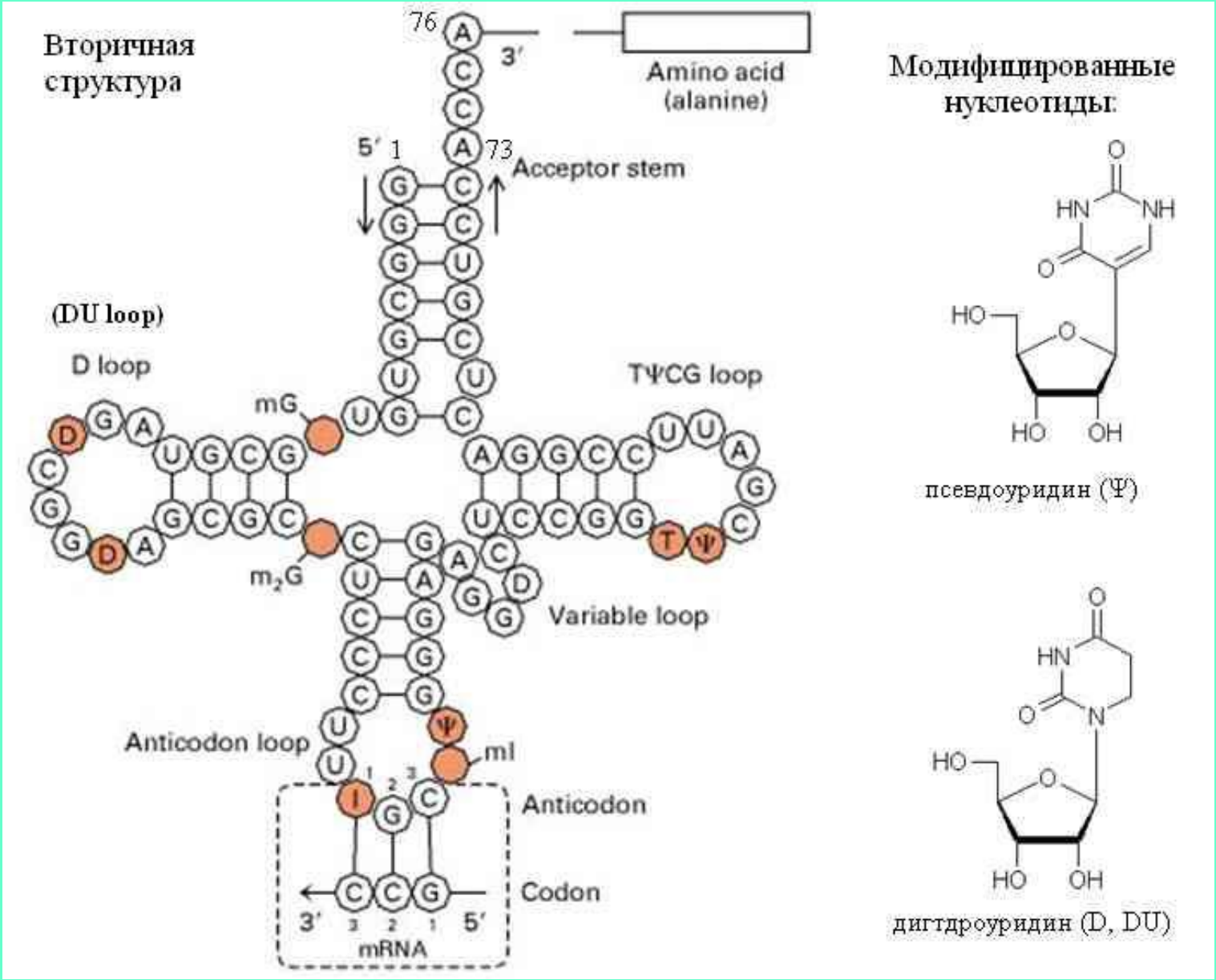
Схема биосинтеза белка на рибосоме



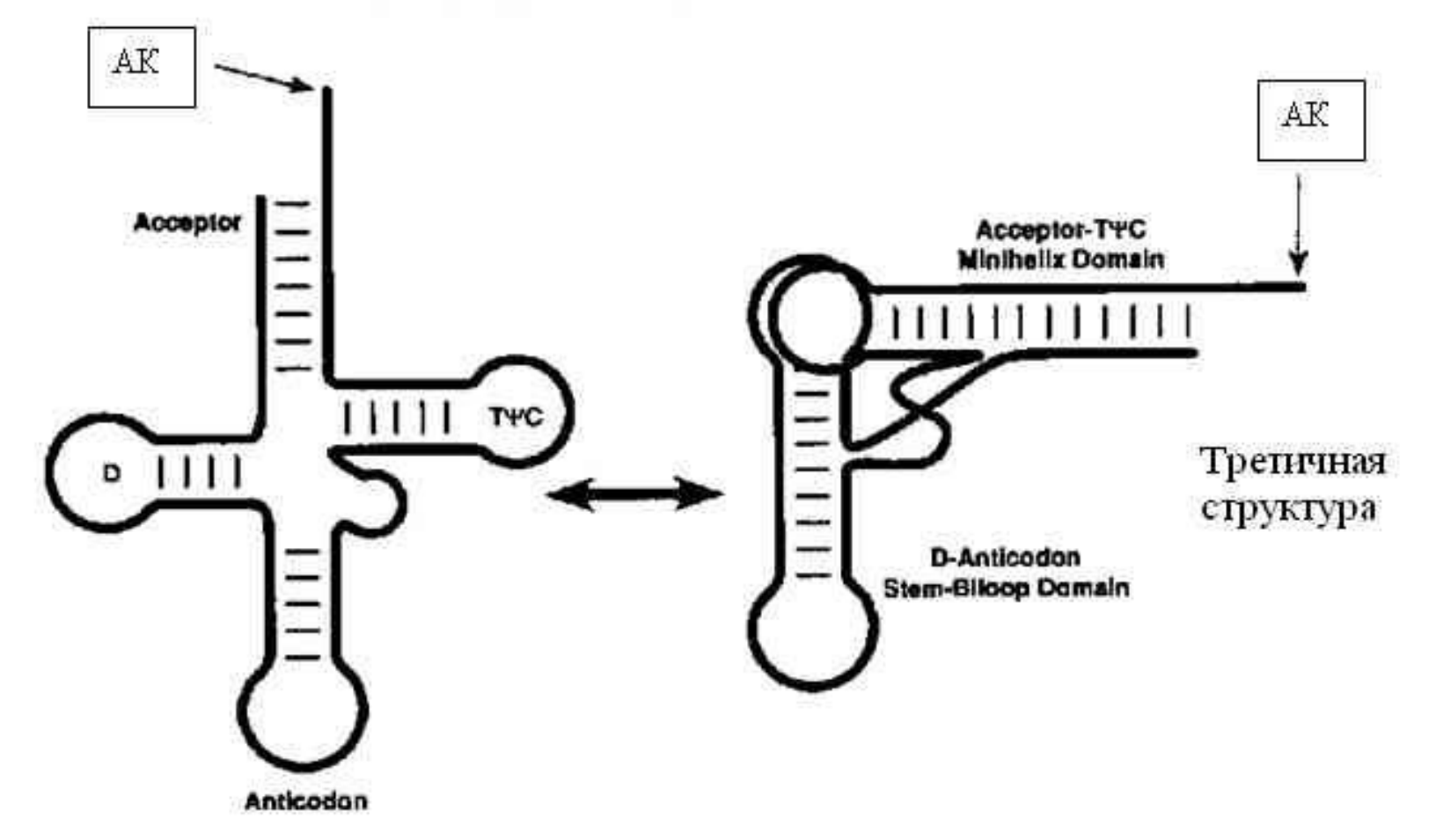
Строение мРНК прокариот и эукариот



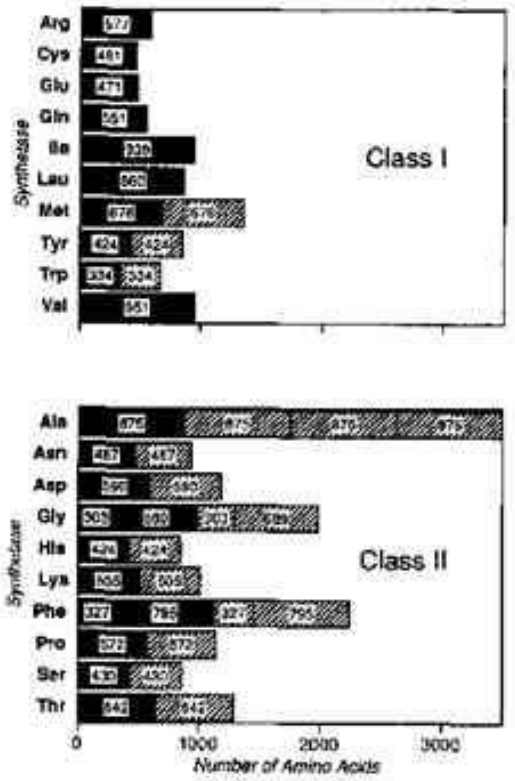
Строение тРНК

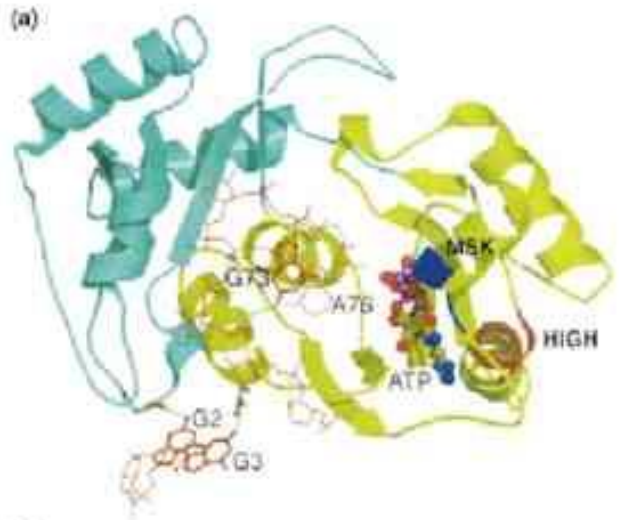


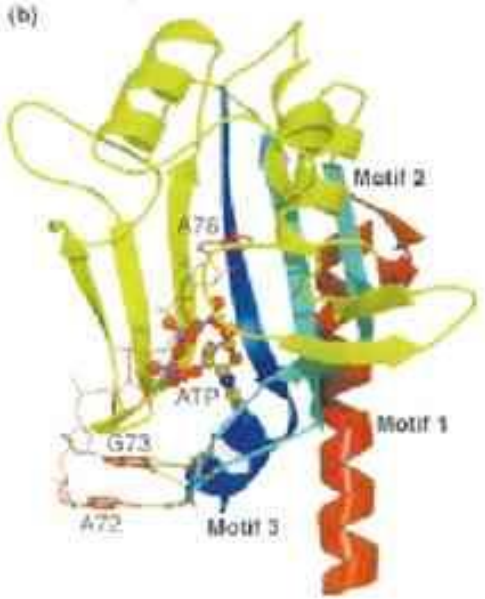
Пространственная структура тРНК



Аминоацил-тРНК-синтетазы





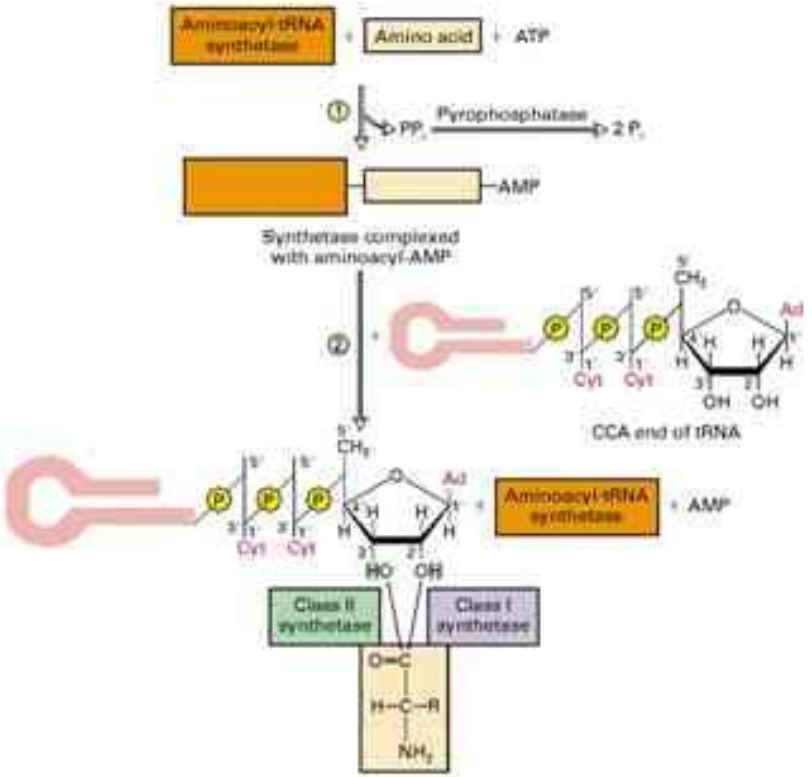


Активные центры aaRS:

Класс I

Класс II

Аминоацилирование тРНК



Общая схема реакции:

1. *Активация аминокислоты:*

АК + АТР + aaRS ↔ aaRS•АК-АМР + PPi

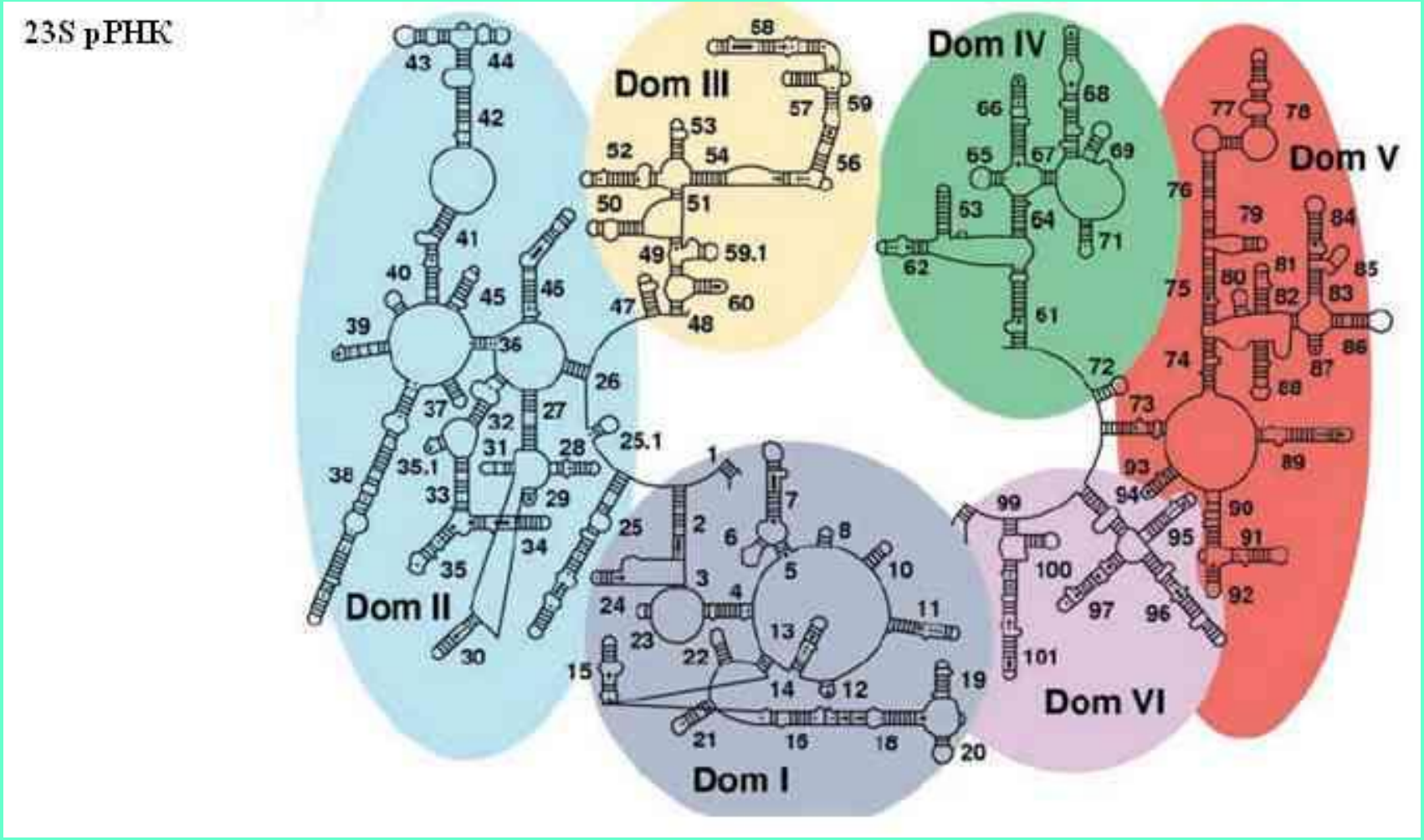
2. *аминоацилирование тРНК:*

aaRS•АК-АМР + тРНК ↔ aaRS + АК-тРНК + АМР

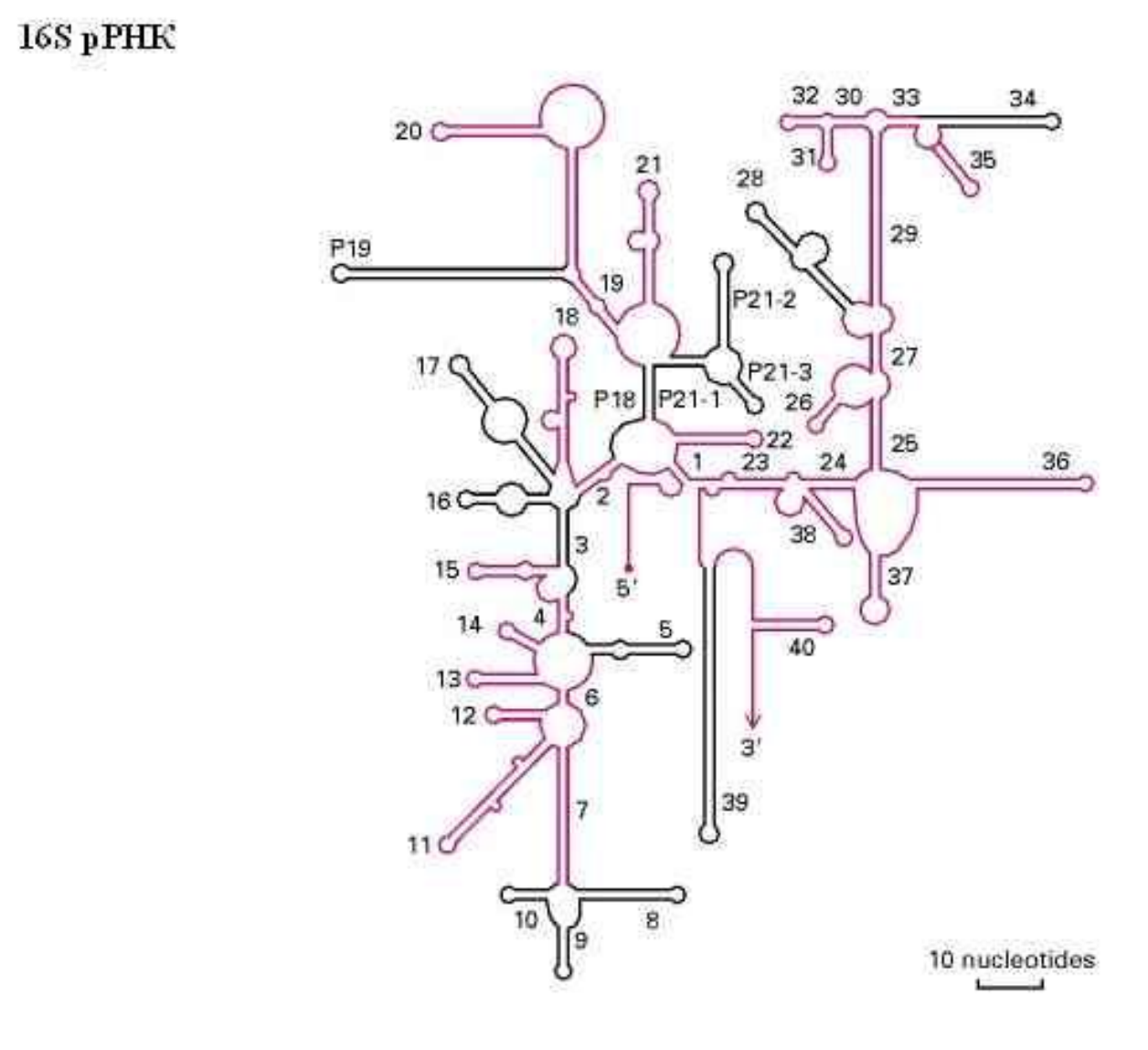
****

АК – аминокислота;
aaRS – аминоацил-тРНК-синтетаза

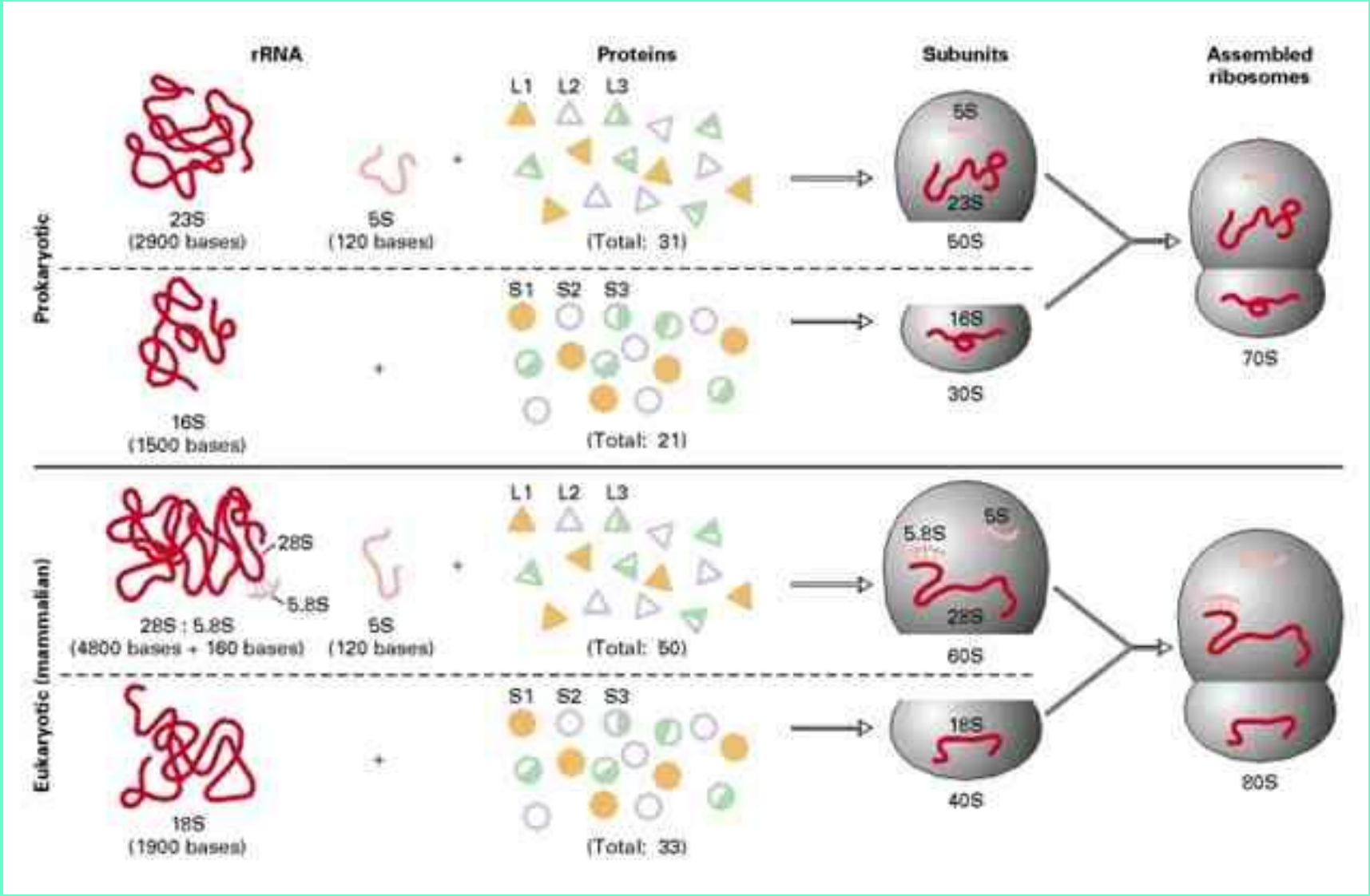
Вторичная структура рРНК (1)



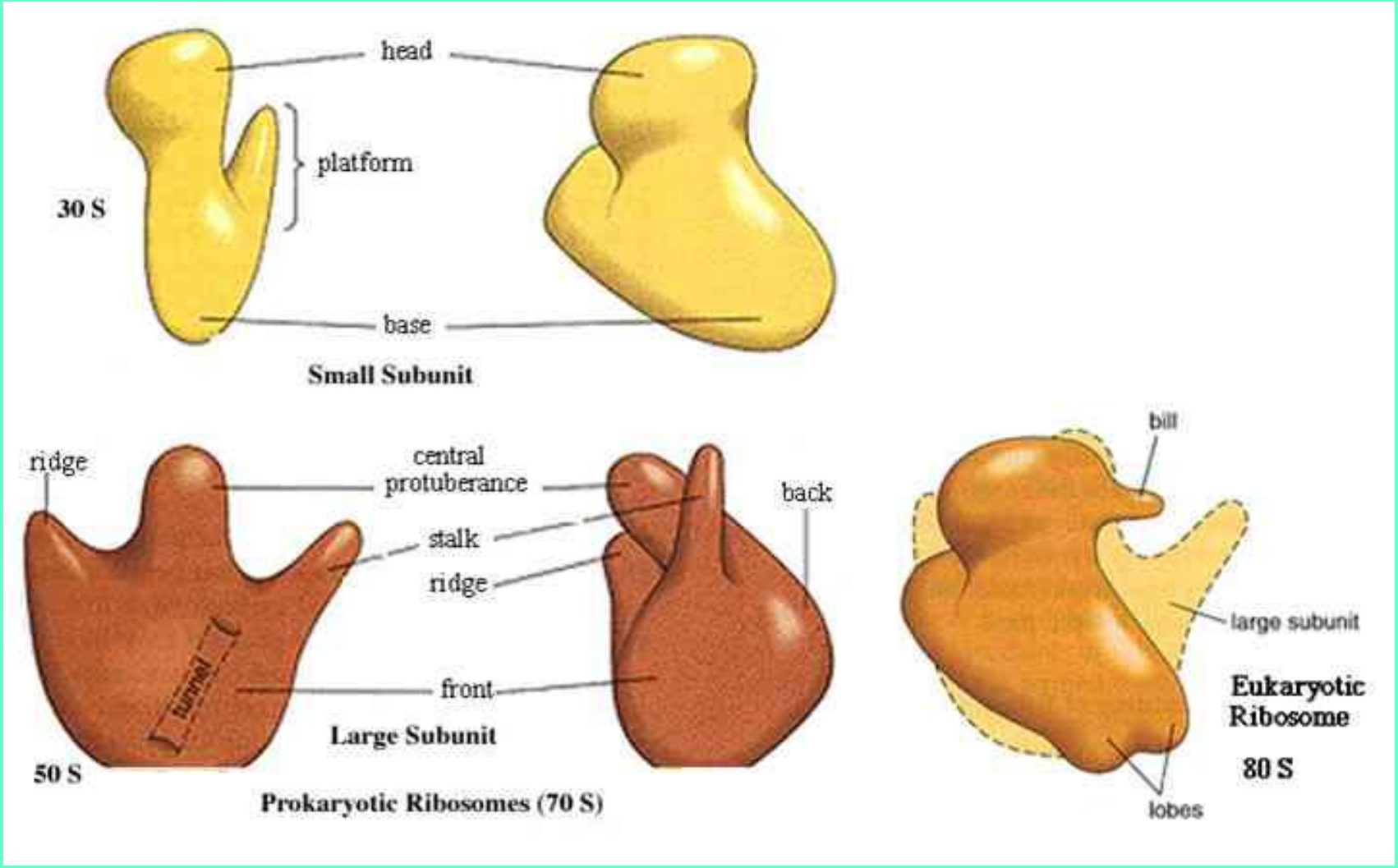
Вторичная структура рРНК (2)



Состав рибосом



Структура рибосом



Большая субчастица рибосомы прокариот

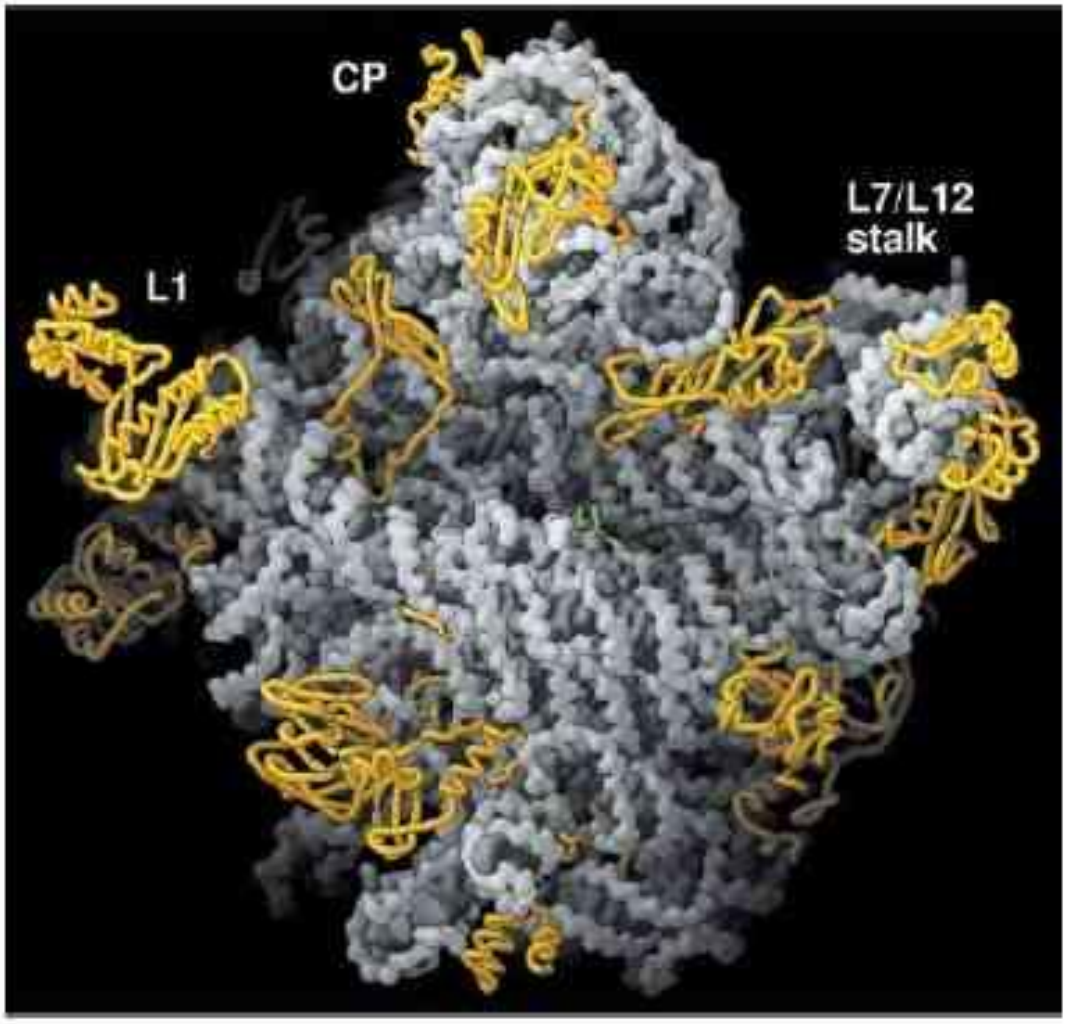
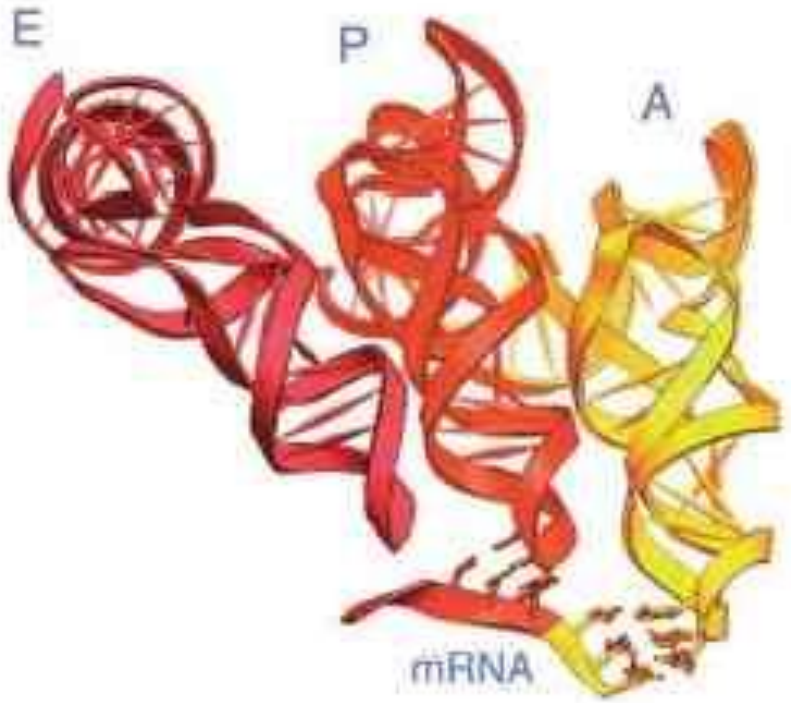


Fig. 2. The *H. marismortui* large ribosomal subunit in the rotated crown view. The L7/L12 stalk is to the right, the L1 stalk is to the left, and the central protuberance (CP) is at the top. In this view, the surface of the subunit that interacts with the small subunit faces the reader. RNA is shown in gray in a pseudo–space-filling rendering. The backbones of the proteins visible are rendered in gold. The Yarus inhibitor bound to the peptidyl transferase site of the subunit is indicated in green (64). The particle is approximately 250 Å across.

Структура тРНК и мРНК, связанных с рибосомой

Изменение структуры тРНК, связанных с А-, Р- и Е-сайтами рибосомы:



Механизм реакции транспептидации

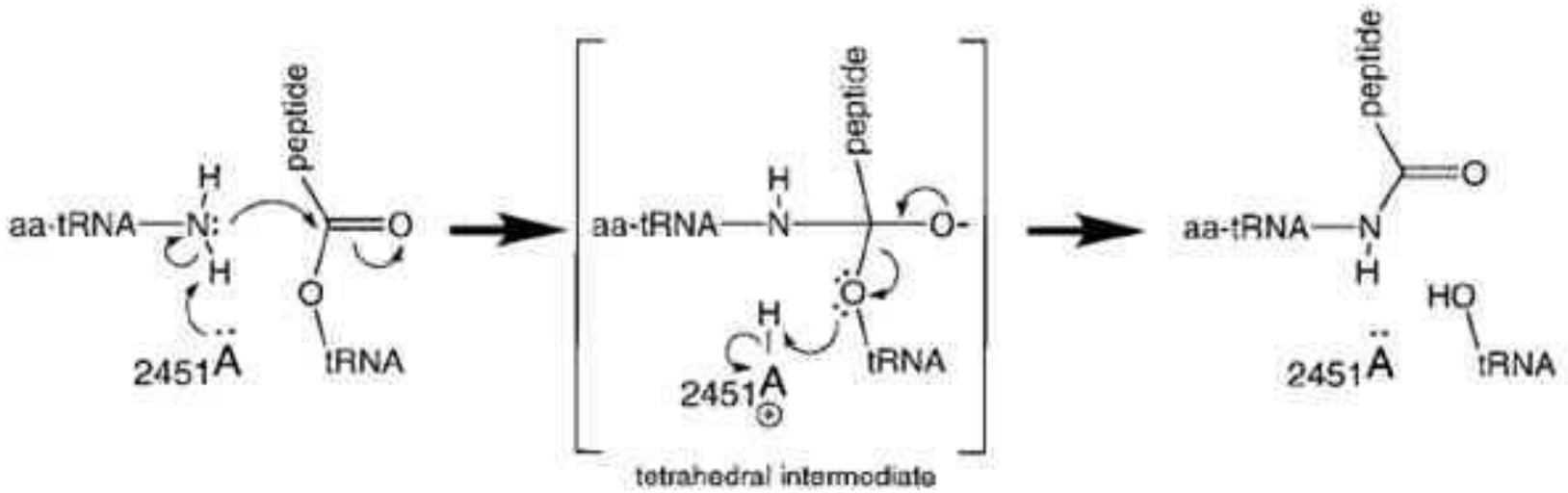
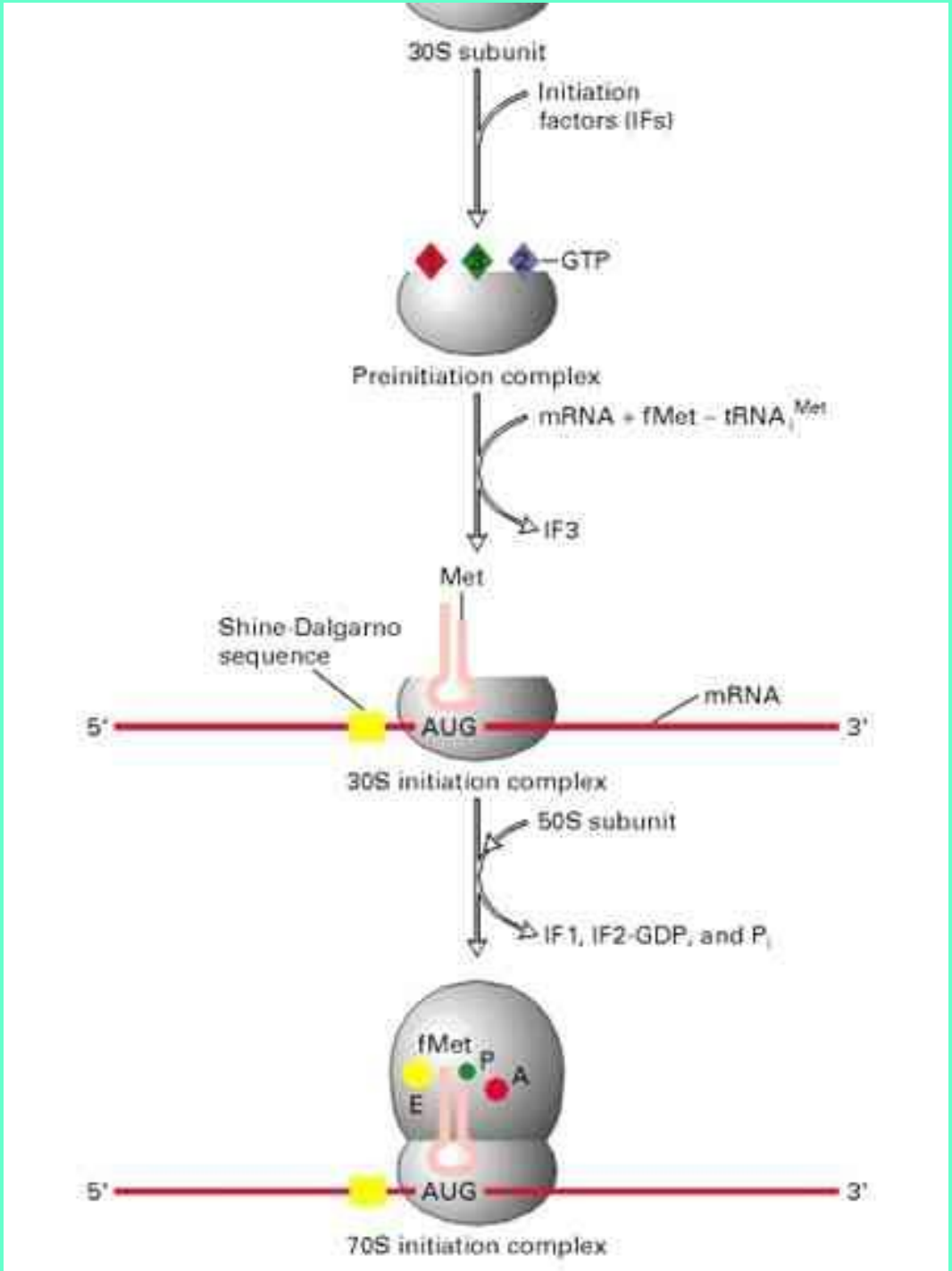


Fig. 2. Proposed general acid-base mechanism for ribosomal catalysis of the peptidyl transfer reaction. The details of the mechanism are discussed in the text. The lone pair of electrons shown on A2451 could be either those of the N1 or N3, although the N3 appears more likely on the basis of the crystal structure (*2*). The positive charge shown next to A2451 in the tetrahedral intermediate could reside on the base or be transferred to adjacent nucleotides by alternative tautomeric forms, as suggested by Nissen *et al.* (*2*).

Инициация трансляции у прокариот



Строение RBS мРНК прокариот и роль белка S1 в инициации

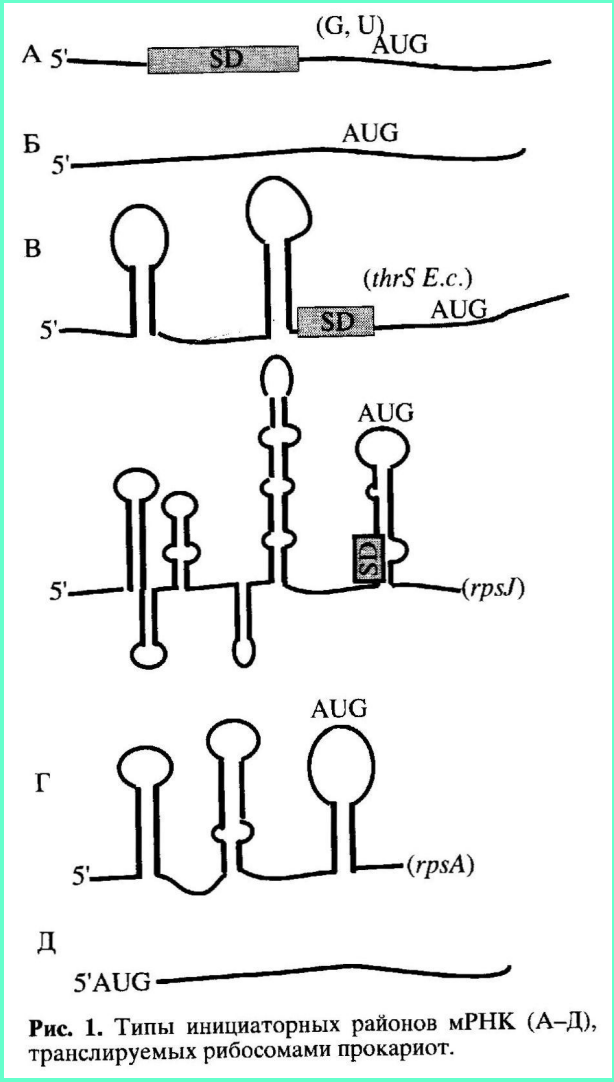
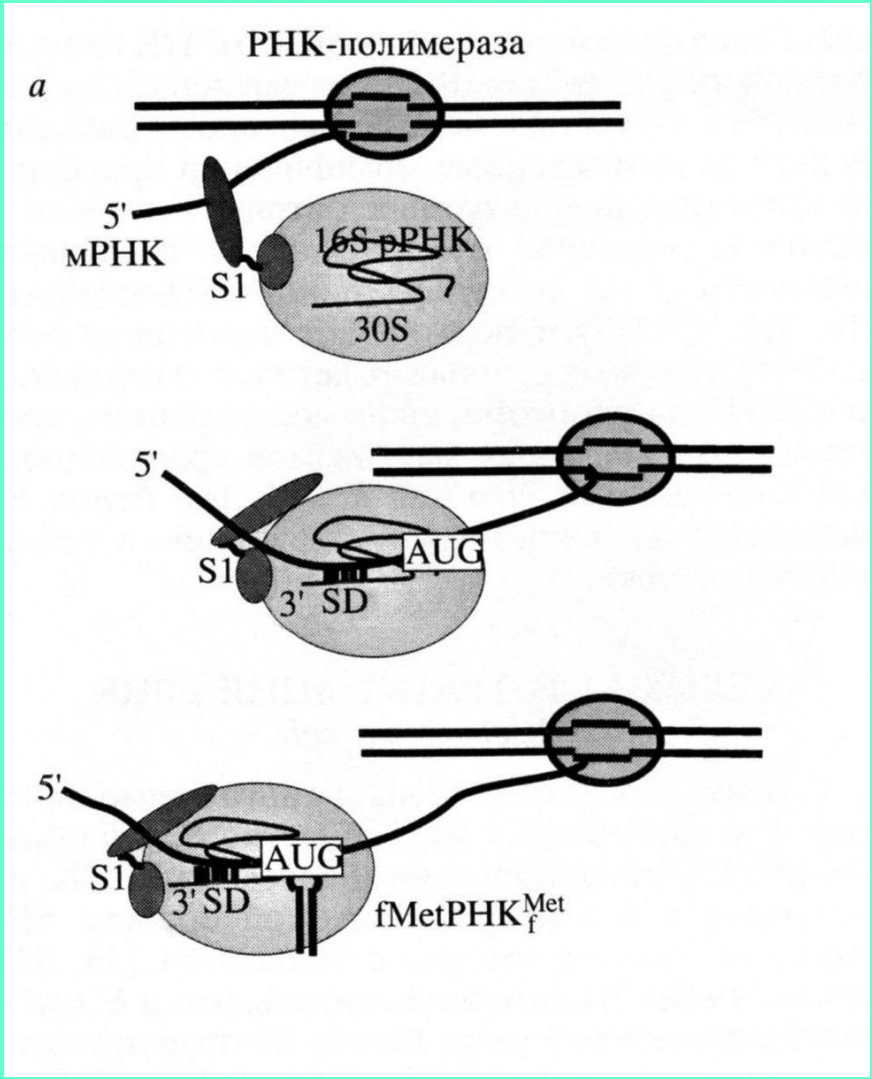


Рис. 1. Типы инициаторных районов мРНК (А–Д), транслируемых рибосомами прокариот.



Факторы инициации, связанные с малой субчастицей рибосомы (прокариоты)

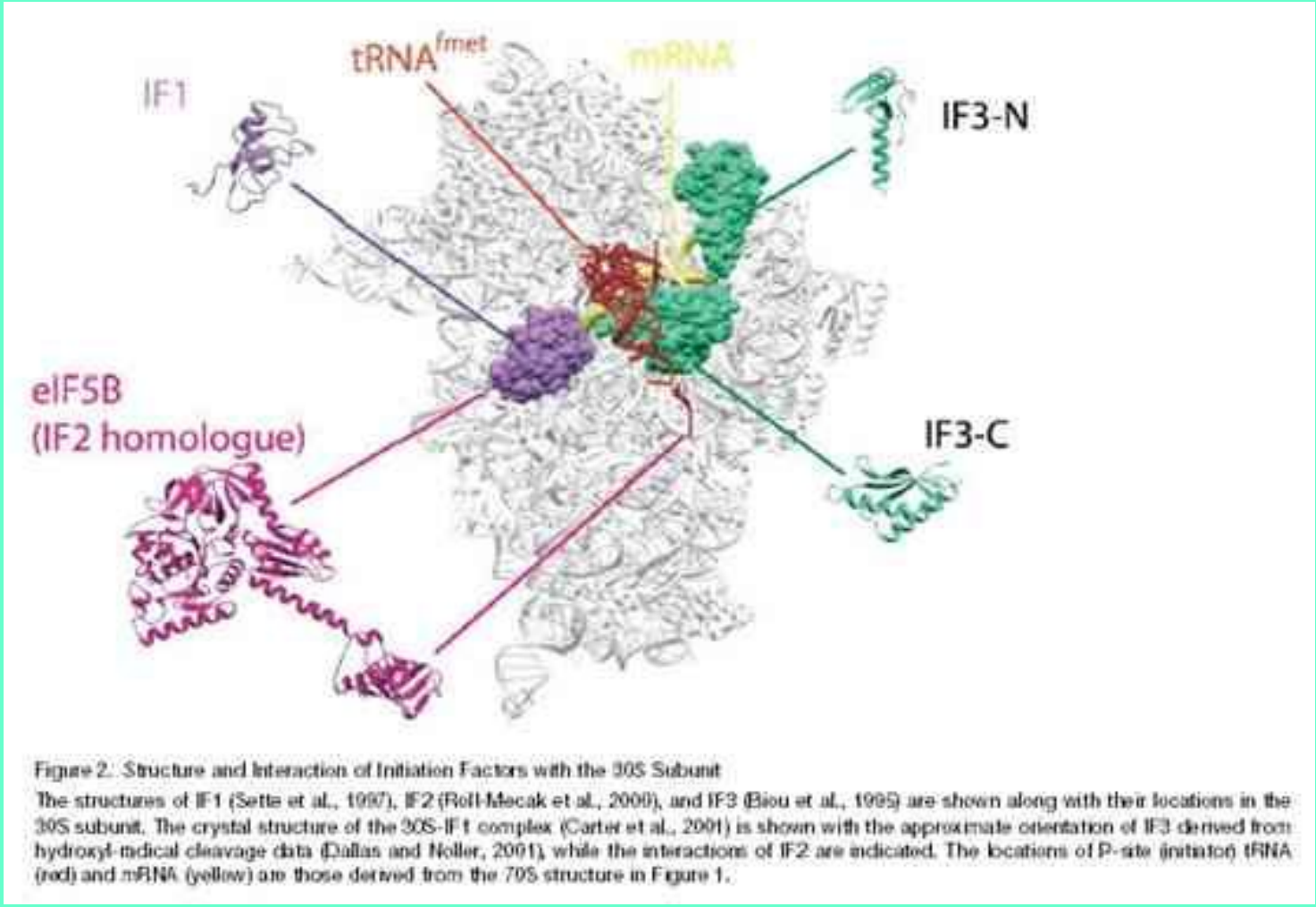


Figure 2: Structure and Interaction of Initiation Factors with the 30S Subunit

The structures of IF1 (Sette et al., 1997), IF2 (Roll-Mecak et al., 2000), and IF3 (Biou et al., 1995) are shown along with their locations in the 30S subunit. The crystal structure of the 30S-IF1 complex (Carter et al., 2001) is shown with the approximate orientation of IF3 derived from hydroxyl-radical cleavage data (Dallas and Noller, 2001), while the interactions of IF2 are indicated. The locations of P-site (initiator) tRNA (red) and mRNA (yellow) are those derived from the 70S structure in Figure 1.

«Макромолекулярная мимикрия» фактора IF3

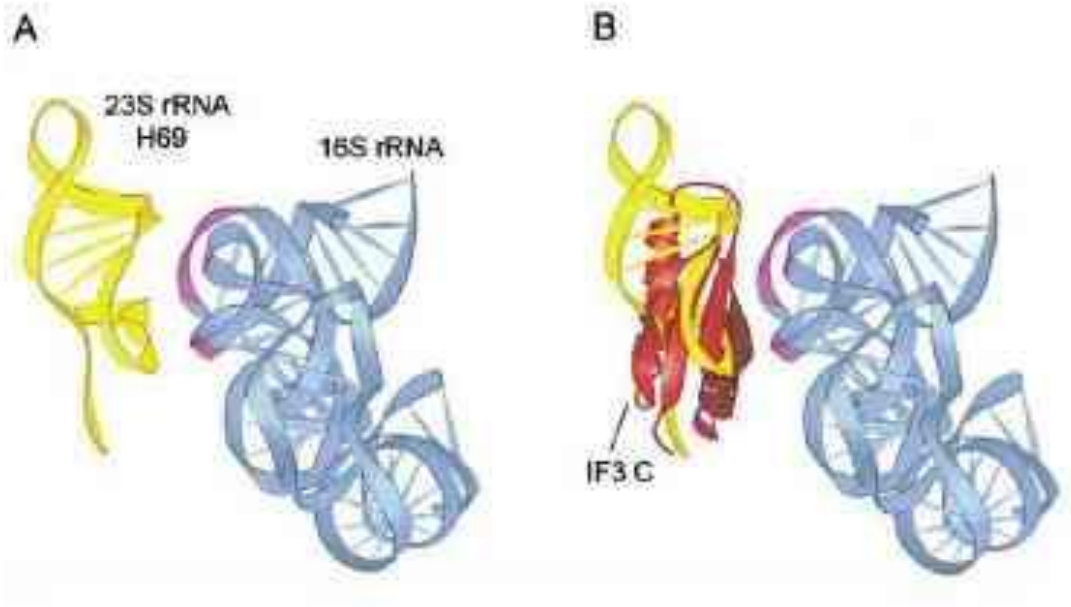
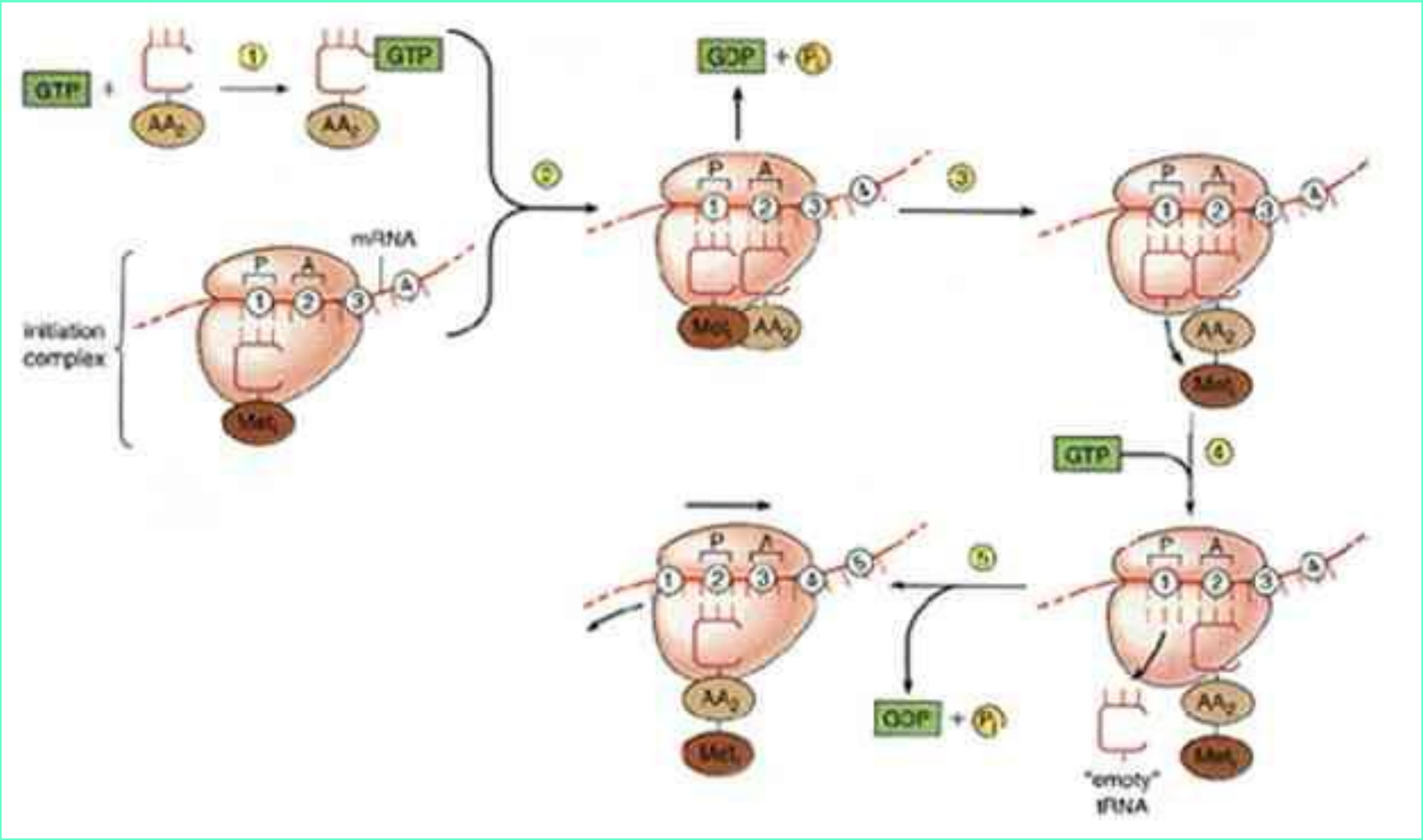


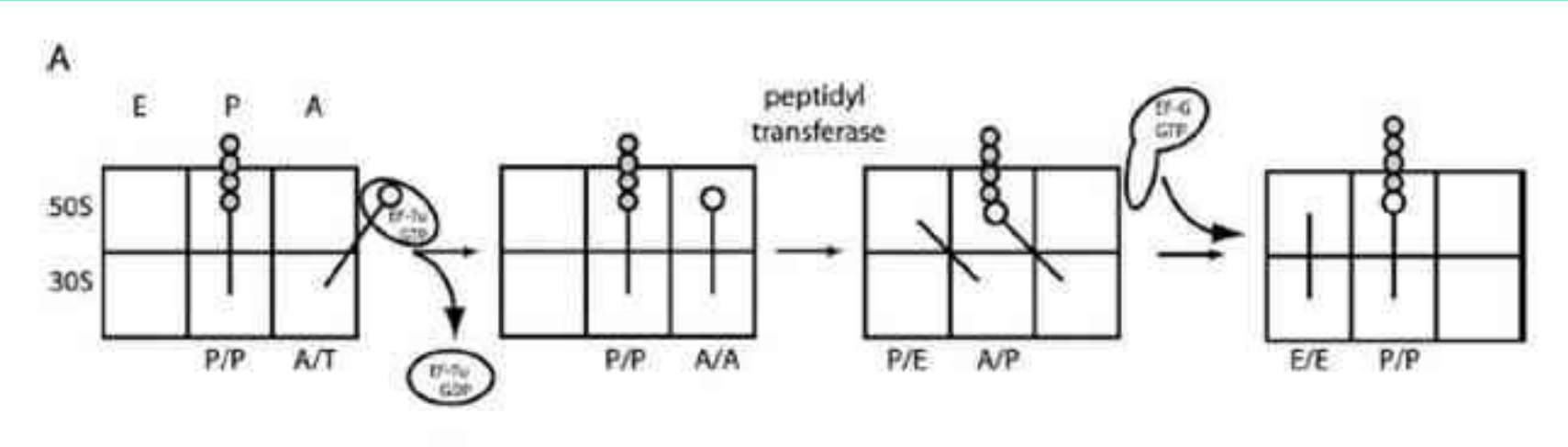
Figure 7. The IF3 C Domain Occupies the Position of Helix 69 of 23S rRNA

(A) A view of the interaction of helix 69 (yellow) of 23S rRNA with helices 23, 24, and 45 of 16S rRNA (blue). The sites of contact between 23S rRNA and 16S rRNA are colored purple. (B) A view showing the overlapping binding site on the 30S subunit of the C domain of IF3 (red) with helix 69 of 23S rRNA (yellow).

Элонгация трансляции у прокариот



Модель гибридных состояний



«Макромолекулярная мимикрия» факторов трансляции

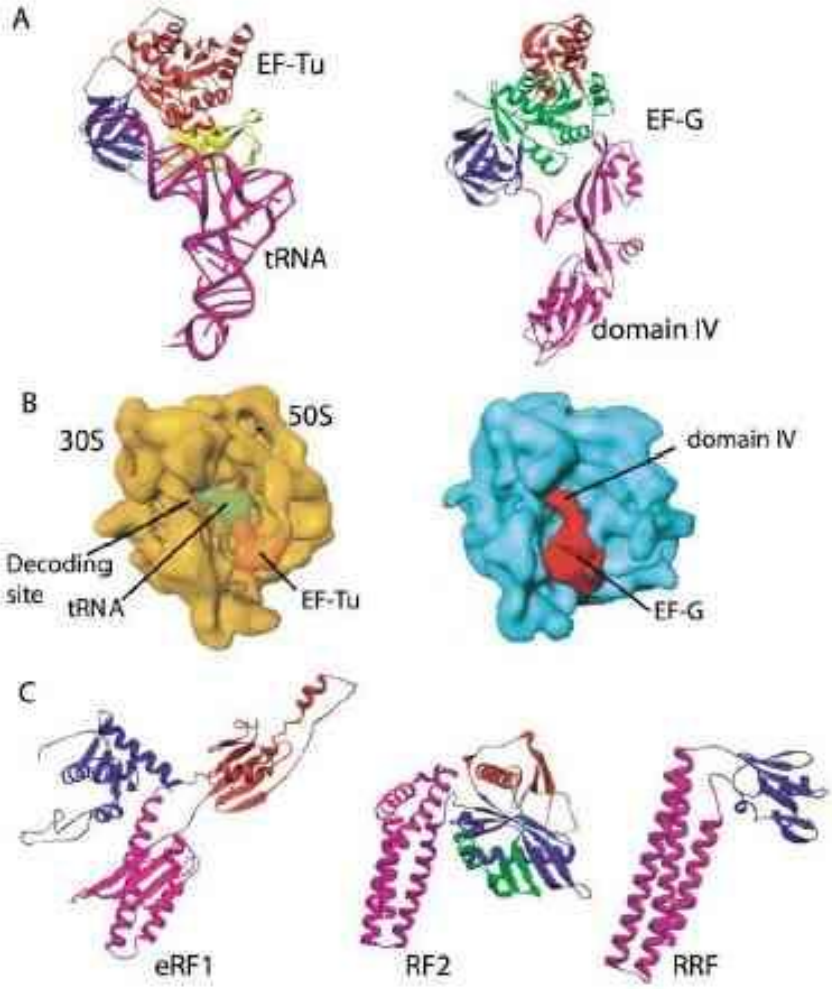


Figure 7. Mimicry among Translation Factors
(A) Crystal structures of (left) the ternary complex of EF-Tu, tRNA, and GDPNP (Nissen et al., 1995) and (right) EF-G (Aevarsson et al., 1994; Czworkowski et al., 1994).
(B) CryoEM reconstructions (left) of the ribosome with the ternary complex (Stark et al., 1997) and EF-G (Agrawal et al., 1998). Reproduced with permission.
(C) Structures of class I release factors eRF1 and RF2 and ribosome recycling factor RRF. The domains that are thought to mimic tRNA are shown in magenta, as is domain IV of EF-G in (A).

Терминация трансляции у прокариот

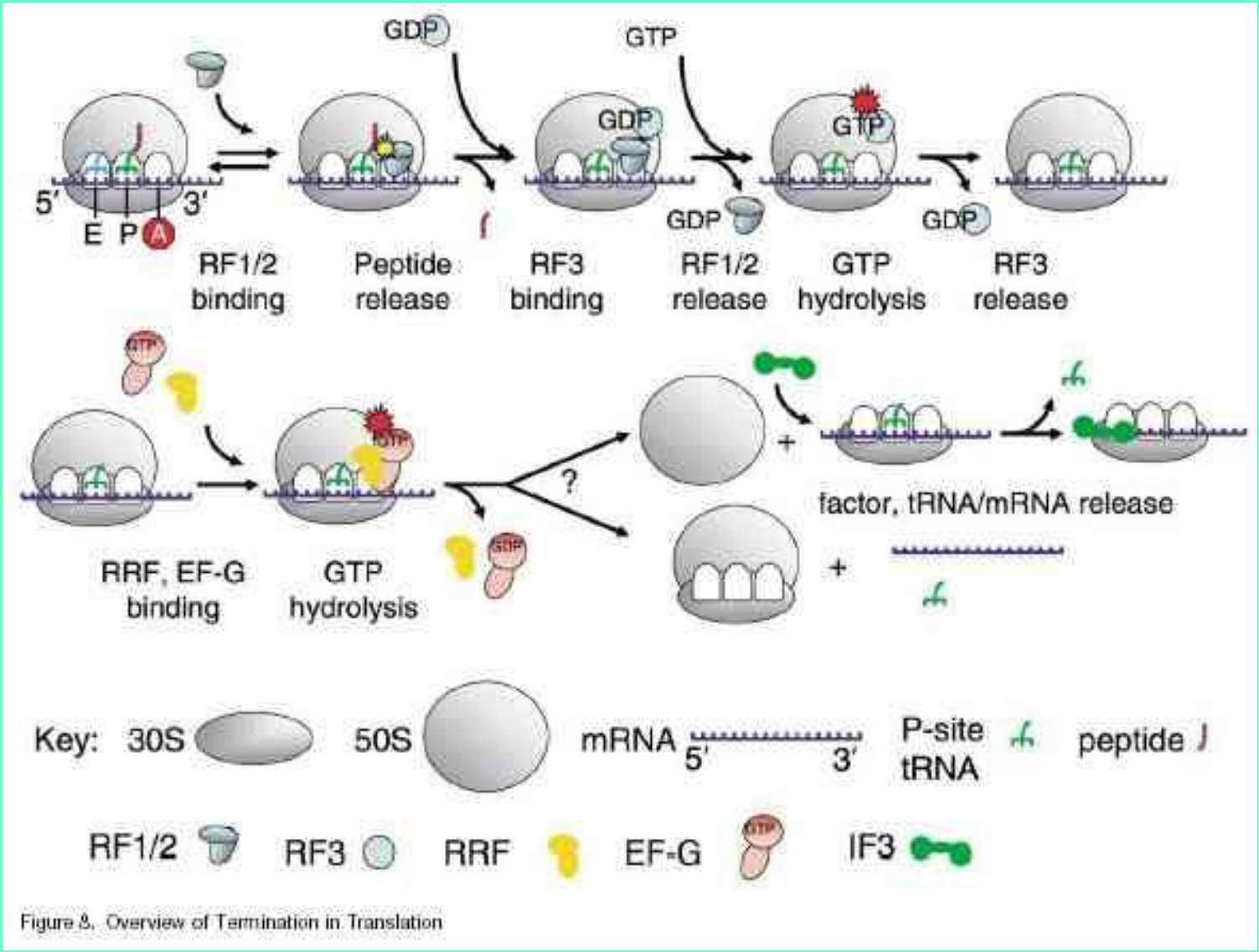


Figure 8. Overview of Termination in Translation

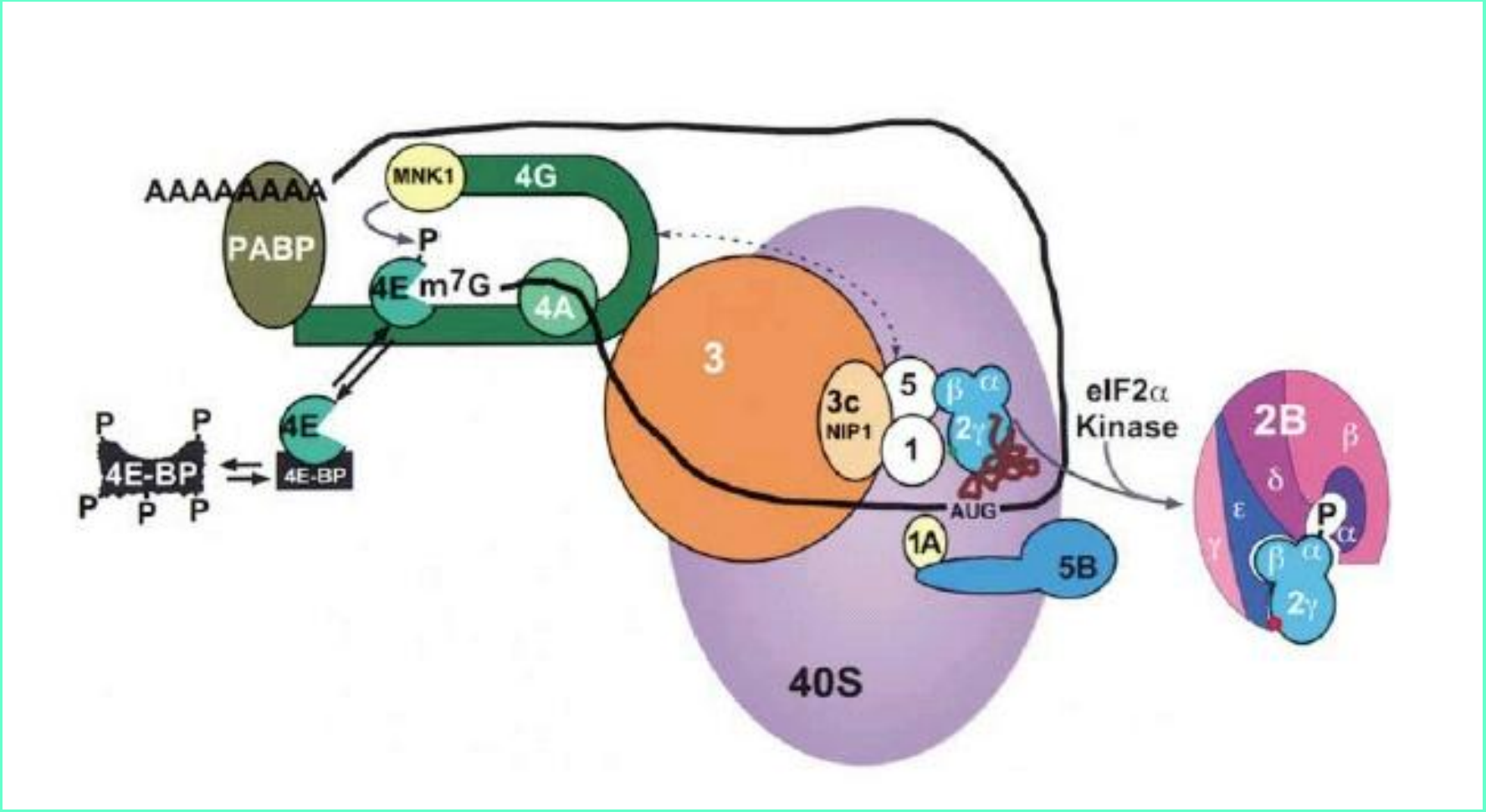
Факторы инициации трансляции у эукариот

Table 1. Translation Initiation Factors

Eukaryotic Factor	Prokaryotic Factor	Archaeal Factor	Function
eIF1	IF3[a]	a-eIF1	Fidelity of AUG codon recognition
eIF1A	IF1	a-eIF1A	Facilitate Met-tRNA$_i^{Met}$ binding to small subunit
eIF2		a-eIF2	Bind Met-tRNA$_i^{Met}$ to 40S subunit; GTPase
eIF2B			Guanine-nucleotide exchange factor for eIF2
eIF3			Promote Met-tRNA$_i^{Met}$ and mRNA binding to 40S subunit
eIF4A		a-eIF4A	DEAD-box helicase
eIF4B			Promote eIF4A activity
eIF4E			m^{7}GpppX cap binding protein
eIF4F			Cap binding complex of eIFs 4A, 4E, and 4G
eIF4G			Adaptor protein interacts with many other factors
eIF4H			Similar to eIF4B
eIF5			AUG recognition and promote eIF2 GTPase activity
eIF5B	IF2	a-eIF5B	Subunit joining; in prokaryotes Met-tRNA$_i^{Met}$ binding

[a]The proposed grouping of eIF1 and IF3 is based on their common function to insure accurate Met-tRNA$_i^{Met}$ and AUG codon selection, and structural similarity of eIF1 (Fletcher et al., 1999) to the C-terminal domain of IF3 (Biou et al., 1995).

Инициирующий комплекс на 40S субчастице



Кэп- и IRES-зависимая инициация

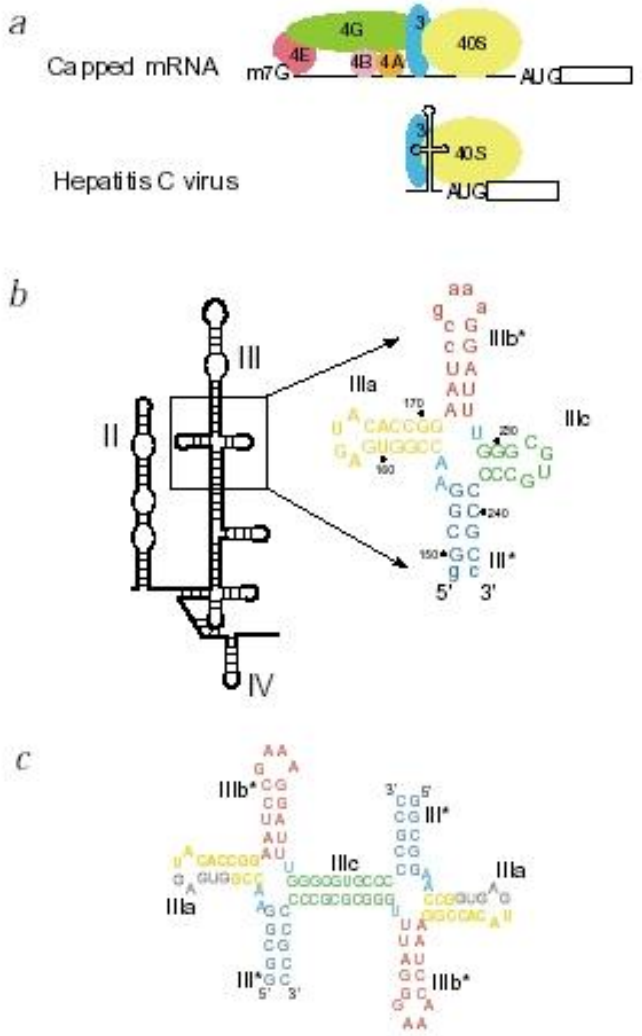
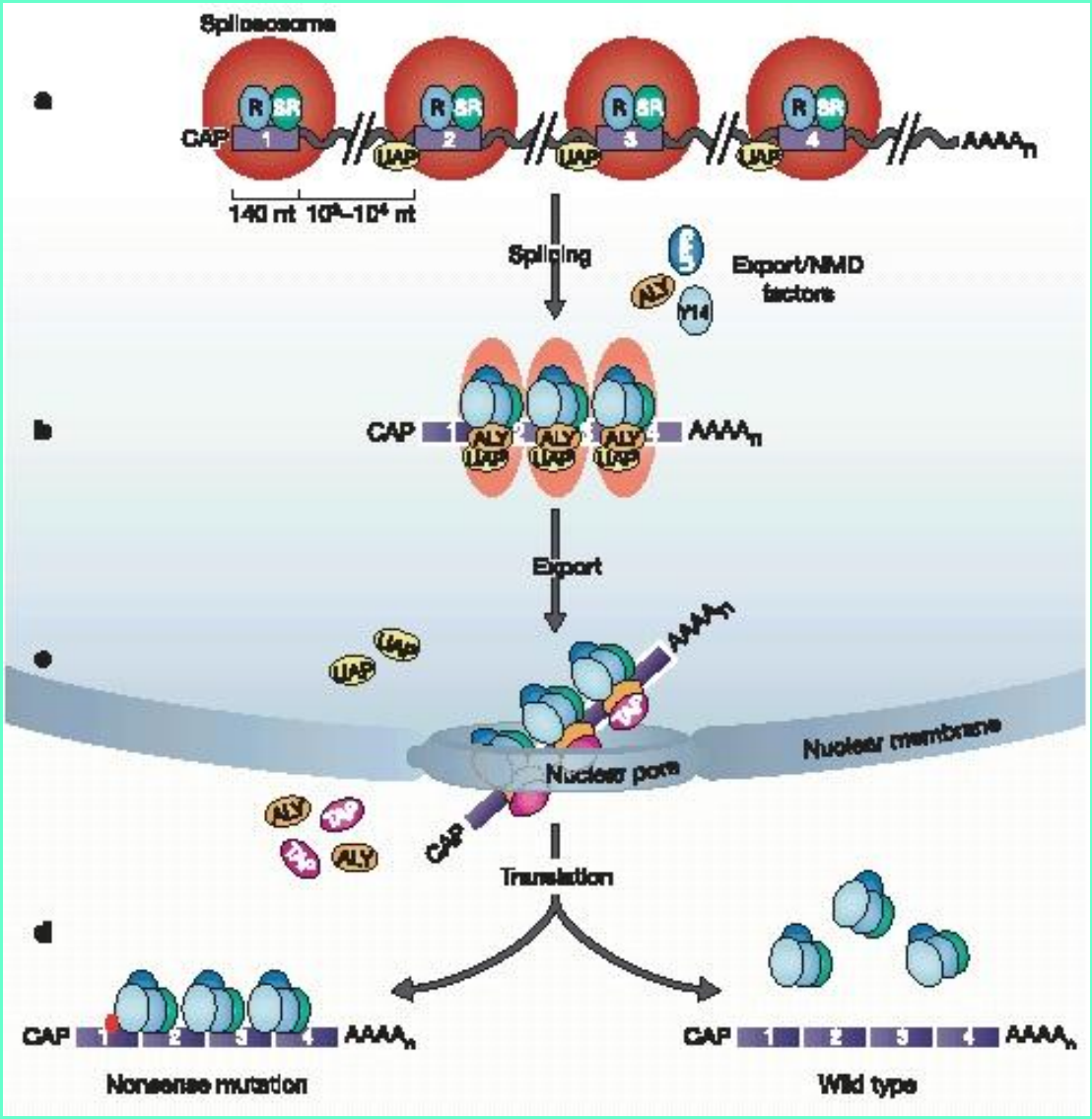
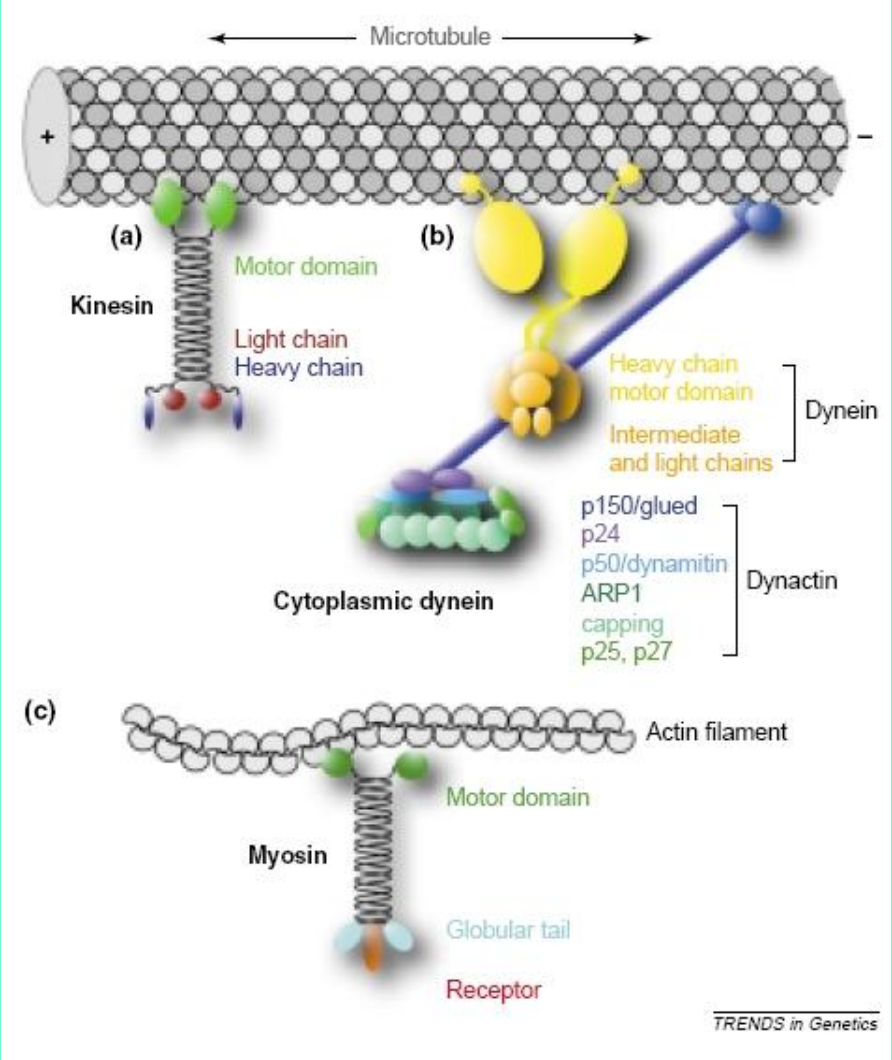


Fig. 1 Function of the HCV IRES and design of the crystallization construct. *a*, Comparison of cap-dependent (top) and internal (bottom) translation initiation. In cap-dependent initiation, recruitment of the 40S subunit is driven by recognition of the modified nucleotide cap by the eIF4F complex. In HCV IRES driven internal initiation, the IRES RNA recruits the translation machinery directly. *b*, Secondary structure of the HCV IRES, showing the location of junction IIIabc and the design of the crystallization construct. Nucleotides that differ from the native sequence are designated in lowercase. *c*, Secondary structural diagram of the crystallization-induced dimer. Loop IIIa nucleotides for which no electron density was observed are shown in outline.

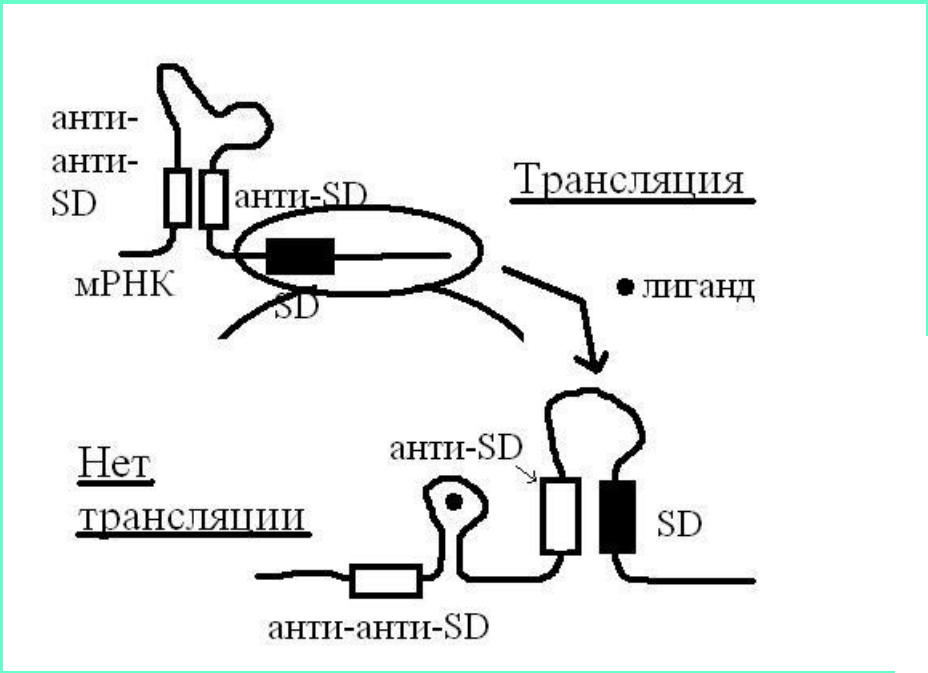
Регуляция трансляции: экспорт мРНК из ядра в цитоплазму

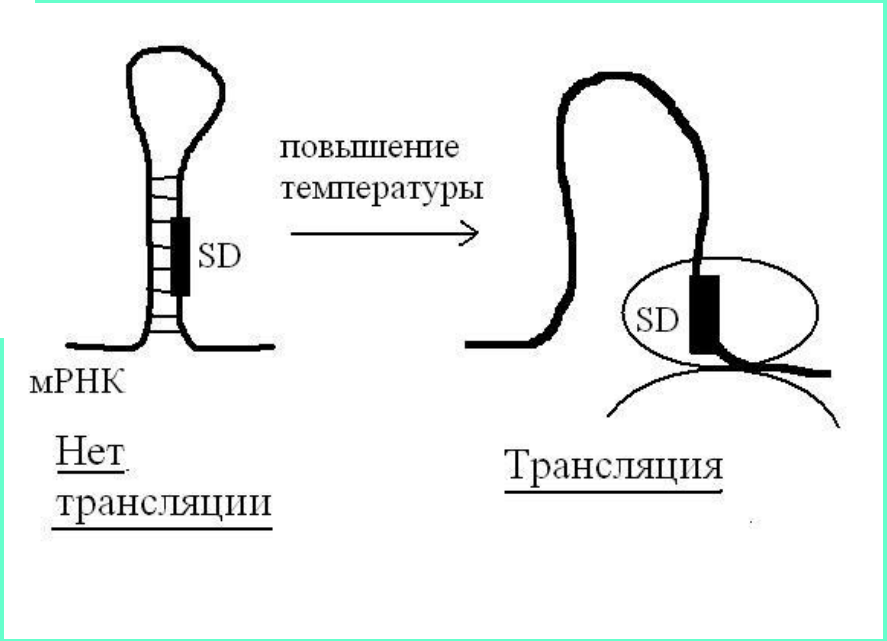


Регуляция трансляции: транспорт мРНК в цитоплазме

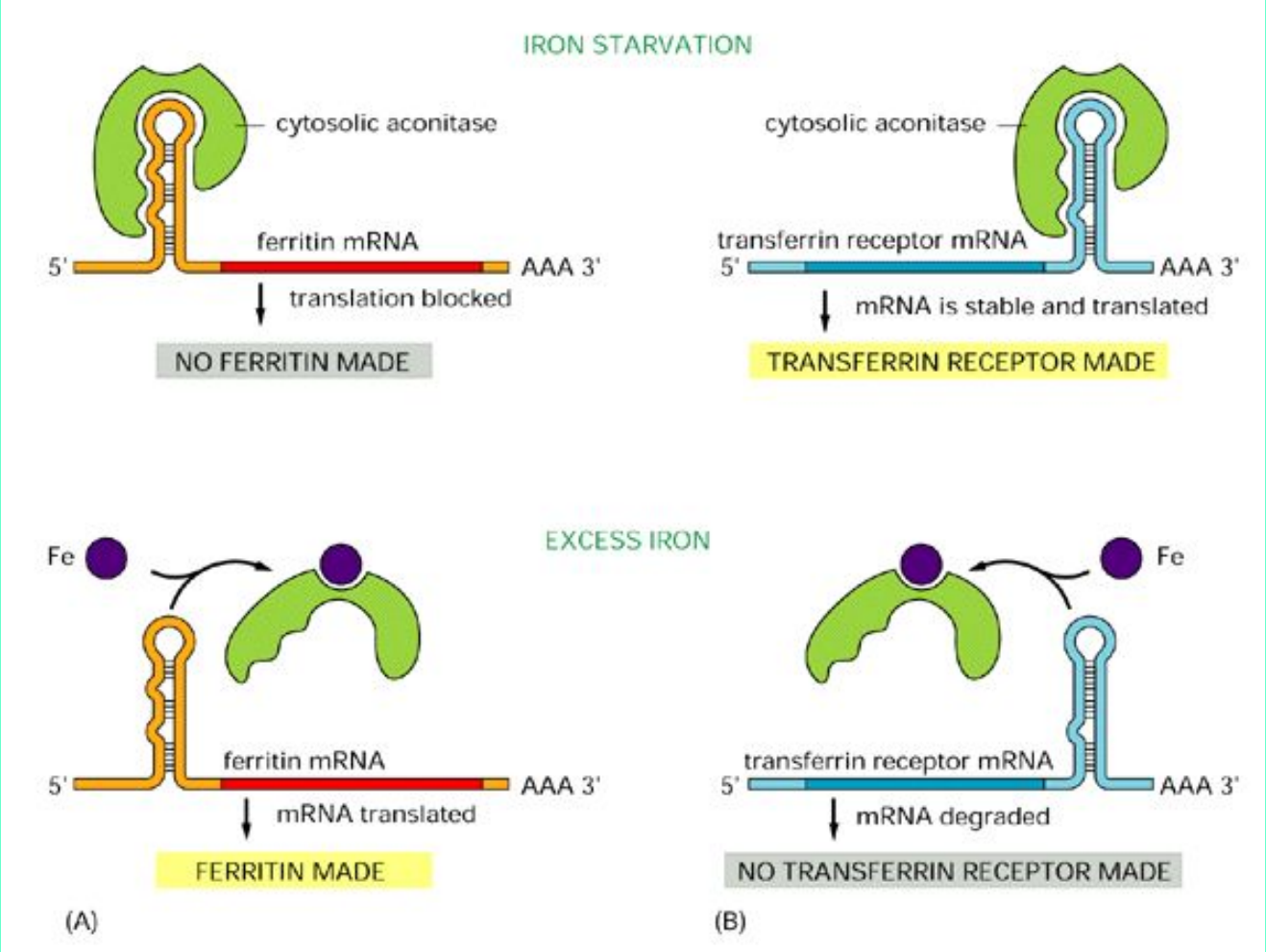


Регуляция трансляции: рибо-переключатели





Регуляция трансляции мРНК ферритина (слева) и рецептора трансферрина (справа) ионами железа



Деградация мРНК экзонуклеазами

Дрожжи:

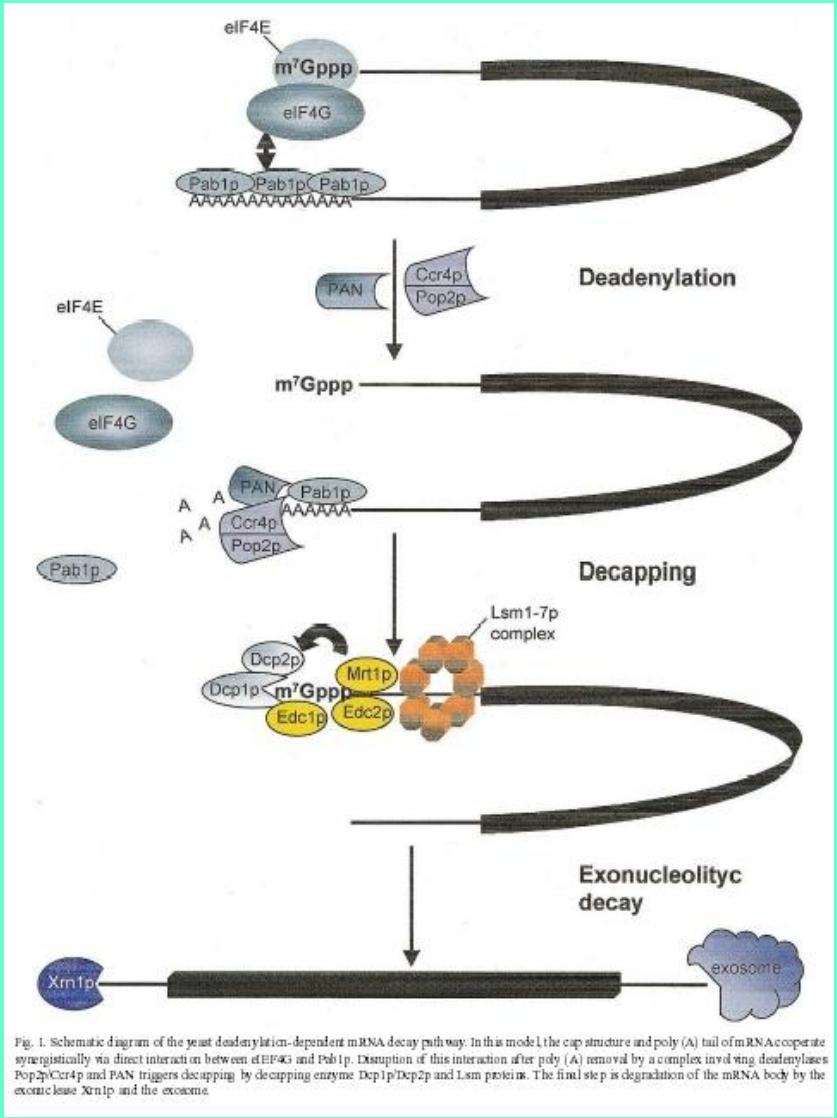


Fig. 1. Schematic diagram of the yeast deadenylation-dependent mRNA decay pathway. In this model the cap structure and poly (A) tail of mRNA cooperate synergistically via direct interaction between eIF4G and Pab1p. Disruption of this interaction after poly (A) removal by a complex involving deadenylases Pop2p/Ccr4p and PAN triggers decapping by decapping enzyme Dcp1p/Dcp2p and Lsm proteins. The final step is degradation of the mRNA body by the exonuclease Xrn1p and the exosome.

Млекопитающие:

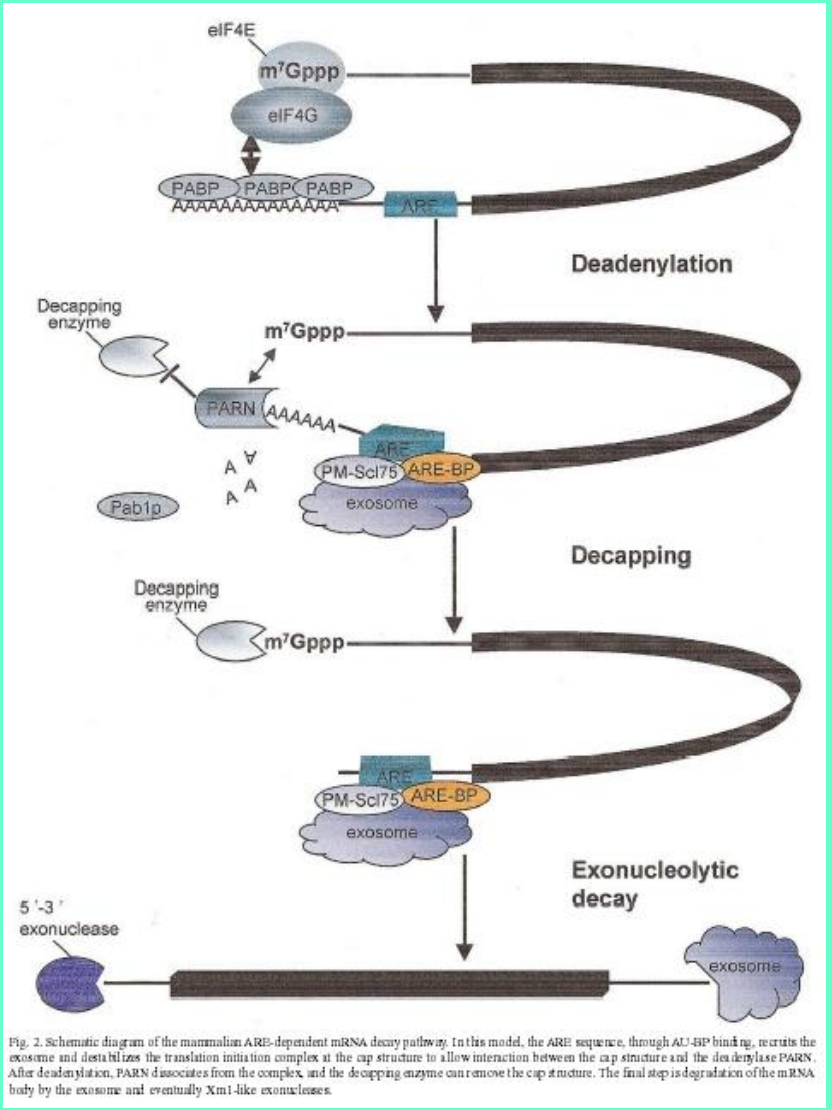


Fig. 2. Schematic diagram of the mammalian ARE-dependent mRNA decay pathway. In this model, the ARE sequence, through AU-BP binding, recruits the exosome and destabilizes the translation initiation complex at the cap structure to allow interaction between the cap structure and the deadenylase PARN. After deadenylation, PARN dissociates from the complex, and the decapping enzyme can remove the cap structure. The final step is degradation of the mRNA body by the exosome and eventually Xrn1-like exonucleases.

Деградация мРНК эндонуклеазами

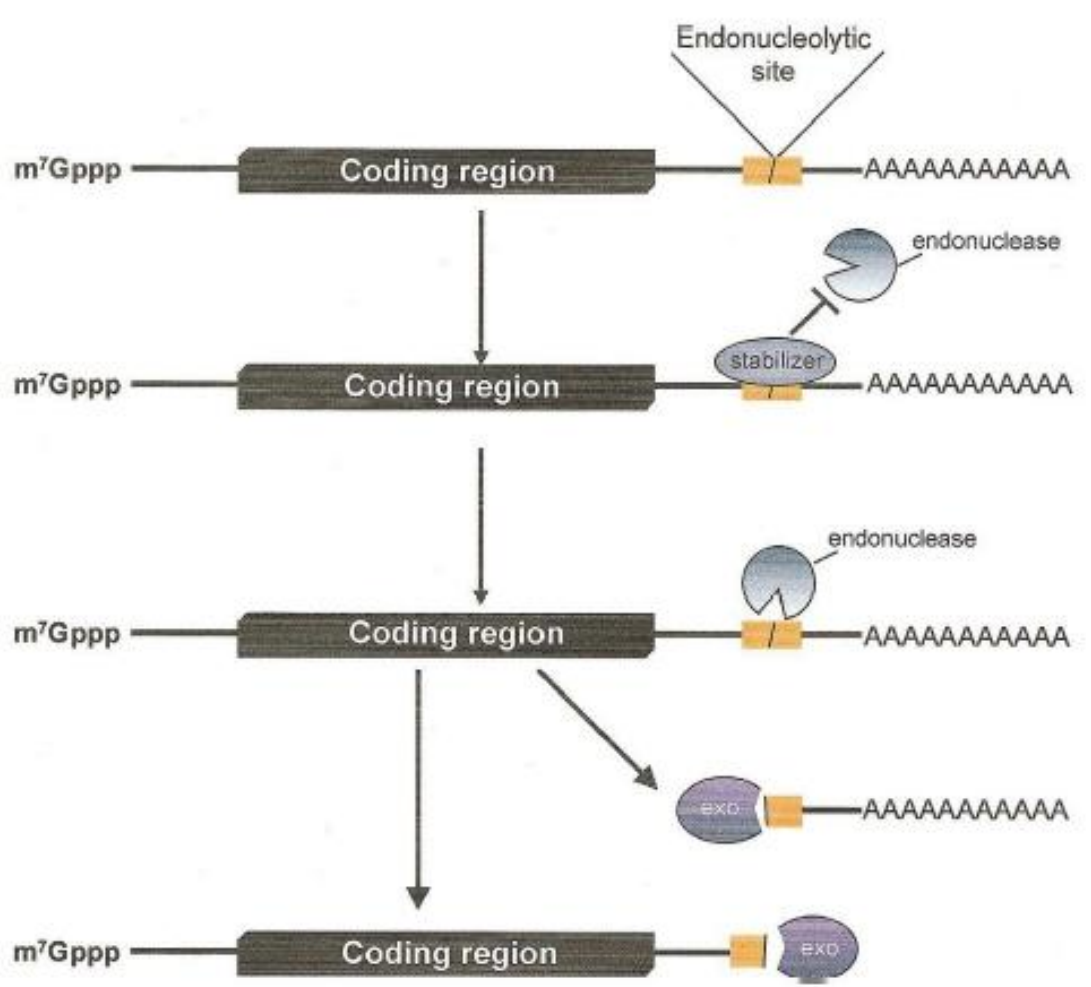
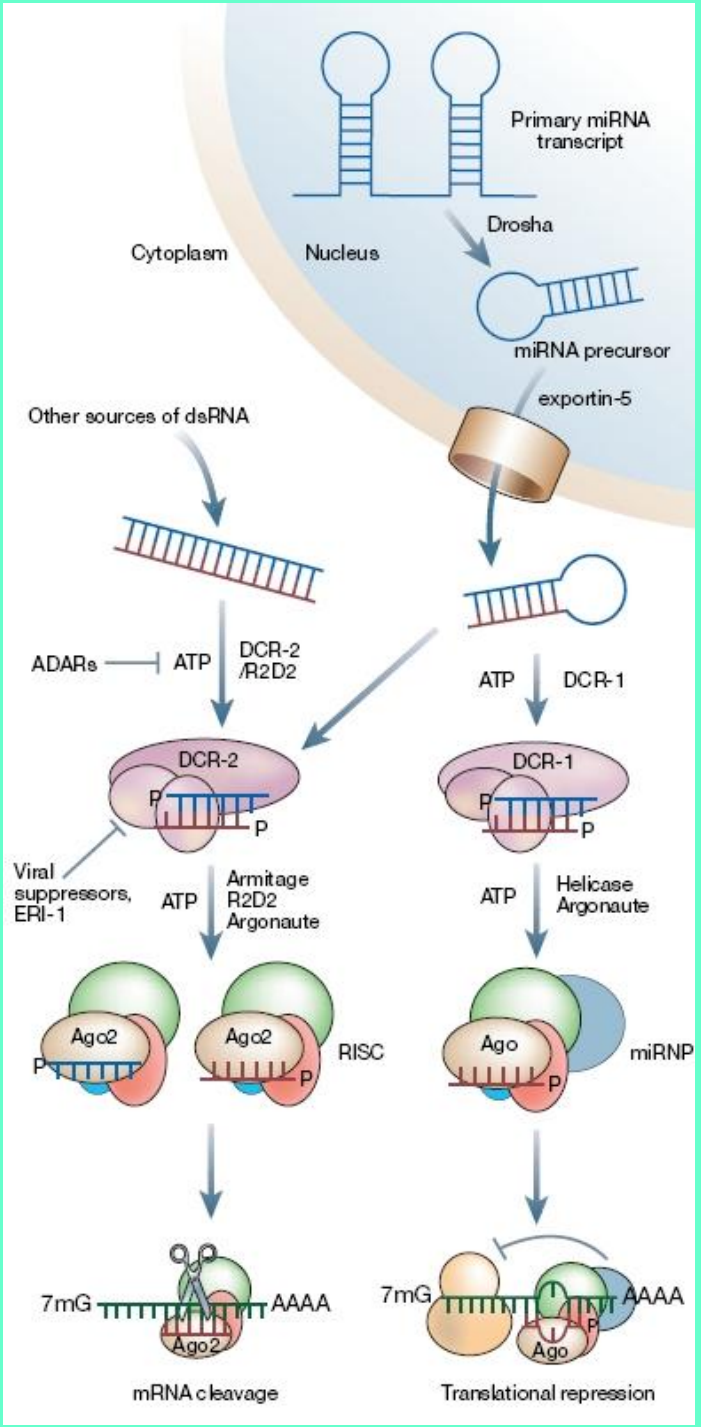
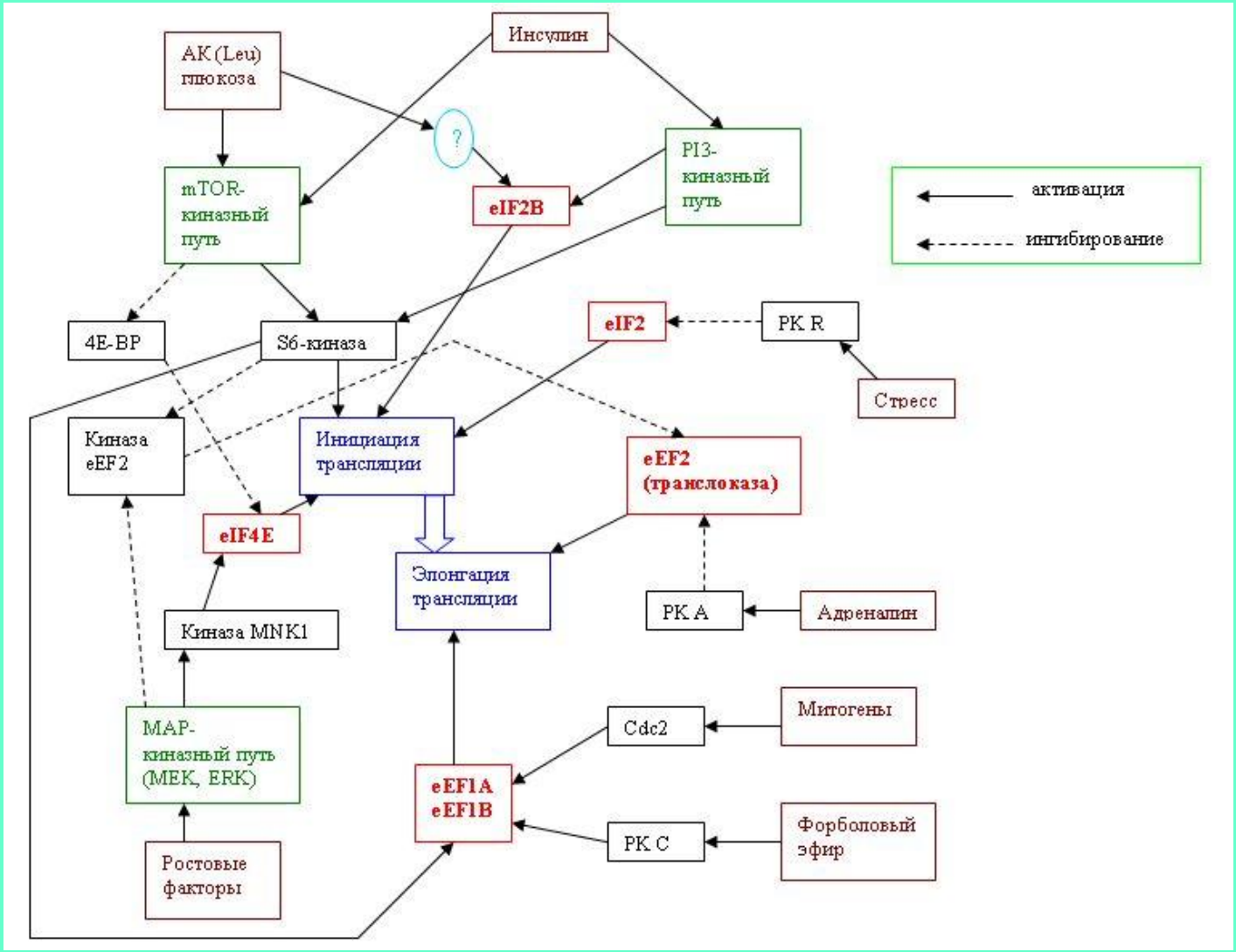


Fig. 3. Schematic diagram of a hypothetical mRNA decay pathway initiated by endonucleolytic cleavage. Some mRNAs can be cleaved internally by an endoribonuclease. This enzyme recognizes and cleaves a specific sequence found frequently in the 3' UTR of mRNA. Then, the two parts of mRNA body are accessible to be rapidly degraded by exonucleases. Interaction of an RNA-binding protein with the cleavage site can block access to endoribonuclease and so stabilizes the mRNA.

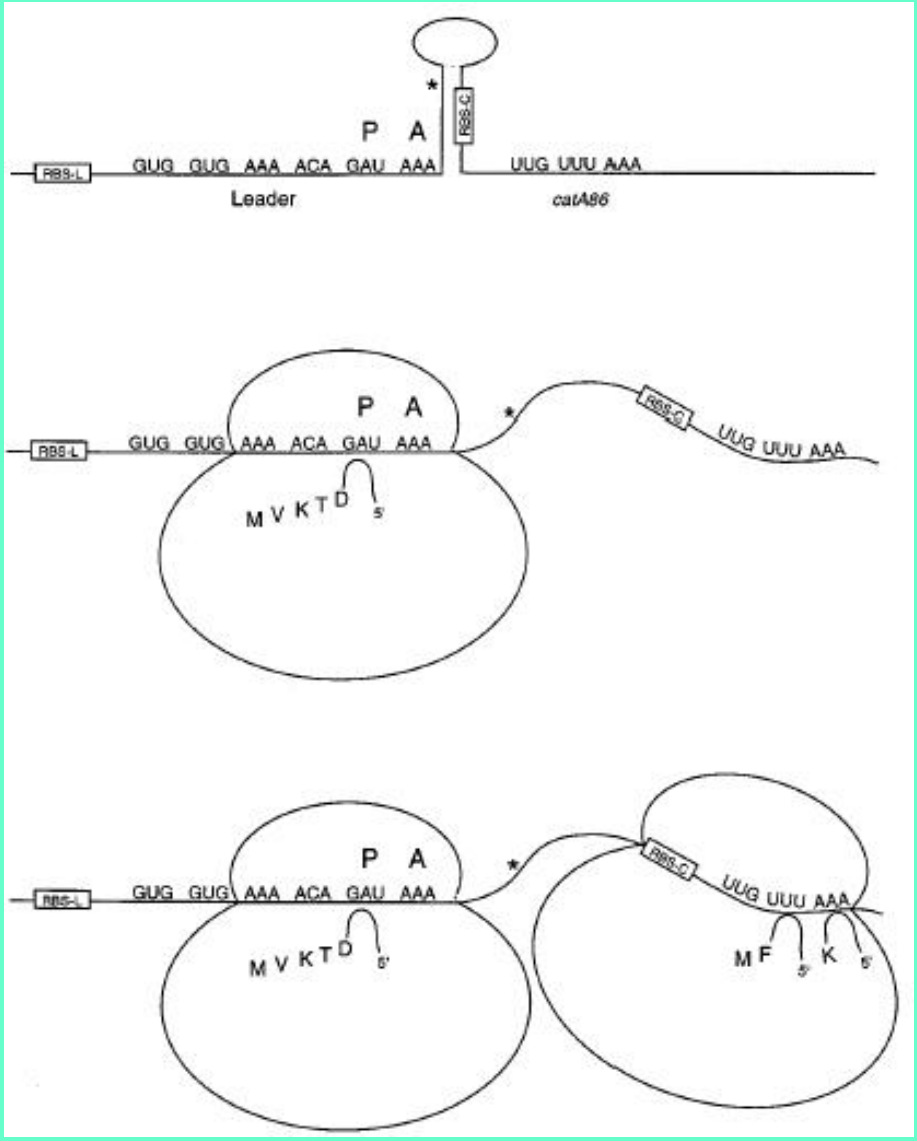
РНКi на уровне трансляции: siРНК и microРНК



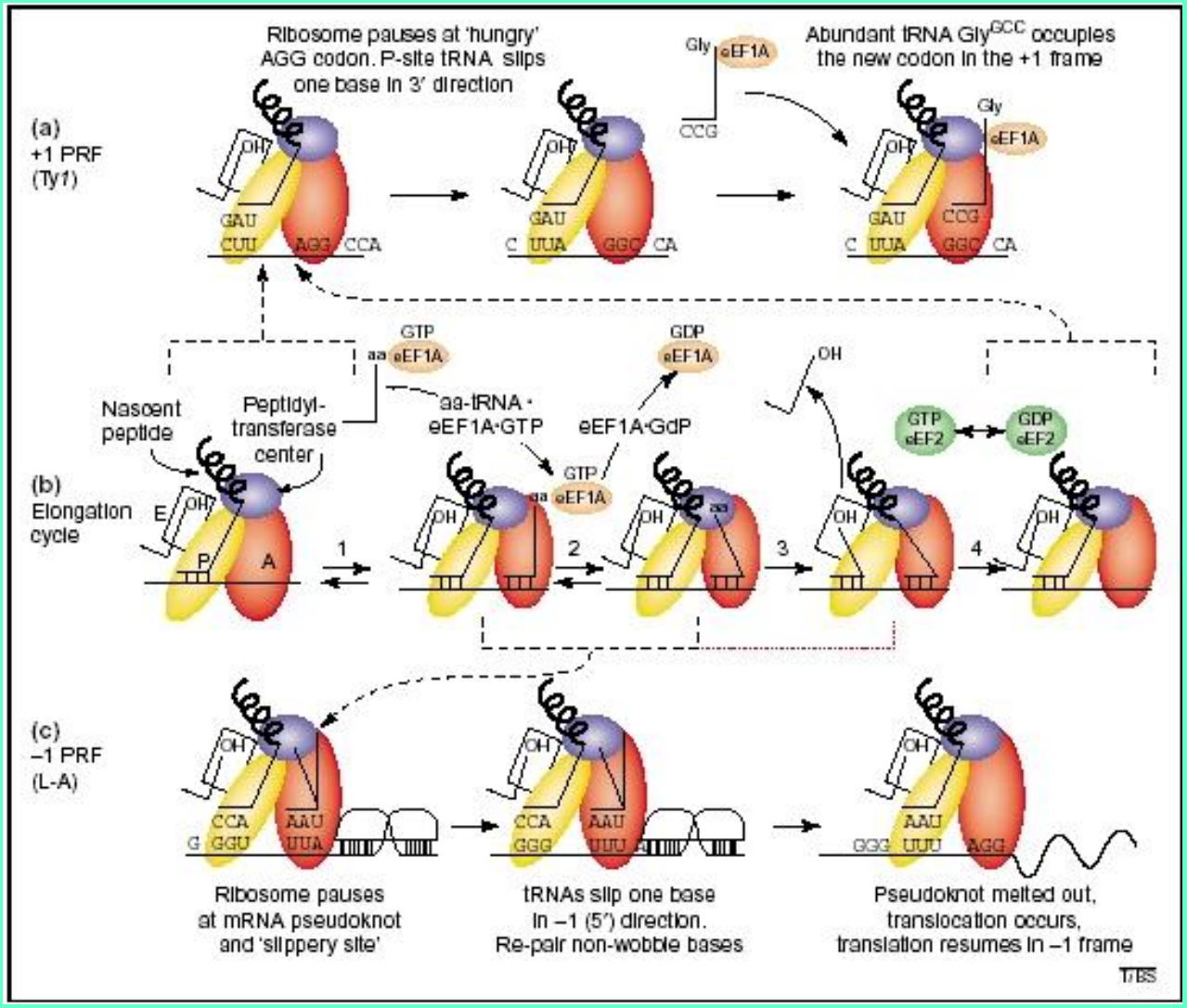
Регуляция разных этапов трансляции у эукариот



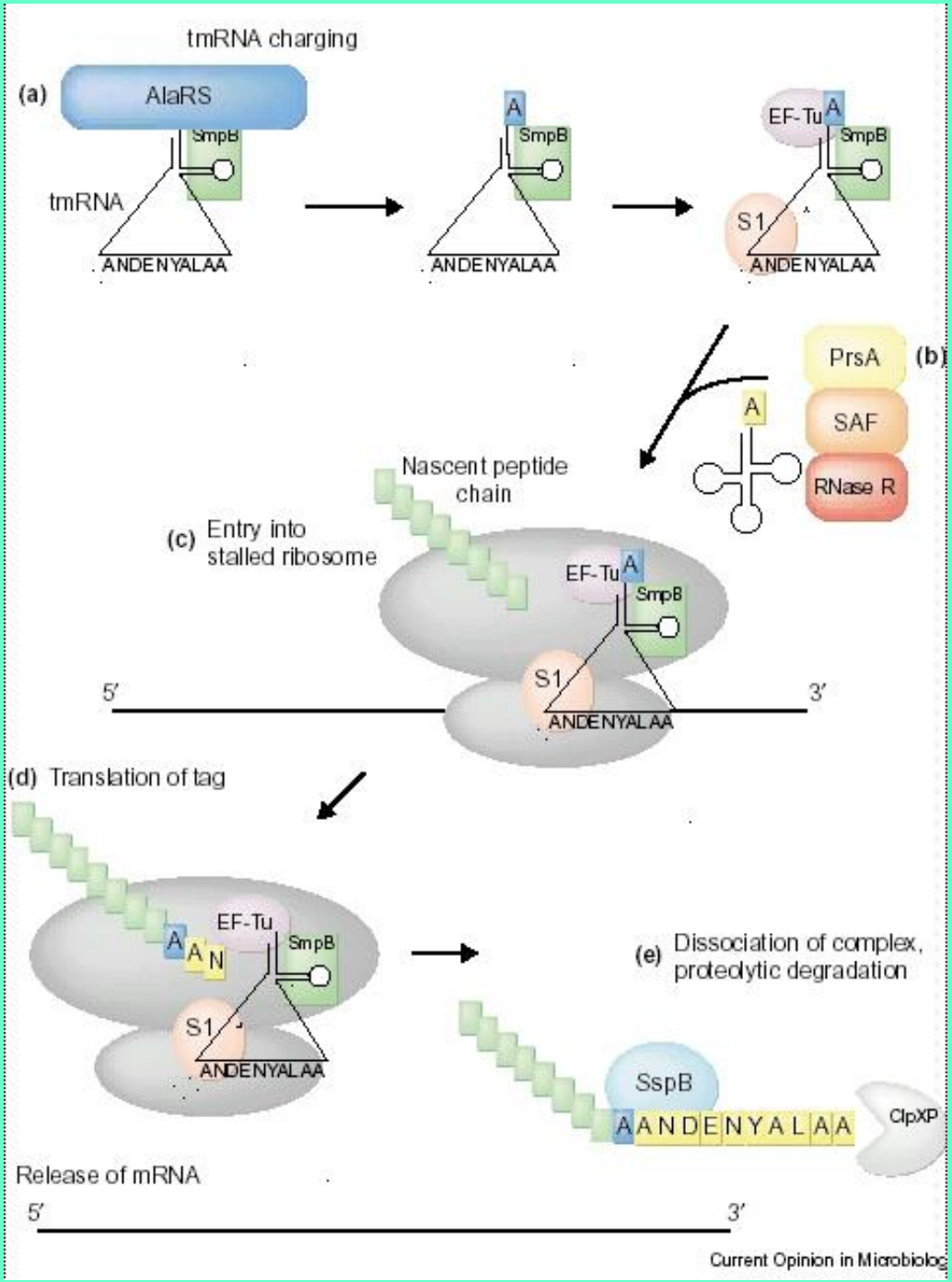
Аттенуация трансляции



Запрограммированный сдвиг рамки считывания



Транс-трансляция



Роль транс-трансляции