Protein Metabolism

Contents

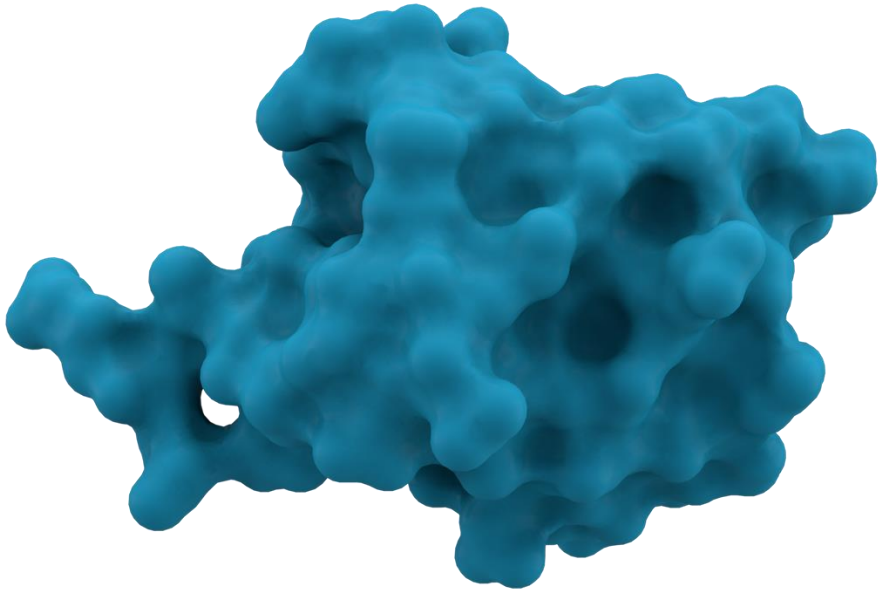
- Degradation of Proteins
- Amino Acid Degradation and Metabolic Conversion
- Biosynthesis of Amino Acids
- Protein Biosynthesis / Translation
- Central Dogma

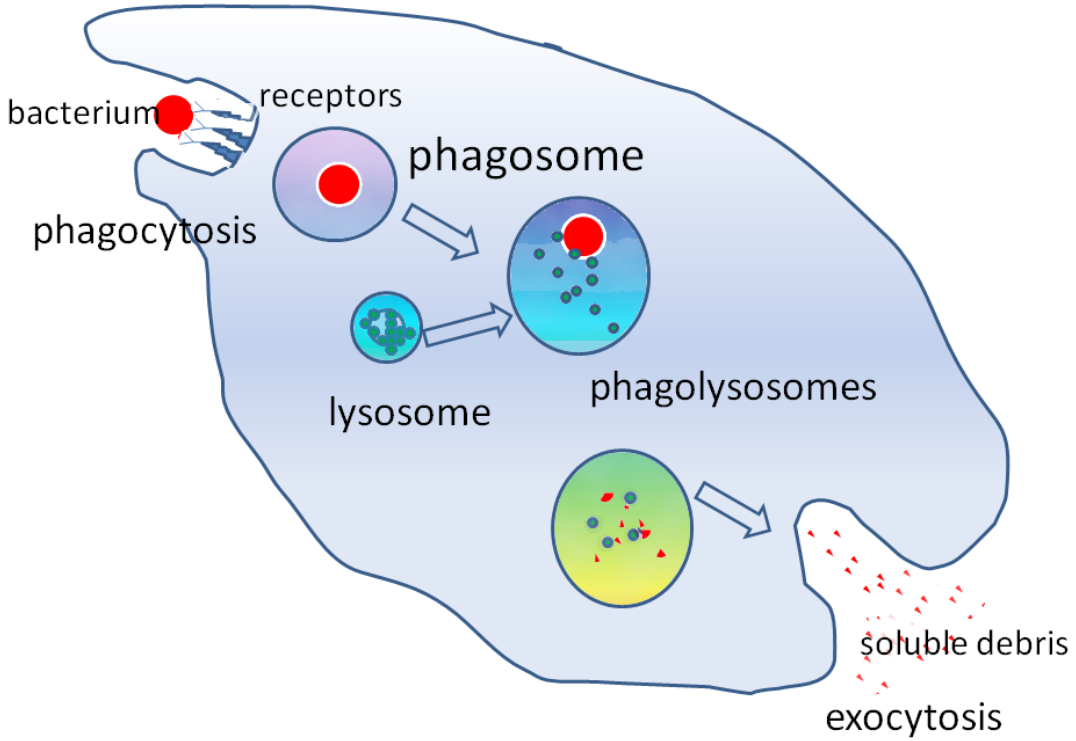
Degradation and Absorption of Exogenous Proteins

- Exogenous proteins（外源蛋白质） are digested in the gastrointestinal tract（胃肠道） into amino acids and small peptides（小肽）, then absorbed and used by tissues.
- Excess amino nitrogen is mainly converted into urea and excreted in urine（尿液）.

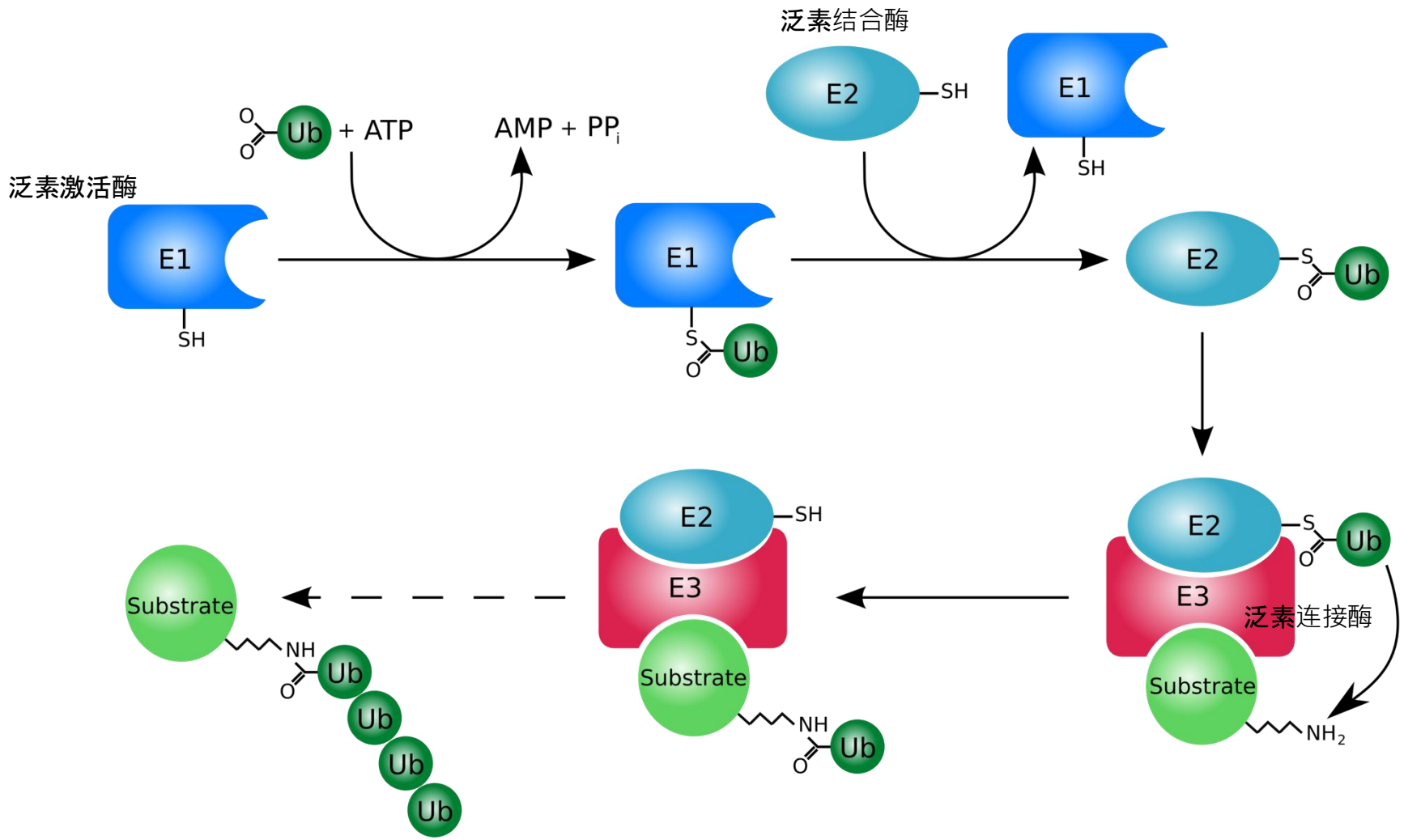
Intracellular proteins are degraded mainly by two systems

- ❖Lysosomal degradation（溶酶体降解）
- ❖Ubiquitin–proteasome system, UPS（泛素-蛋白酶体系统）





The UPS is ATP-dependent and is especially important for selective degradation of short-lived, damaged, or misfolded proteins.



Enzymes

1. Endopeptidases（肽链内切酶）

Endopeptidases, also called **proteinases（蛋白酶）**, hydrolyze peptide bonds **inside the polypeptide chain（多肽链内部的肽键）**. This converts large proteins into shorter polypeptides and oligopeptides（寡肽）.

- **Pepsin（胃蛋白酶）**
- **Trypsin（胰蛋白酶）**
- **Chymotrypsin（糜蛋白酶）**
- **Elastase（弹性蛋白酶）**

Enzymes

2. Exopeptidases（肽链外切酶）

Exopeptidases remove amino acids from the free ends（游离末端） of peptides.

- **Aminopeptidases（氨肽酶）** act at the N-terminus（N端 / 氨基末端）.
- **Carboxypeptidases（羧肽酶）** act at the C-terminus（C端 / 羧基末端）.
  - ✓ **Carboxypeptidase A（羧肽酶A）** prefers hydrophobic (疏水性) or aromatic (芳香族) residues.
  - ✓ **Carboxypeptidase B（羧肽酶B）** prefers basic residues, especially lysine（赖氨酸） and arginine（精氨酸）.

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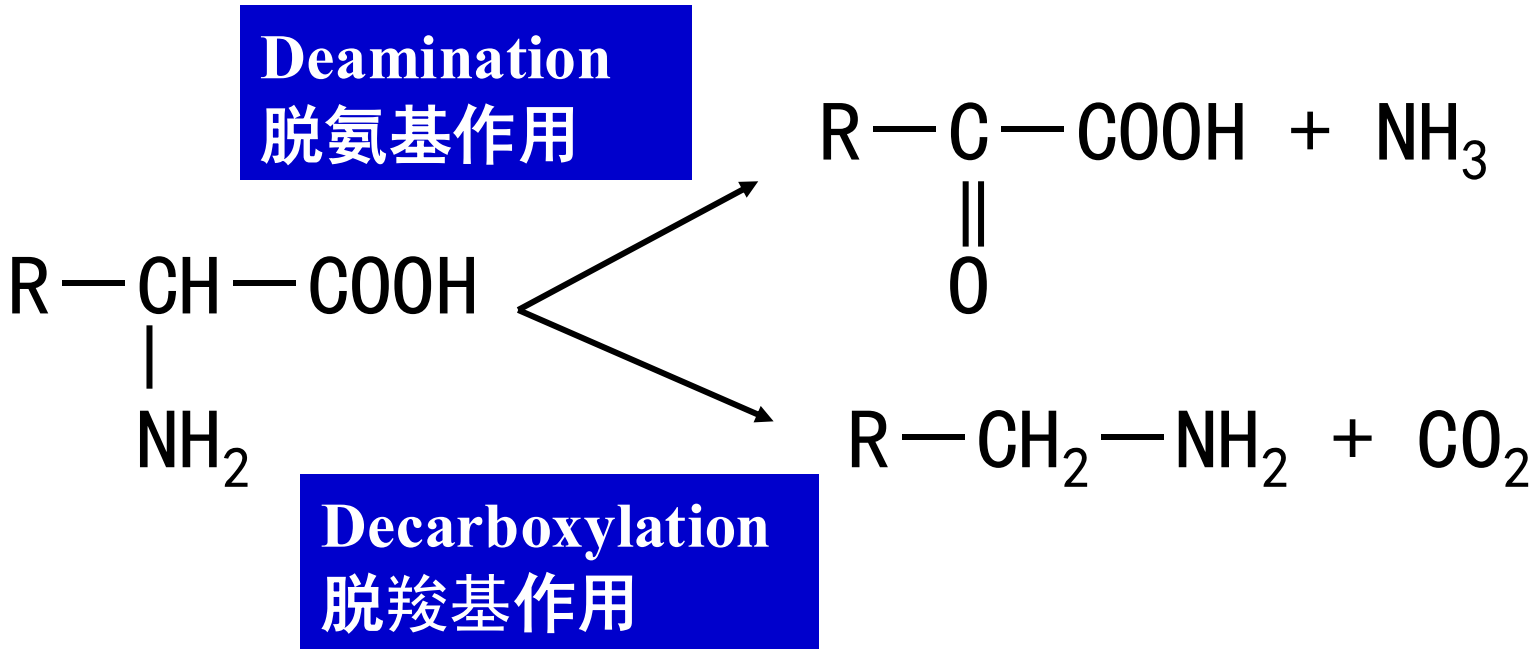
Common Metabolic Pathways of Amino Acids



Common Metabolic Pathways of Amino Acids

Deamination（脱氨基作用）

The amino group（氨基） is removed from an amino acid, forming an **α-keto acid（α-酮酸）** and **NH_4^+（铵离子）**.

- ❖ Removes amino nitrogen（氨基氮）
- ❖ Provides carbon skeletons（碳骨架） for energy metabolism
- ❖ Produces ammonia/ammonium that enters the urea cycle（尿素循环）

Decarboxylation（脱羧基作用）

The carboxyl group（羧基） is removed as CO_2（二氧化碳）, forming an **amine（胺类）**.

- ❖ Produces biologically active amines（生物活性胺）
- ❖ Examples include histamine（组胺）, GABA（γ-氨基丁酸）, dopamine（多巴胺）, and serotonin（5-羟色胺）

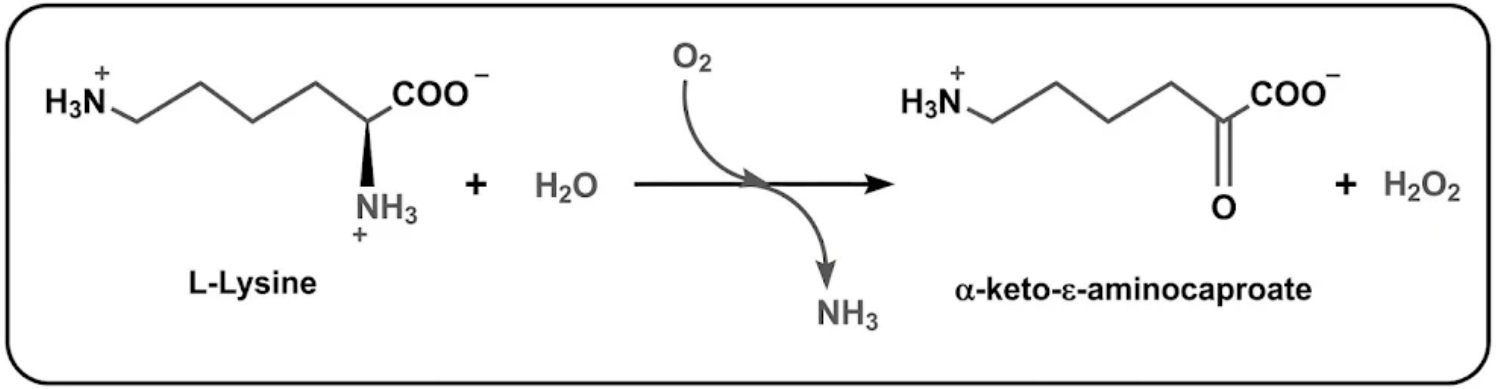
Deamination（脱氨基作用）

1. Oxidative Deamination（氧化脱氨基作用）

A. L-Amino Acid Oxidase（L-氨基酸氧化酶）

L-amino acid oxidase
(L-氨基酸氧化酶)

$$\text{L-amino acid} + O_2 + H_2O \longrightarrow \alpha\text{-keto acid} + NH_4^+ + H_2O_2$$



It is found in some animal tissues, kidney, liver, and microorganisms, but because its physiological activity is limited, it is not the central pathway of human amino acid catabolism.

Deamination（脱氨基作用）

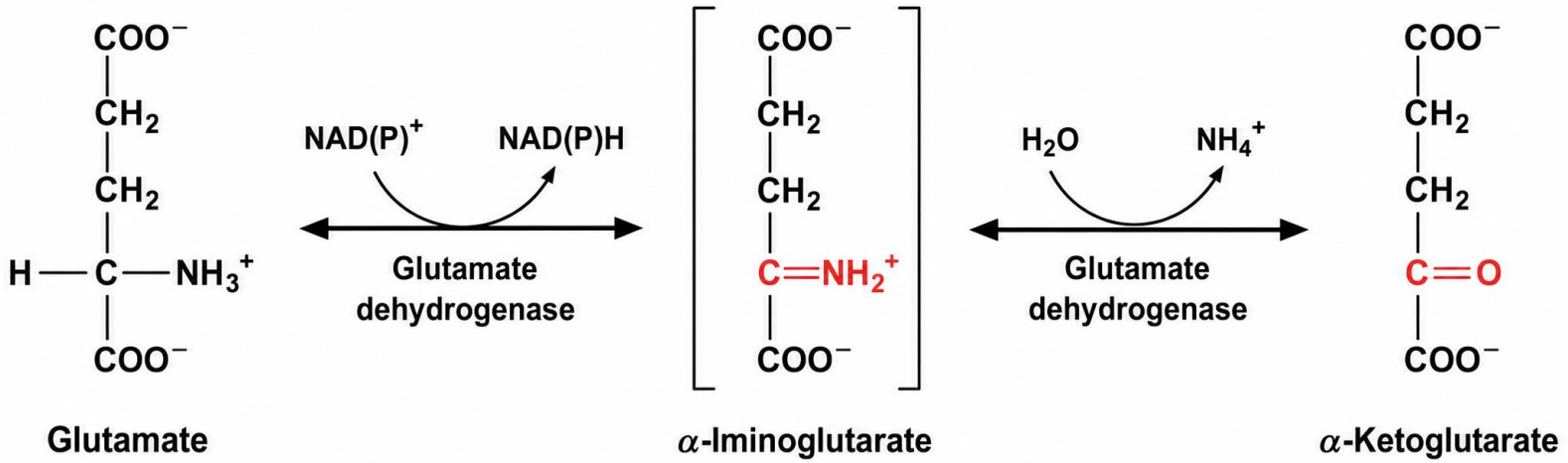
1. Oxidative Deamination（氧化脱氨基作用）

B. Glutamate Dehydrogenase（GDH, 谷氨酸脱氢酶）

This is the key oxidative deamination enzyme in human amino acid metabolism.

$$\text{Glutamate} + NAD^+ \text{ or } NADP^+ + H_2O \xrightleftharpoons{\text{GDH}} \alpha\text{-ketoglutarate} + NH_4^+ + NADH \text{ or } NADPH + H^+$$

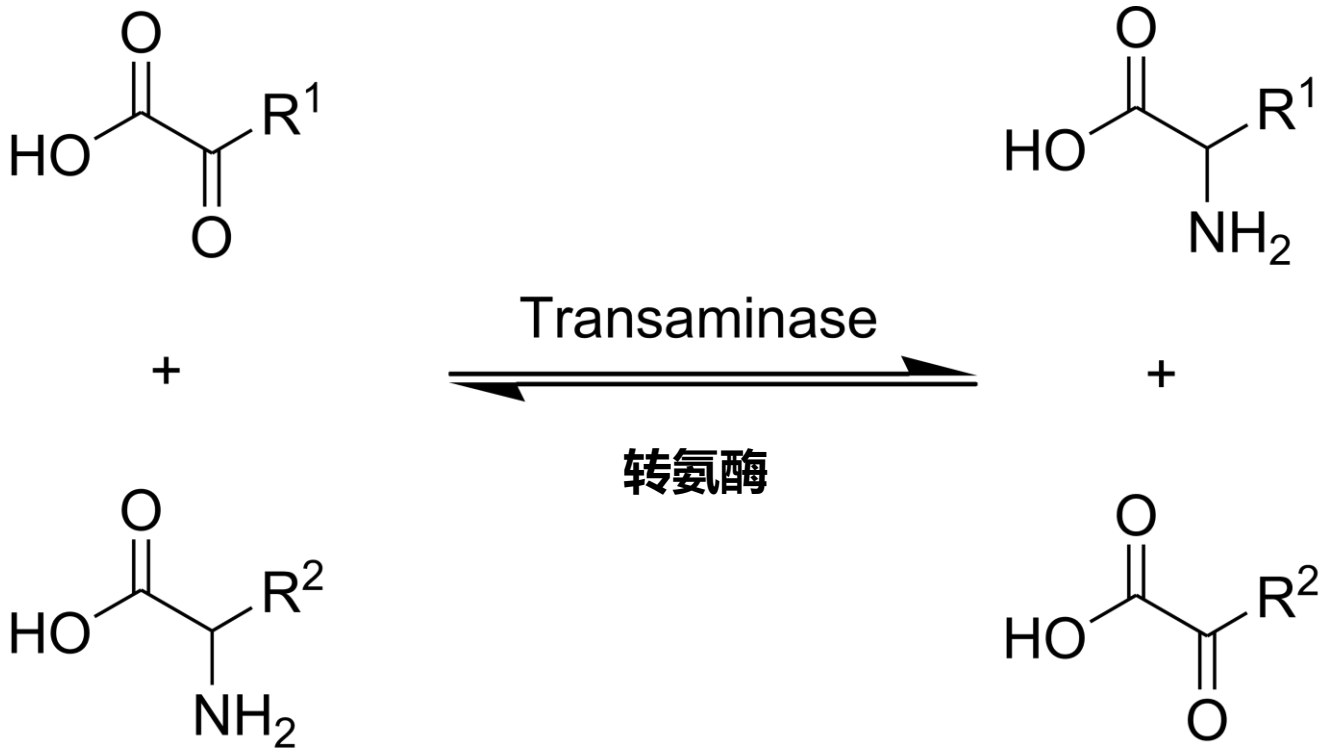
- ❖ Mainly in mitochondria
- ❖ Widely distributed in living organisms
- ❖ Uses either **NAD^+** or **$NADP^+$**
- ❖ Reversible reaction
- ❖ Allosterically regulated（变构调节）



Deamination（脱氨基作用）

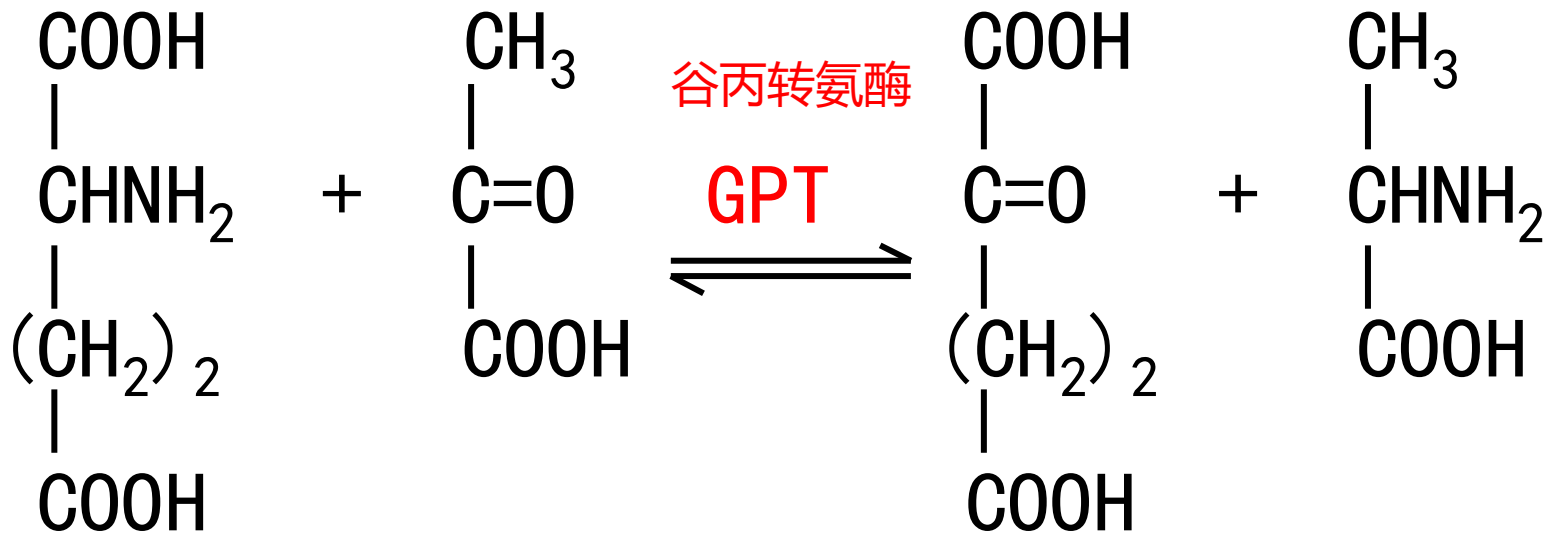
2. Transamination（转氨基作用）

Transamination is the transfer of an amino groupfrom an amino acid to an α-keto acid, forming a new amino acid and a new α-keto acid.



Deamination（脱氨基作用）

2. Transamination（转氨基作用）

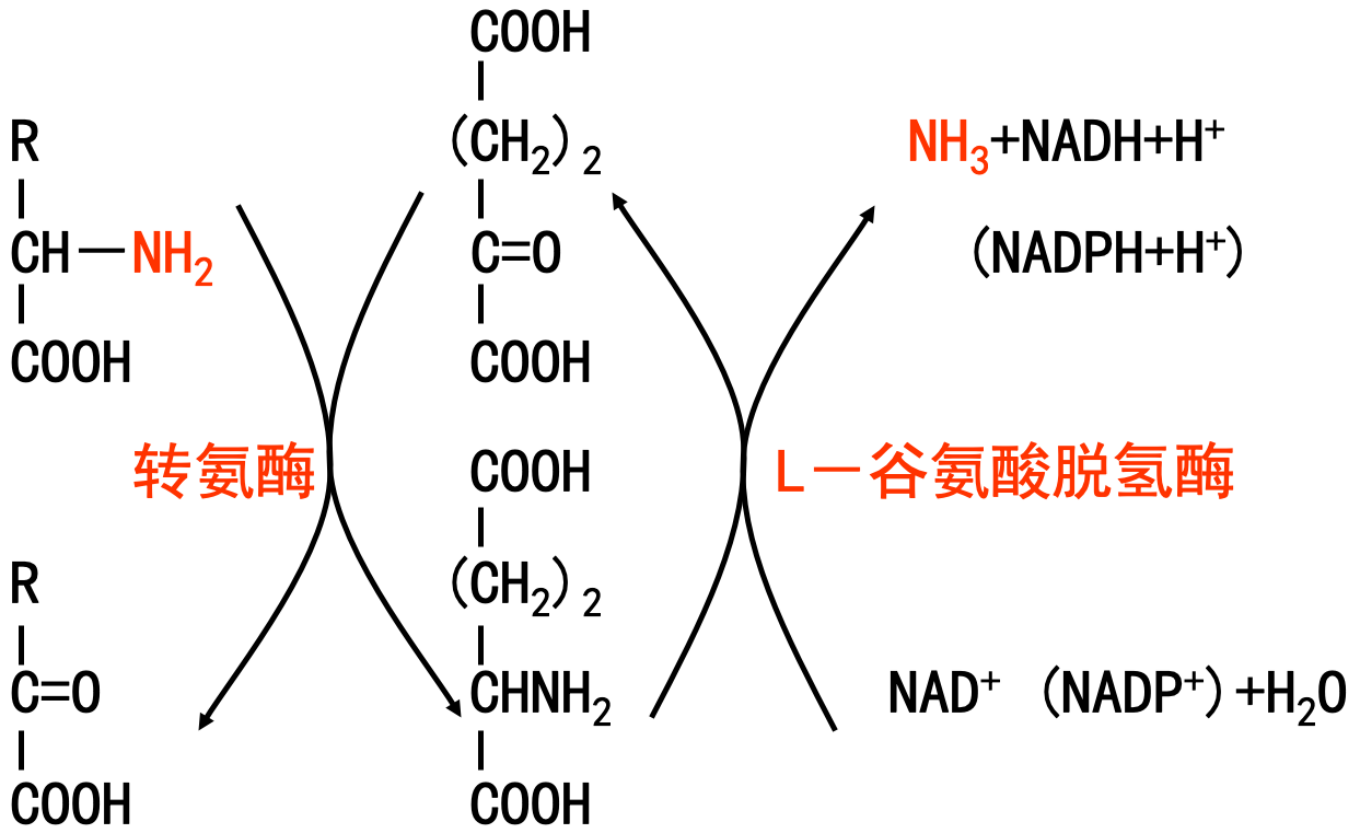


Glu　　Pyr　　α-Kg　　Ala

Most amino acids can undergo transamination, but lysine（赖氨酸）, threonine（苏氨酸）, proline（脯氨酸）, and hydroxyproline（羟脯氨酸） generally do not undergo typical transamination.

Transdeamination（转氨脱氨作用）

Combined deamination（联合脱氨基作用），also called transdeamination（转氨脱氨作用），is the combination of: Transamination（转氨基作用） and Oxidative deamination of glutamate（谷氨酸的氧化脱氨基作用）



Transdeamination（转氨脱氨作用）

Fate of Amino Nitrogen（氨基氮的代谢去向）

❖ **Reuse for amino acid synthesis（重新用于氨基酸合成）**

Amino groups are transferred between carbon skeletons by transamination（转氨基作用）.

❖ **Formation of glutamate and glutamine（生成谷氨酸和谷氨酰胺）**

Glutamate is the amino-group collection center（氨基汇集中心）; glutamine is the major nontoxic transport form of ammonia（氨的主要无毒运输形式）.

❖ **Formation and excretion of NH_4^+（形成并排泄铵离子）**

In the kidney, NH_3 binds H^+ to form NH_4^+, helping maintain acid–base balance（酸碱平衡）.

❖ **Conversion to urea（转变为尿素）**

In mammals, ammonia is detoxified mainly in the liver through the urea cycle（尿素循环 / 鸟氨酸循环） and excreted by the kidney.

Transdeamination（转氨脱氨作用）

Metabolic Fate of α-Keto Acids（α-酮酸的代谢转变）

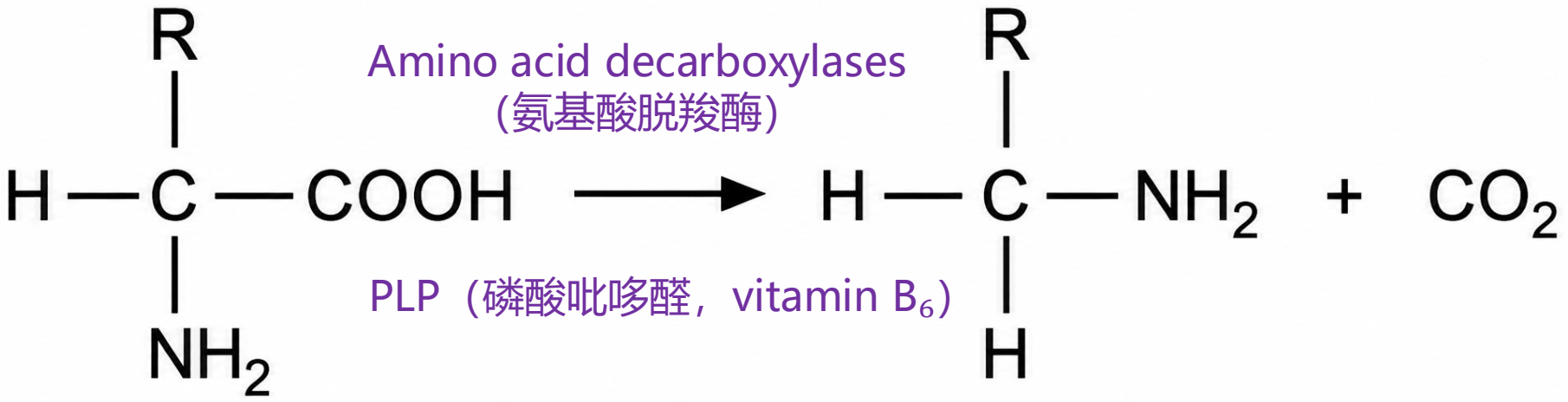
After amino acids lose their amino groups, the remaining carbon skeletons are usually converted into α-keto acids. These carbon skeletons can enter central metabolism.

- ❖ **Be reaminated to form amino acids（重新氨基化生成氨基酸）**
- ❖ **Enter gluconeogenesis or lipid metabolism（进入糖异生或脂质代谢）**
- ❖ **Be completely oxidized to CO_2 and H_2O（彻底氧化为 CO_2 和 H_2O）**

- ✓ Glucogenic amino acids（生糖氨基酸） can contribute to glucose synthesis because they are degraded into pyruvate（丙酮酸） or TCA-cycle intermediates.
- ✓ Ketogenic amino acids（生酮氨基酸） can contribute to ketone body synthesis because they are degraded into acetyl-CoA or acetoacetate.

Decarboxylation（脱羧基作用）

Decarboxylation is not the main pathway for energy metabolism of amino acids. Its major importance is the formation of biogenic amines（生物胺）, many of which act as neurotransmitters（神经递质）, hormones（激素）, or local signaling molecules.



Amino acid **Amine（胺）**

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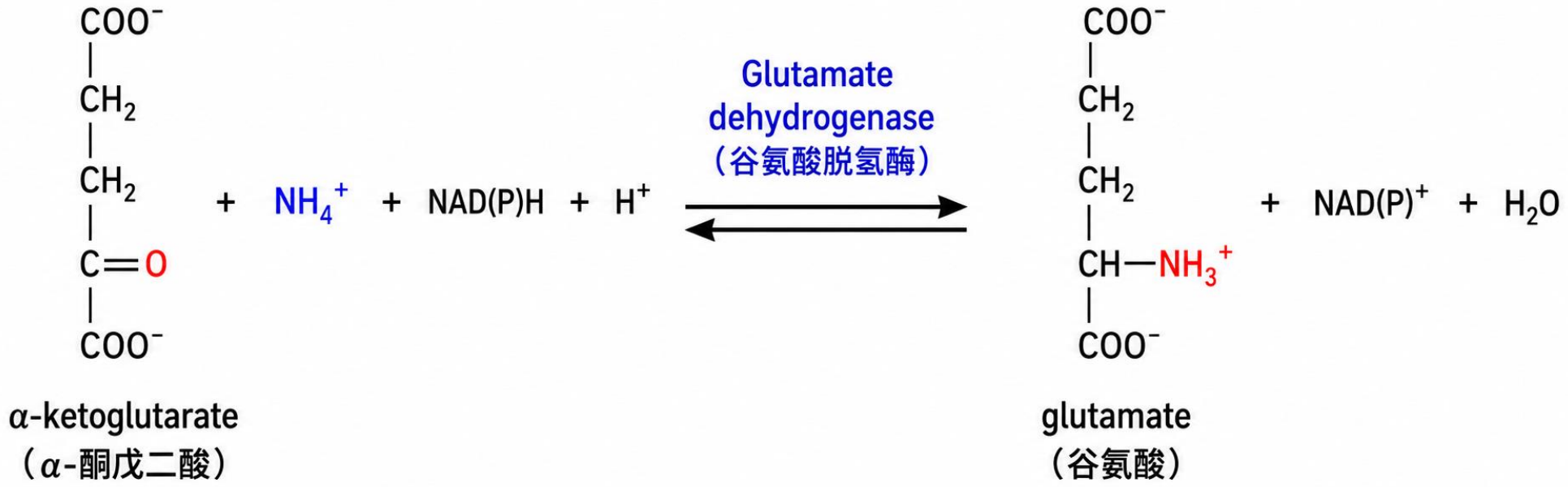
❖ Amination: Direct Incorporation of Ammonia（氨基化作用：直接氨基化）

NH_3 / NH_4^+ + α-keto acid ⟶ amino acid

A common example



Biosynthesis of Amino Acids

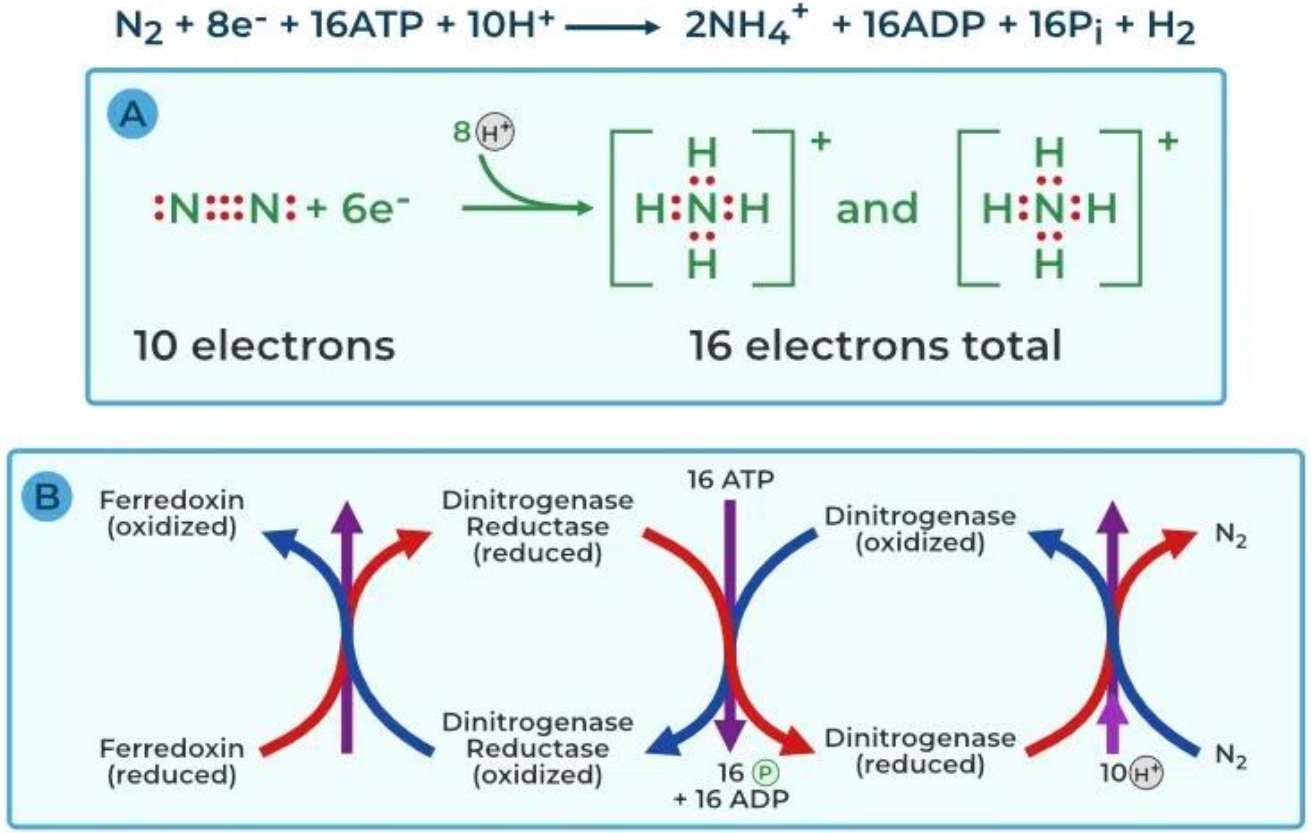
❖ Amination: Direct Incorporation of Ammonia（氨基化作用：直接氨基化）

Source of Nitrogen（氮的来源）

Biological nitrogen fixation

（生物固氮）

Some prokaryotes convert atmospheric N_2 into NH_3 through nitrogenase（固氮酶）, making nitrogen available for biosynthesis.



Biosynthesis of Amino Acids

❖ Amination: Direct Incorporation of Ammonia（氨基化作用：直接氨基化）

Biological nitrogen fixation（生物固氮）

Free-living nitrogen-fixing organisms (游离固氮生物)

These live independently in soil or water and fix nitrogen without a plant host.

Examples:

- **Azotobacter（固氮菌属）**
- **Clostridium（梭菌属）**
- **Some cyanobacteria（蓝细菌）**

Symbiotic nitrogen-fixing organisms (共生固氮生物)

These live in association with host plants, especially legumes（豆科植物）.

Examples:

- **Rhizobium（根瘤菌） in root nodules**
- **Bradyrhizobium（慢生根瘤菌）**

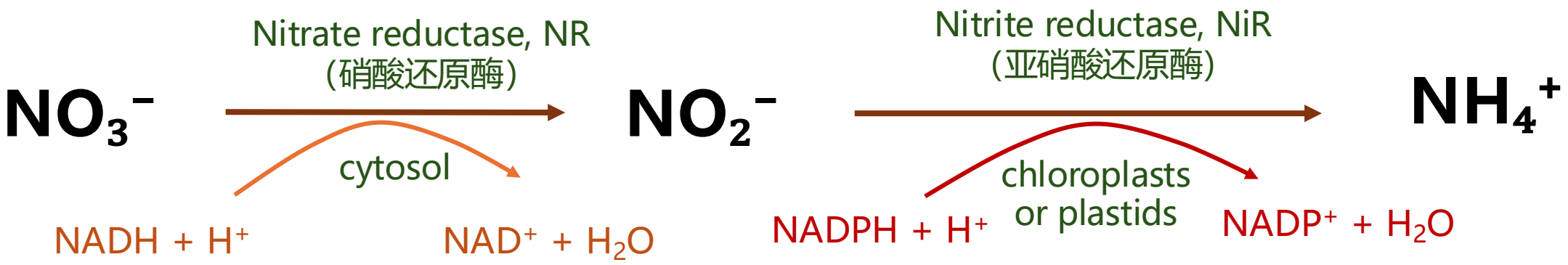
Biosynthesis of Amino Acids

❖ Amination: Direct Incorporation of Ammonia（氨基化作用：直接氨基化）

Source of Nitrogen（氮的来源）

Nitrate Reduction in Plants（植物体内硝酸盐的还原作用）

In plants, nitrogen can enter amino acid biosynthesis mainly in the reduced form NH_4^+. However, the major inorganic nitrogen source absorbed by many plants from soil is nitrate (NO_3^-）.



Biosynthesis of Amino Acids

❖ Amination: Direct Incorporation of Ammonia（氨基化作用：直接氨基化）

Source of Nitrogen（氮的来源）

Catabolic Production of Ammonia（分解代谢产生氨）

Ammonia/ammonium（NH_3 / NH_4^+） can be produced during the degradation of nitrogen-containing compounds, especially:

- ❖ **Amino acid deamination（氨基酸脱氨基作用）.**
- ❖ **Amide hydrolysis（酰胺水解）.** Glutamine（谷氨酰胺）and asparagine（天冬酰胺）can release NH_4^+ through glutaminase（谷氨酰胺酶）and asparaginase（天冬酰胺酶）.
- ❖ **Nucleotide degradation（核苷酸降解）.** Purine（嘌呤）and pyrimidine（嘧啶）degradation can release amino nitrogen.
- ❖ **Urea hydrolysis by urease（脲酶水解尿素）.** In plants and many microorganisms, urease（脲酶）hydrolyzes urea to release NH_3/NH_4^+.

Biosynthesis of Amino Acids

❖ Amination: Direct Incorporation of Ammonia（氨基化作用：直接氨基化）

Sources of α-Keto Acids（α-酮酸的来源）

Carbohydrate metabolism
(糖代谢)

- ❖ Pyruvate, Pyr
- ❖ Oxaloacetate, OAA
- ❖ α-Ketoglutarate, α-KG

Glyoxylate cycle
(乙醛酸循环)

- ❖ Glyoxylate can be converted to glycine（甘氨酸）
- ❖ Important in plants and microorganisms

Lipid metabolism
(脂类代谢)

- ❖ Glycerol（甘油） via carbohydrate metabolism
- ❖ Odd-chain fatty acids can form succinyl-CoA（琥珀酰辅酶A）
- ❖ In plants and microorganisms, acetyl-CoA can enter the glyoxylate cycle

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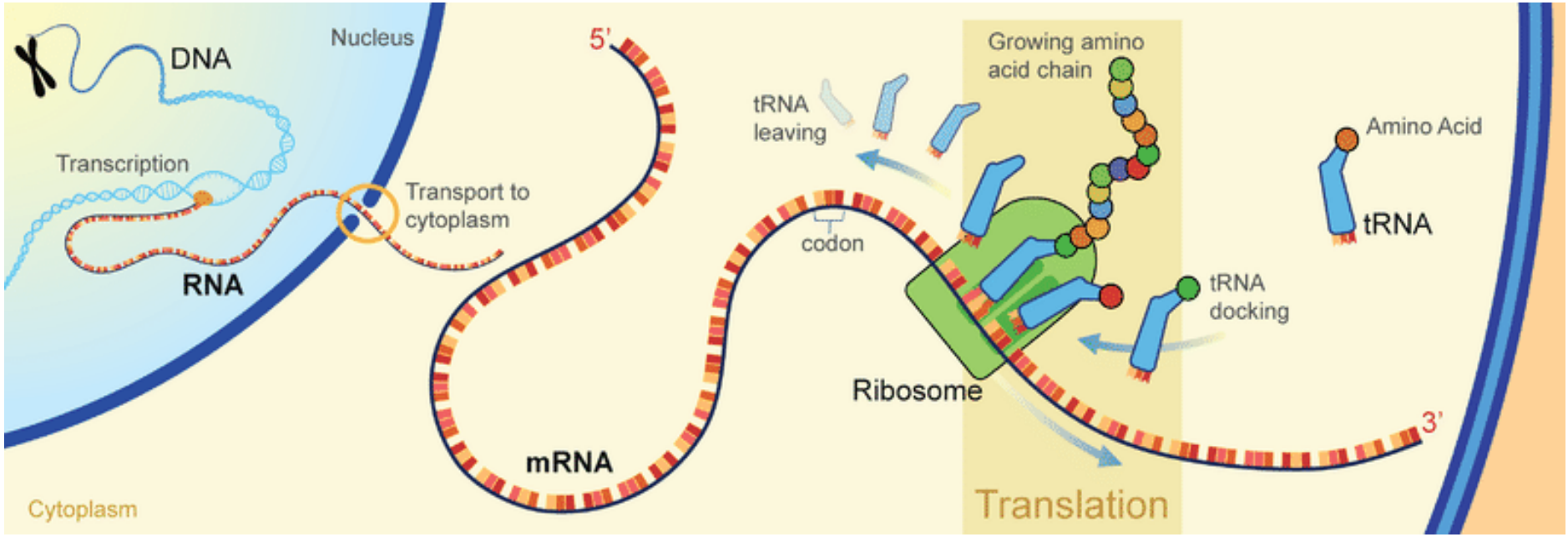
Protein Biosynthesis / Translation

Translation (翻译) is mRNA-directed protein synthesis on ribosomes.

During translation, the ribosome reads the mRNA in the 5′ → 3′ direction. According to the codon sequence（密码子序列） of mRNA, specific amino acids are added one by one to the growing polypeptide chain（正在延长的多肽链）.



Protein Biosynthesis / Translation

❖ **Location of Translation（翻译发生的场所）** **in the cytosol**

In prokaryotes（原核生物）

In the cytoplasm on 70S ribosomes. As prokaryotes have no nucleus, transcription and translation can be coupled

In eukaryotes（真核生物）

- ❖ Proteins for the cytosol, nucleus, mitochondria, and peroxisomes are usually synthesized on free ribosomes.
- ❖ Secreted proteins（分泌蛋白）, membrane proteins（膜蛋白）, and lysosomal proteins（溶酶体蛋白） are usually synthesized on RER-bound ribosomes（粗面内质网结合核糖体）.

Protein Biosynthesis / Translation

❖ Main Components Required for Translation

- ❖ **mRNA** provides the codon sequence（密码子序列）.
- ❖ **Ribosome** provides the platform for decoding and peptide-bond formation（肽键形成）.
- ❖ **tRNA** carries specific amino acids and recognizes codons through anticodons（反密码子）.
- ❖ **Amino acids**（氨基酸）are building blocks of the polypeptide chain.
- ❖ **Aminoacyl-tRNA synthetases**（氨酰-tRNA合成酶）attach each amino acid to its correct tRNA.
- ❖ **Translation factors**（翻译因子）include Initiation factors（起始因子）, elongation factors（延长因子）, and release factors（释放因子）.
- ❖ Energy: **ATP** is used for tRNA charging; **GTP** is used during initiation, elongation, and termination.

Protein Biosynthesis / Translation

❖ Codon（密码子）

Codon: a triplet of nucleotides on mRNA that encodes one amino acid or a stop signal. 密码子是mRNA上编码一种氨基酸或终止信号的三个连续核苷酸。

❖ Genetic code（遗传密码）

The correspondence between mRNA codons and amino acids or stop signals during protein synthesis. mRNA密码子与氨基酸或终止信号之间的对应规则。

Nobel Prize in Physiology or Medicine 1968

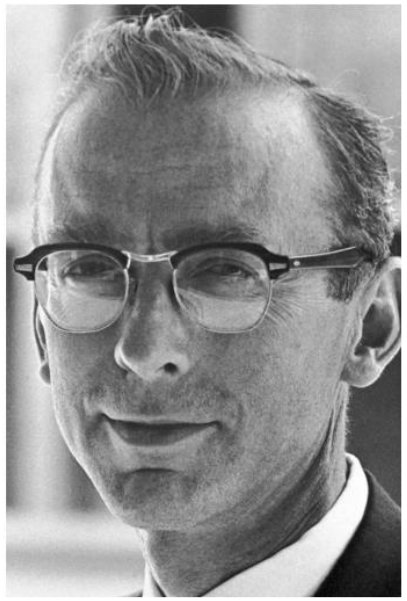


Photo from the Nobel Foundation archive.

Robert W. Holley

Prize share: 1/3



Photo: Harold Hone. Nobel Foundation archive

Har Gobind Khorana

Prize share: 1/3

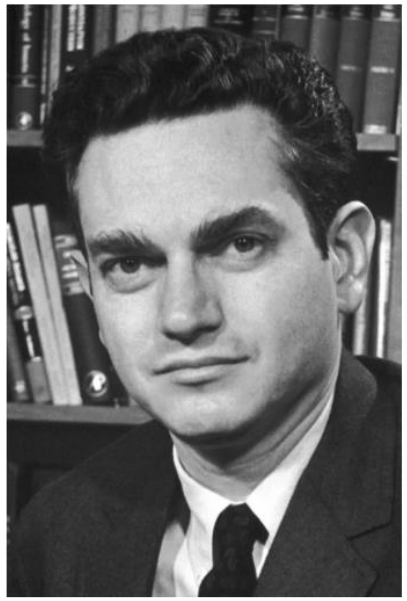


Photo from the Nobel Foundation archive.

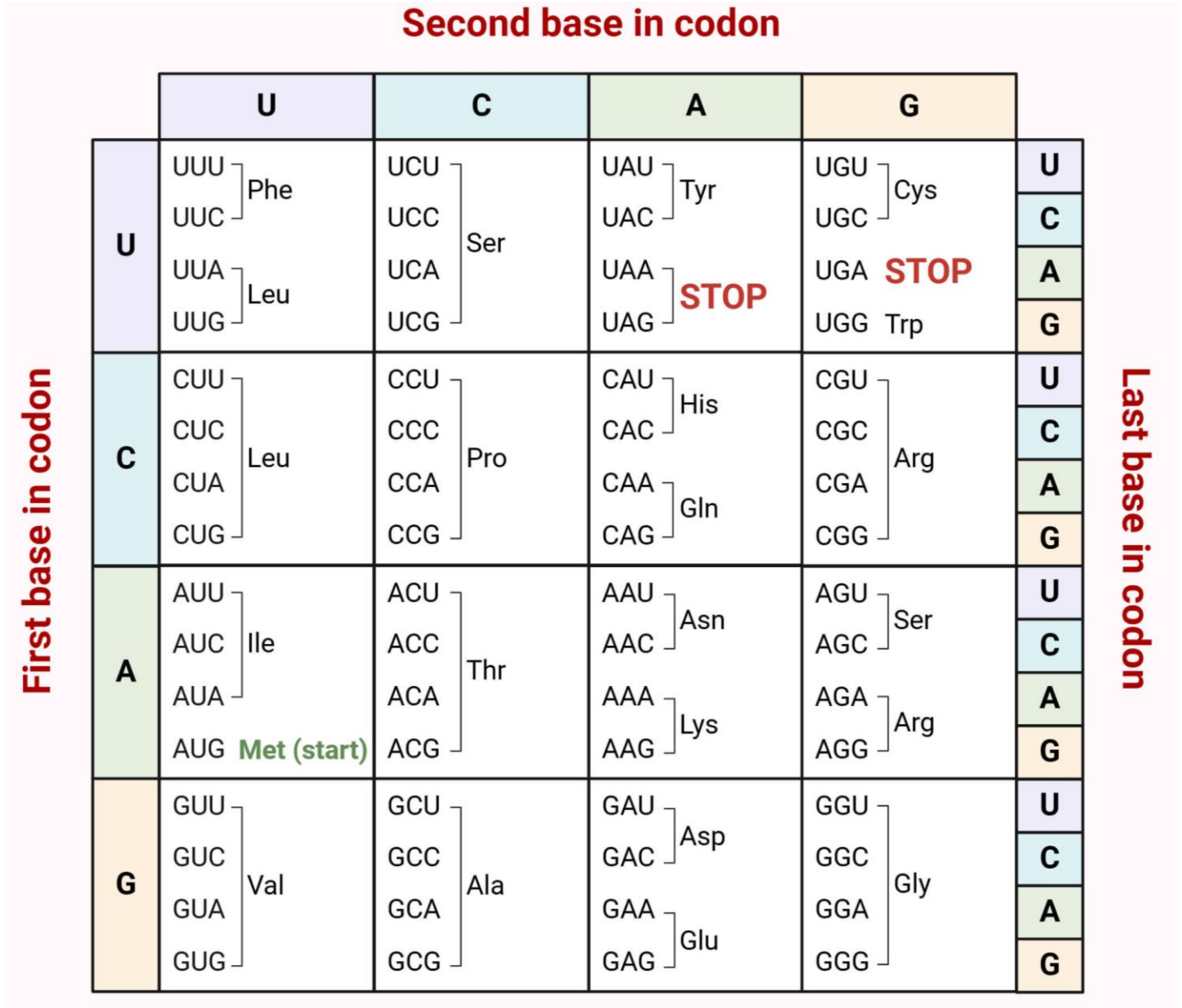
Marshall W. Nirenberg

Prize share: 1/3

From 1961 to 1966, Nirenberg, Khorana, Holley and others helped decipher the genetic code, establishing the correspondence between the 64 codons and amino acids or stop signals. They received the 1968 Nobel Prize in Physiology or Medicine.

Protein Biosynthesis / Translation

Codon Table（遗传密码子表）



First base	U	C	A	G	Last base
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
	UUA Leu	UCA Ser	UAA STOP	UGA STOP	A
	UUG Leu	UCG Ser	UAG STOP	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC Leu	CCC Pro	CAC His	CGC Arg	C
	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
	AUG Met (start)	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

- ❖ 61 sense codons（有义密码子）encode amino acids.
- ❖ 3 stop codons（终止密码子）terminate translation: **UAA**, **UAG**, **UGA**

AUG usually serves as the start codon and encodes:

- ❖ Methionine, **Met** in eukaryotes
- ❖ N-formylmethionine, **fMet**（N-甲酰甲硫氨酸） in bacteria and organelles

Protein Biosynthesis / Translation

Key Properties of the Genetic Code

1. **Triplet（三联体）**: three bases form one codon.
2. **read 5′→3′,** and the protein is synthesized **N→C.**
3. **Degenerate（简并性）**: most amino acids have multiple codons.
4. **Specific（专一性）**: each codon specifies only one amino acid or stop signal.
5. **Non-overlapping and comma-less（不重叠、无标点）**: codons are read continuously.
6. **Nearly universal（通用性）**: most organisms use the same code, with minor exceptions.
7. **Wobble（摇摆性）**: the third codon base often pairs flexibly with tRNA anticodons.

Protein Biosynthesis / Translation

Degeneracy of the Genetic Code（遗传密码的简并性）

Most amino acids are encoded by more than one codon. This property is called degeneracy.

Only two amino acids have a single codon:

- **Methionine, Met（甲硫氨酸）: AUG**
- **Tryptophan, Trp（色氨酸）: UGG**

Examples of synonymous codons（同义密码子）:

- **Glu（谷氨酸）**: GAA, GAG
- **Asp（天冬氨酸）**: GAU, GAC
- **Leu（亮氨酸）**: UUA, UUG, CUU, CUC, CUA, CUG

Protein Biosynthesis / Translation

Degeneracy of the Genetic Code（遗传密码的简并性）

Synonymous codons（同义密码子） encode the same amino acid, but they are not always used equally. Different organisms, tissues, or genes may prefer different synonymous codons. This is called codon usage bias（密码子使用偏好）.

Codon usage bias is related to:

- Evolutionary history（进化历史）
- Genome GC content（基因组GC含量）
- tRNA abundance（tRNA丰度）
- Translational efficiency and accuracy（翻译效率与准确性）
- Gene expression level（基因表达水平）

Protein Biosynthesis / Translation

Wobble of Codons（密码子的摆动性 / 变偶性）

The specificity of codon recognition is mainly determined by the **first two bases** of the codon. **The third base** often allows more flexible pairing with the first base of the tRNA anticodon（反密码子第一位碱基）. This flexibility is called **wobble**.

Valine（缬氨酸） is encoded by four codons: GUU, GUC, GUA, GUG. These codons share the first two bases, GU, and differ only at the third base U, C, A, or G

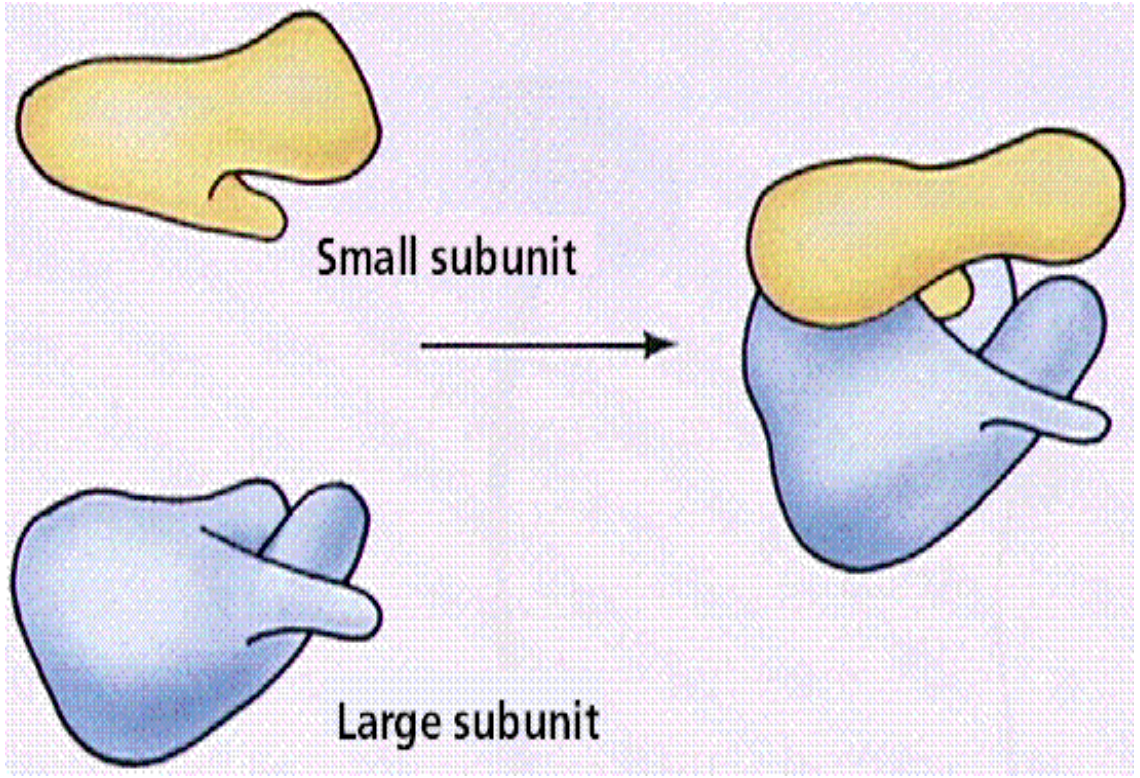
But not always…

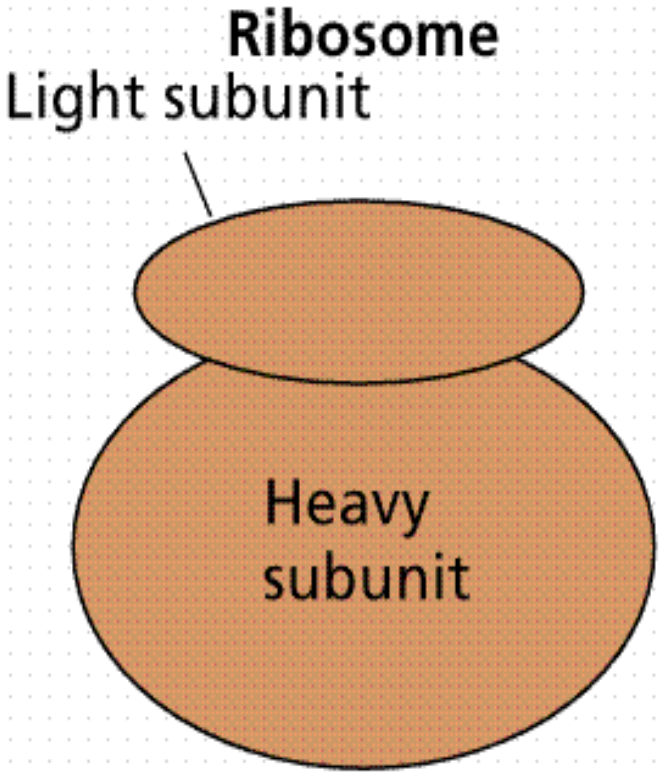
Leucine（亮氨酸）: UUA, UUG, CUU, CUC, CUA, CUG

Protein Biosynthesis / Translation

❖ Ribosome, the Site of Protein Synthesis

Ribosomes are composed mainly of rRNA and ribosomal proteins; rRNA forms the structural and catalytic core of the ribosome.





Protein Biosynthesis / Translation

❖ Ribosome, the Site of Protein Synthesis

- ❖ **Small subunit（小亚基）**: recognizes mRNA codons and tRNA anticodons（识别密码子和反密码子）
- ❖ **Large subunit（大亚基）**: catalyzes peptide-bond formation（催化肽键形成）

The ribosome contains three tRNA-binding sites:

- ❖ **A site（A位点 / 氨酰位点）**: incoming aminoacyl-tRNA
- ❖ **P site（P位点 / 肽酰位点）**: growing peptidyl-tRNA
- ❖ **E site（E位点 / 出口位点）**: exiting deacylated tRNA

Protein Biosynthesis / Translation

❖ tRNA, The Adaptor for Amino Acid Transfer

tRNA links mRNA codons with amino acids during translation.

- **Carries amino acids（携带氨基酸）：**Amino acids attach to the **3’ CCA end**.
- **Recognizes codons（识别密码子）：**The anticodon（反密码子） pairs with the mRNA codon.
- **Delivers amino acids to the ribosome（将氨基酸送入核糖体）：**tRNA brings amino acids to the correct position during translation.
- **Ensures specificity through aminoacyl-tRNA synthetase（通过氨酰-tRNA合成酶保证专一性）：**Each aminoacyl-tRNA synthetase attaches the correct amino acid to the correct tRNA.

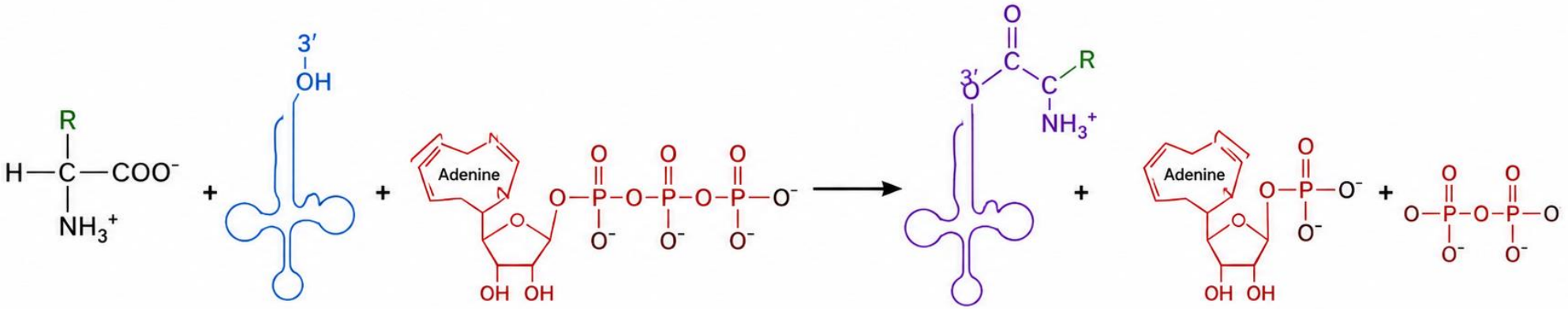
Protein Biosynthesis / Translation

❖ Aminoacyl-tRNA Formation（氨酰-tRNA的形成）

Amino acid + tRNA + ATP ⟶ aminoacyl-tRNA + AMP + PPi

This reaction is catalyzed by:

Aminoacyl-tRNA synthetase
（氨酰-tRNA合成酶）

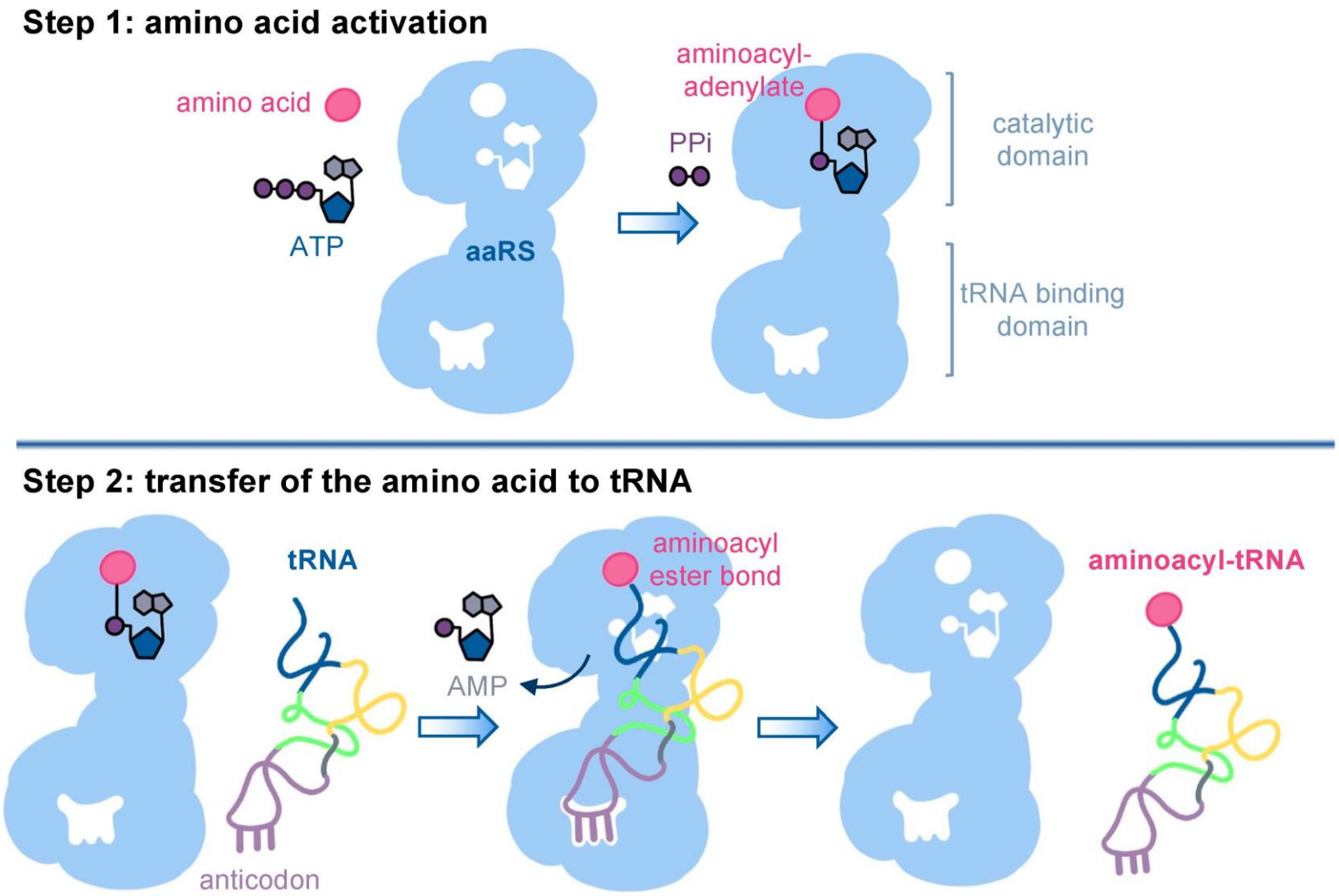


Amino acid（氨基酸） | tRNA（tRNA） | ATP（ATP） | aminoacyl-tRNA（氨酰-tRNA） | AMP（AMP） | PPi（PPi）

The product, aminoacyl-tRNA（氨酰-tRNA）, carries an activated amino acid for protein synthesis.

Protein Biosynthesis / Translation

❖ Aminoacyl-tRNA Formation（氨酰-tRNA的形成）



氨酰-tRNA 合成酶具有很强的底物识别能力，部分酶还具有校对功能。

Protein Biosynthesis / Translation

❖ Main Enzymes and Factors in Translation（主要酶系及辅助因子）

Enzymes / catalytic activities

- ❖ Aminoacyl-tRNA synthetase（氨酰-tRNA合成酶）
- ❖ Peptidyl transferase activity（肽酰转移酶活性）

Translation factors

- ❖ Initiation factors, IFs / eIFs（起始因子）, help assemble the initiation complex.
- ❖ Elongation factors, EFs / eEFs（延长因子）, deliver aminoacyl-tRNA and promote translocation.
- ❖ Release factors, RFs / eRFs（释放因子）, recognize stop codons and release the completed polypeptide.

Energy and ions

- ❖ ATP for amino acid activation
- ❖ GTP for initiation, elongation, translocation, and termination
- ❖ K^+ and Mg^{2+}（K^+和Mg^{2+}） for ribosome function

Process of Translation

1. Initiation（起始）
2. Elongation（延长）
3. Termination and recycling（终止与核糖体循环）

Process of Translation

Step 1. Initiation（翻译起始）

Initiation assembles the ribosome, mRNA, and initiator tRNA at the start codon（起始密码子）.

Small ribosomal subunit binds the mRNA and locates the start codon

↓

Initiator tRNA binds the start codon.

fMet-tRNA^{fMet}（甲酰甲硫氨酰-起始tRNA） in bacteria & Met-tRNA$_i^{Met}$(甲硫氨酰-起始tRNA) in eukaryotes

↓

Large ribosomal subunit joins to form the complete initiation complex

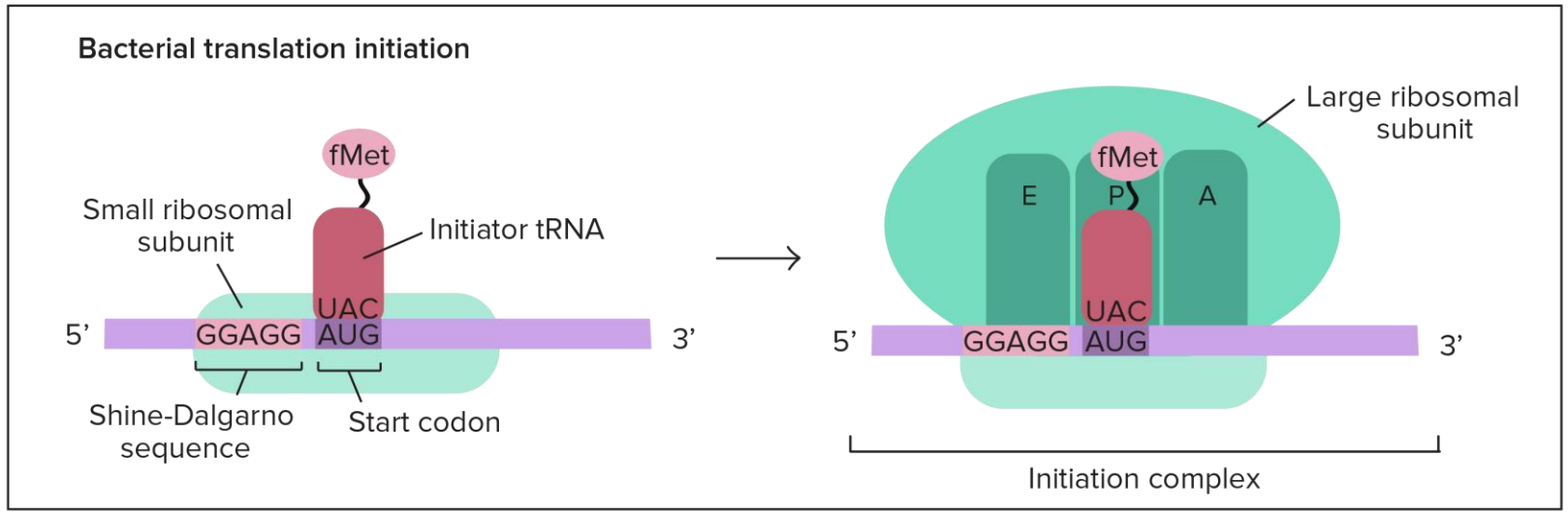
After initiation:

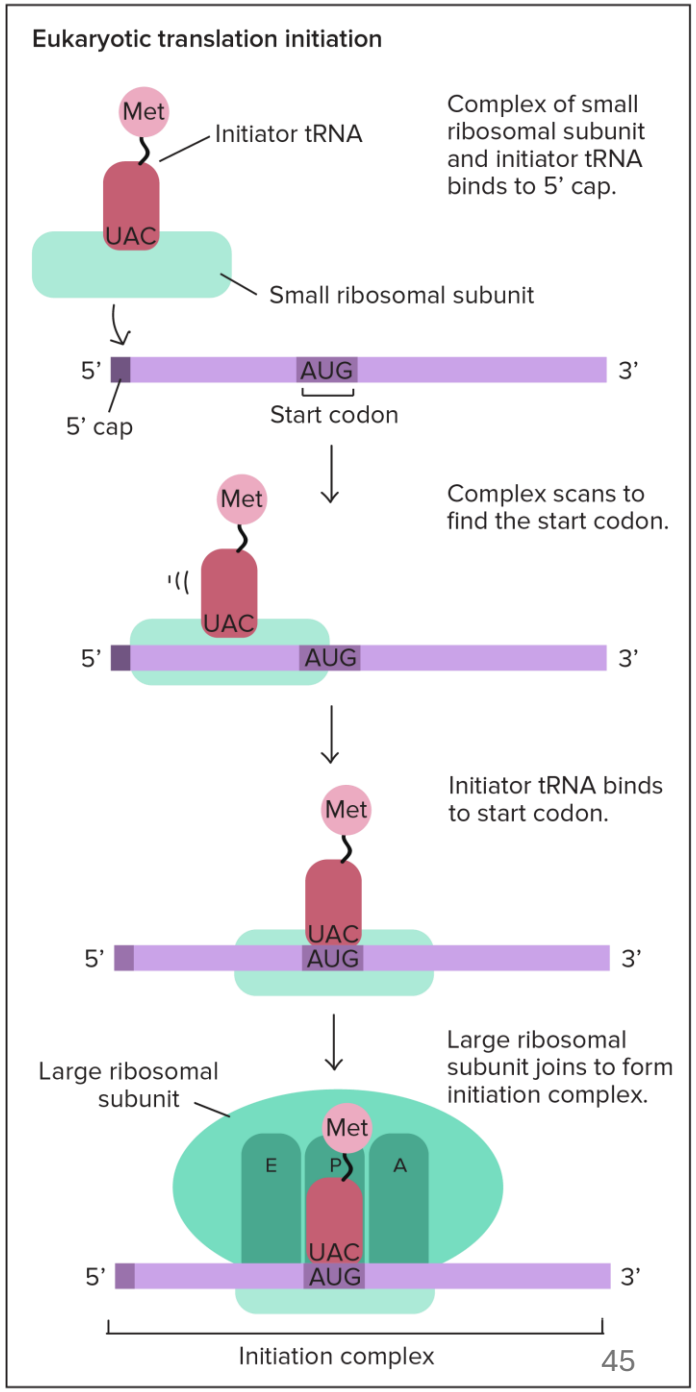
- **P site（P位点）** contains the initiator tRNA.
- **A site（A位点）** is empty and ready for the next aminoacyl-tRNA.
- **E site（E位点）** is empty.

Process of Translation

Step 1. Initiation（翻译起始）

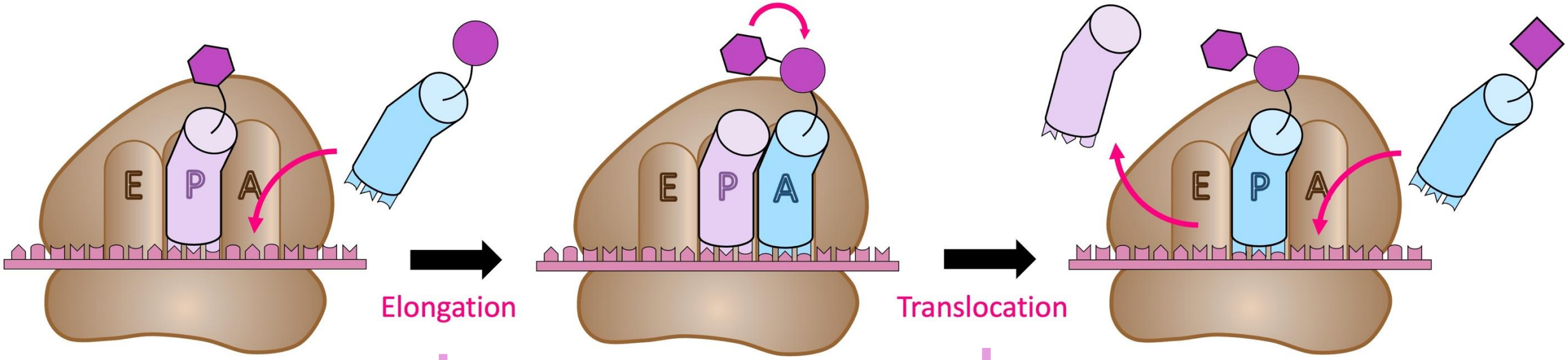
Initiation complex





Process of Translation

Step 2. Elongation（翻译延长）



Aminoacyl-tRNA entry into the A site
(氨酰-tRNA进入A位点)

Requires elongation factors（延长因子） and GTP

Peptide-bond formation
肽键形成

This reaction is catalyzed by the peptidyl transferase center（肽酰转移酶中心） of the large ribosomal subunit.

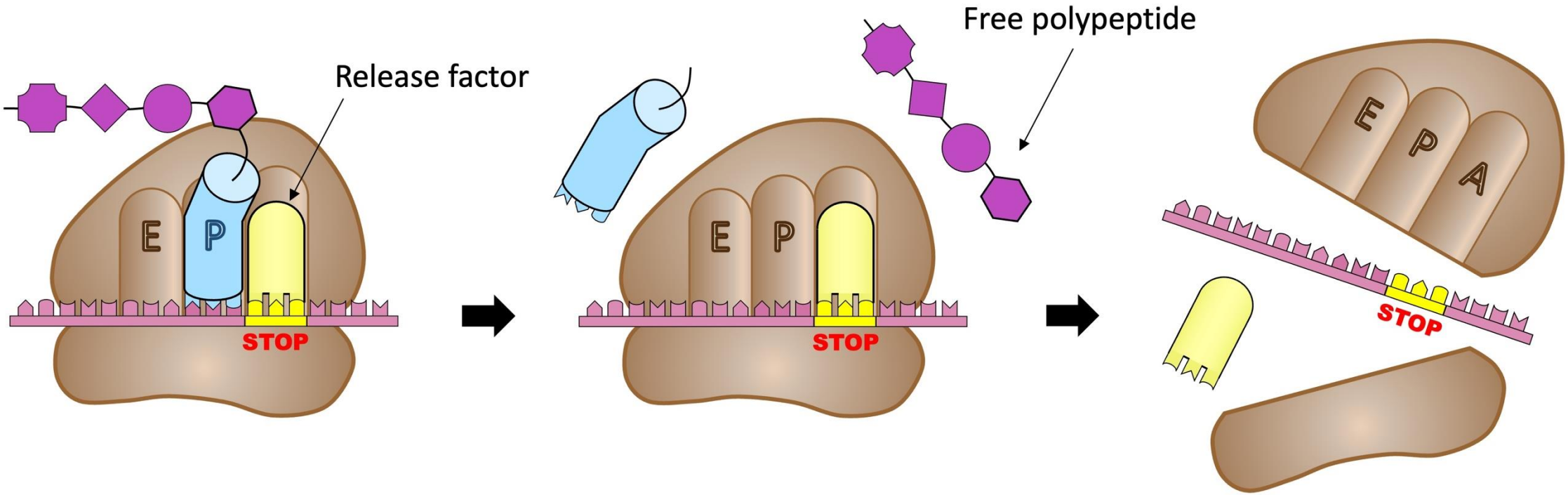
Translocation
移位

- Peptidyl-tRNA（肽酰-tRNA） moves from the A site to the P site.
- Empty tRNA moves from the P site to the E site.
- The empty tRNA exits from the E site.
- The A site becomes free for the next aminoacyl-tRNA.

Process of Translation

Step 3. Termination（翻译终止）

- Elongation and translocation continue in a repeating cycle until the ribosome reaches a stop codon
- These codons do not recruit a tRNA molecule, but instead recruit a release factor that signals for translation to stop
- The polypeptide is released and the ribosome disassembles back into its two independent subunits



Post-Translational Events

After termination, the ribosome is recycled for another round of translation.

The newly synthesized polypeptide may undergo:

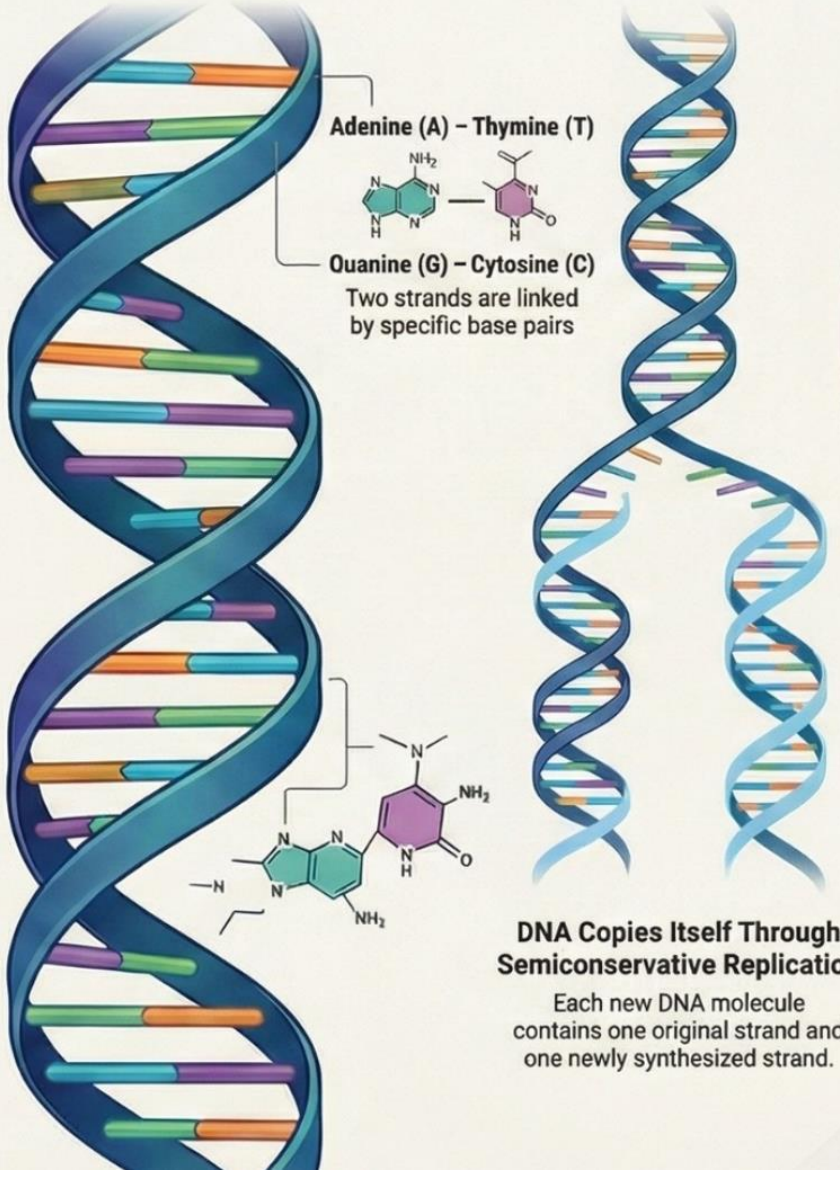
- **Folding（折叠）**
- **Chaperone-assisted folding（分子伴侣辅助折叠）**
- **Proteolytic processing（蛋白水解加工）**
- **Post-translational modification, PTM（翻译后修饰）**
- **Protein targeting（蛋白质定位）**

Contents

- Degradation of Proteins
- Amino Acid Degradation and Metabolic Conversion
- Biosynthesis of Amino Acids
- Protein Biosynthesis / Translation
- **Central Dogma**

From DNA to Protein: The Central Dogma of Biology

The Blueprint: DNA Structure & Replication



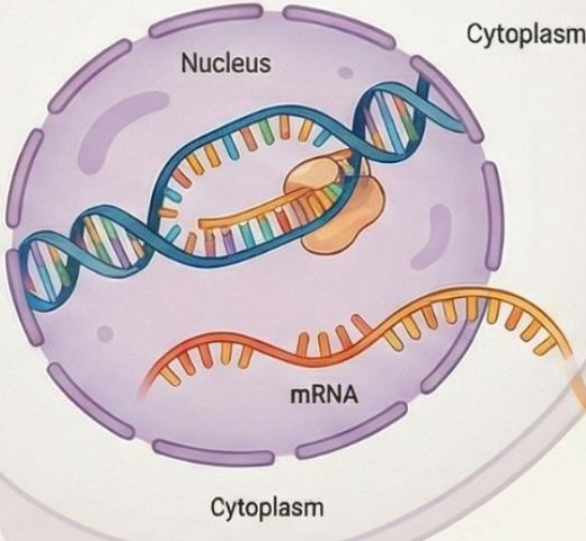
DNA Copies Itself Through Semiconservative Replication

Each new DNA molecule contains one original strand and one newly synthesized strand.

The Factory: From Gene to Protein

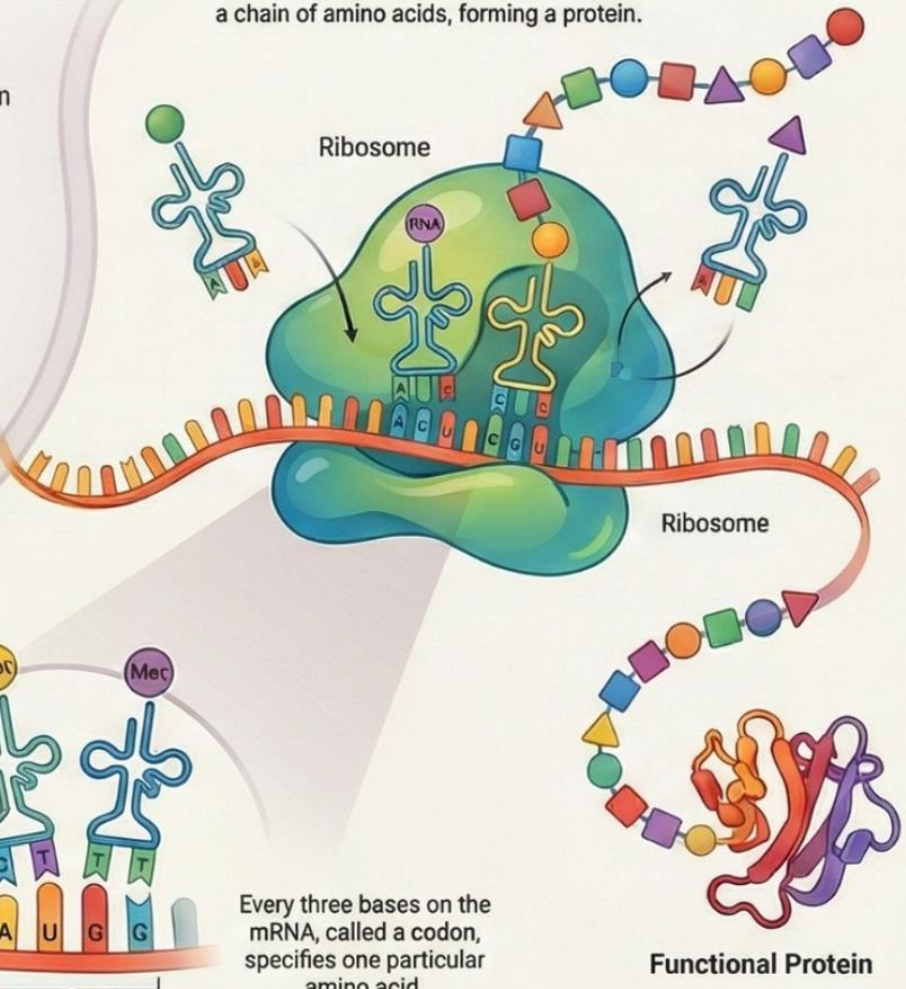
Step 1: Transcription (DNA → RNA)

A segment of DNA is used as a template to create a complementary messenger RNA (mRNA) molecule.

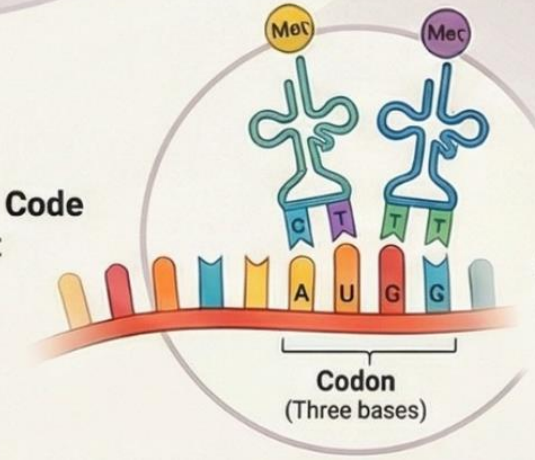


Step 2: Translation (RNA → Protein)

A ribosome reads the mRNA's code to assemble a chain of amino acids, forming a protein.



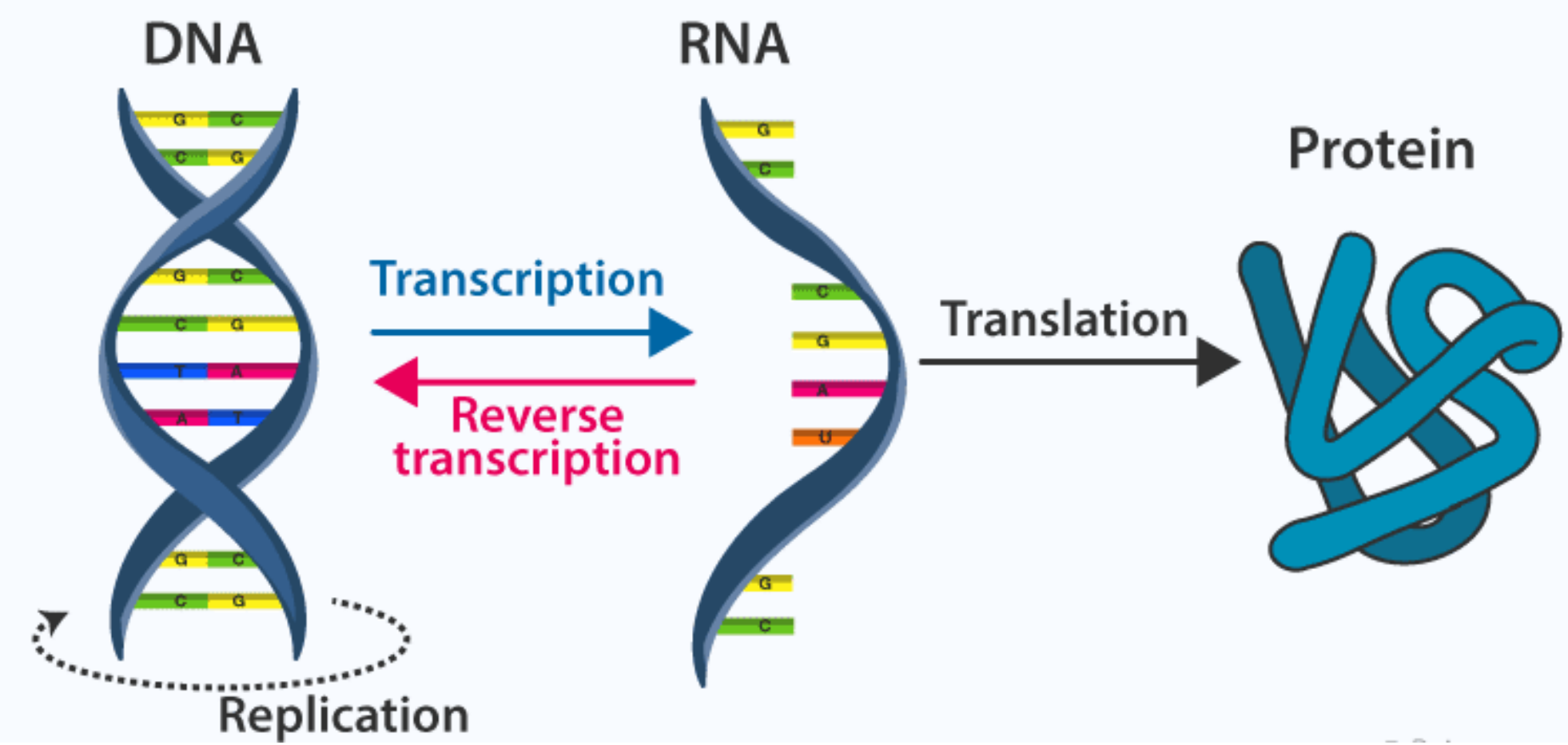
The Genetic Code is a Triplet

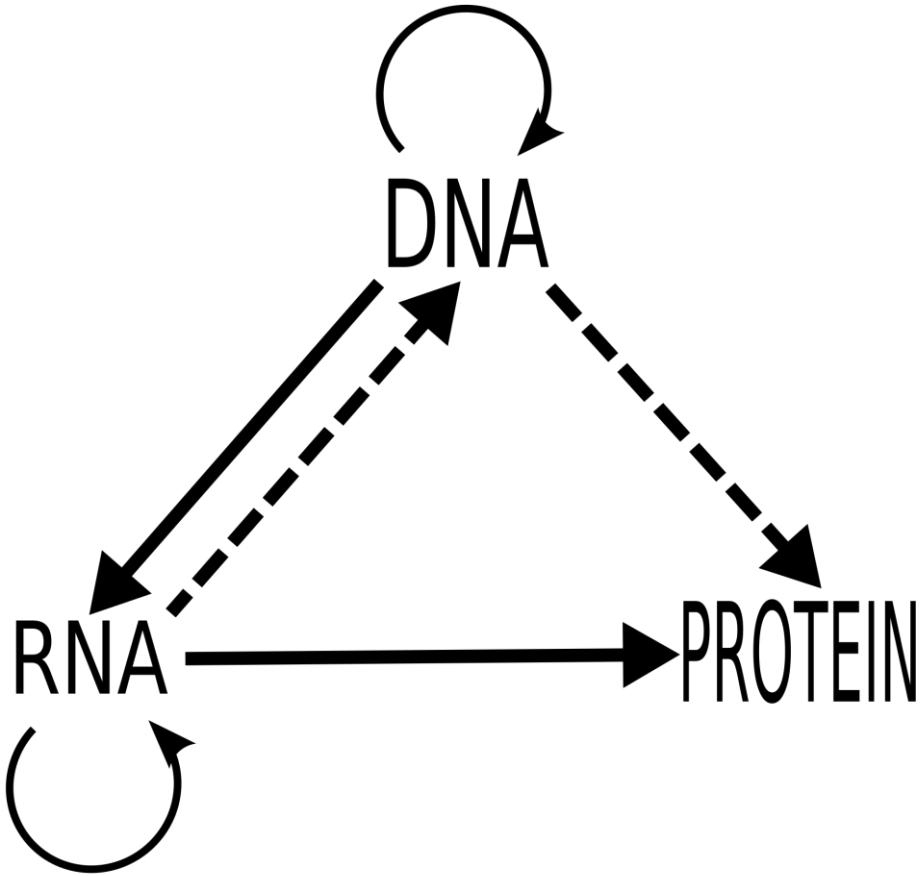


Every three bases on the mRNA, called a codon, specifies one particular amino acid.

Central dogma（中心法则）

The central dogma of molecular biology describes the flow of genetic information in biological systems.





RESEARCH ARTICLE

Protein-templated synthesis of dinucleotide repeat DNA by an antiphage reverse transcriptase

PUJUAN DENG, HYUNBIN LEE, CARLO ARMIJO, HAOQING WANG, AND ALEX GAO Authors Info & Affiliations

NEWS | BIOLOGY

Scientists stunned by ‘fundamentally new way’ life produces DNA

Bacterial system uses protein in novel way to build mysterious repetitive DNA sequence that defends against viruses

16 APR 2026 · 2:00 PM ET · BY RICHARD STONE

Homework Assignments

Model 1: DNA is actively transcribed, producing much mRNA. Ribosomes translate rapidly, so many proteins are synthesized. However, protein degradation is weak, so misfolded proteins accumulate.
Model 2: Transcription and translation are slower, so fewer proteins are synthesized. However, protein degradation is efficient, so damaged proteins are removed quickly.

Task 1: Explain the roles of **DNA**, **mRNA**, **tRNA**, **ribosomes**, **amino acids**, and **ATP/GTP** in protein synthesis.
Task 2: Which model is more successful for long-term cell survival: rapid protein synthesis or efficient protein quality control? Explain why.
Task 3: Suggest one way to improve each model. Consider **mRNA stability**, **ribosome activity**, **ATP/GTP supply**, **molecular chaperones**, or **protein degradation systems**.

Challenge: A codon changes from **GAA** to **UAA**. Explain how this affects protein synthesis.