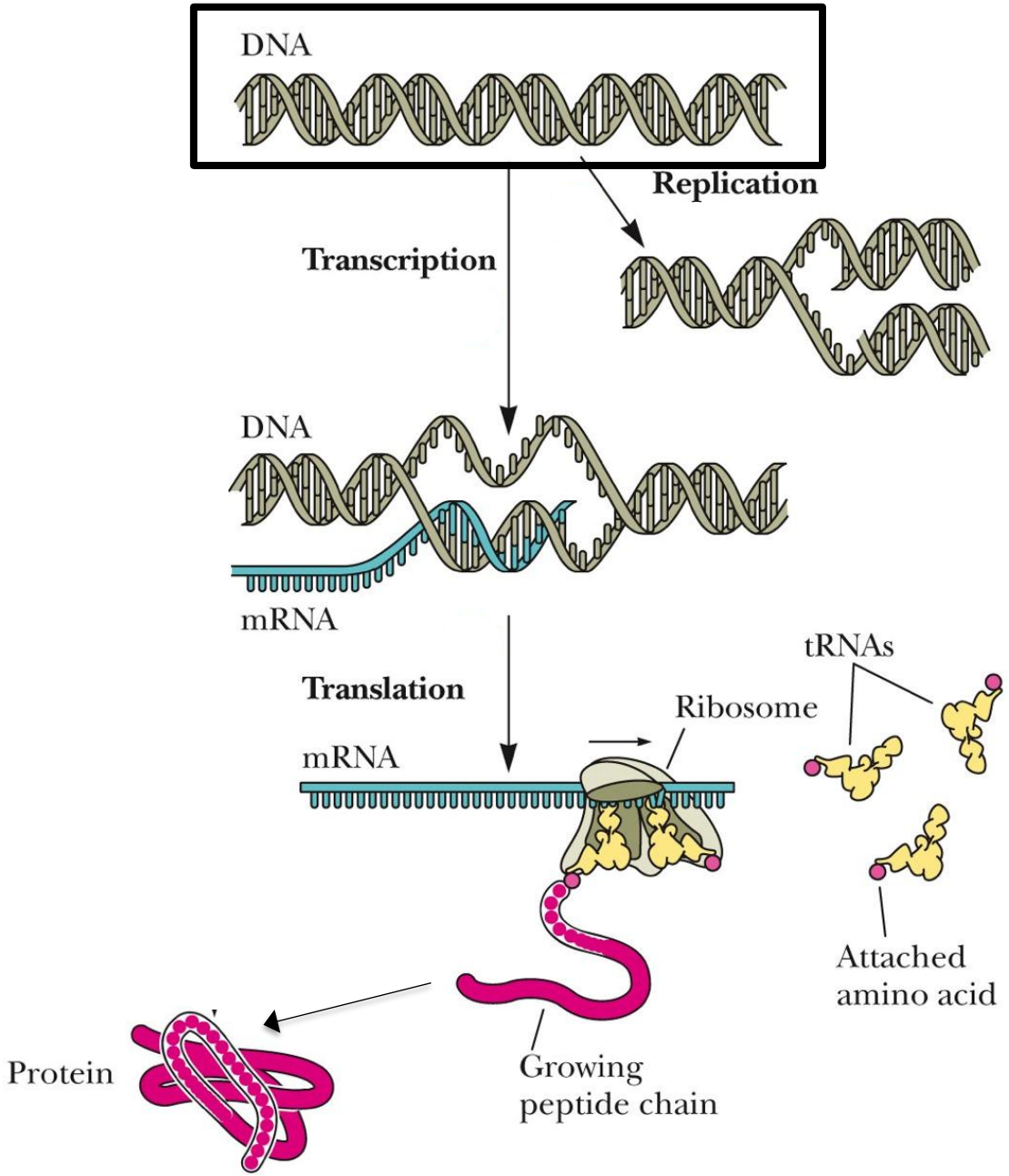
Nucleotide Biosynthesis

The central dogma of molecular biology



Learning Objectives

1. Know the building blocks for the biosynthesis of both purine and pyrimidine nucleotides.

2. Identify the differences between purine and pyrimidine synthesis pathways.

3. Be able to describe the structure and function of ribonucleotide reductase.

4. Understand how enzymes within the biosynthetic pathways are regulated.

Close

0 response submitted

Purines have _____ rings and pyrimidines have _____ rings

Scan the QR or use link to join

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2, 2

Treemap

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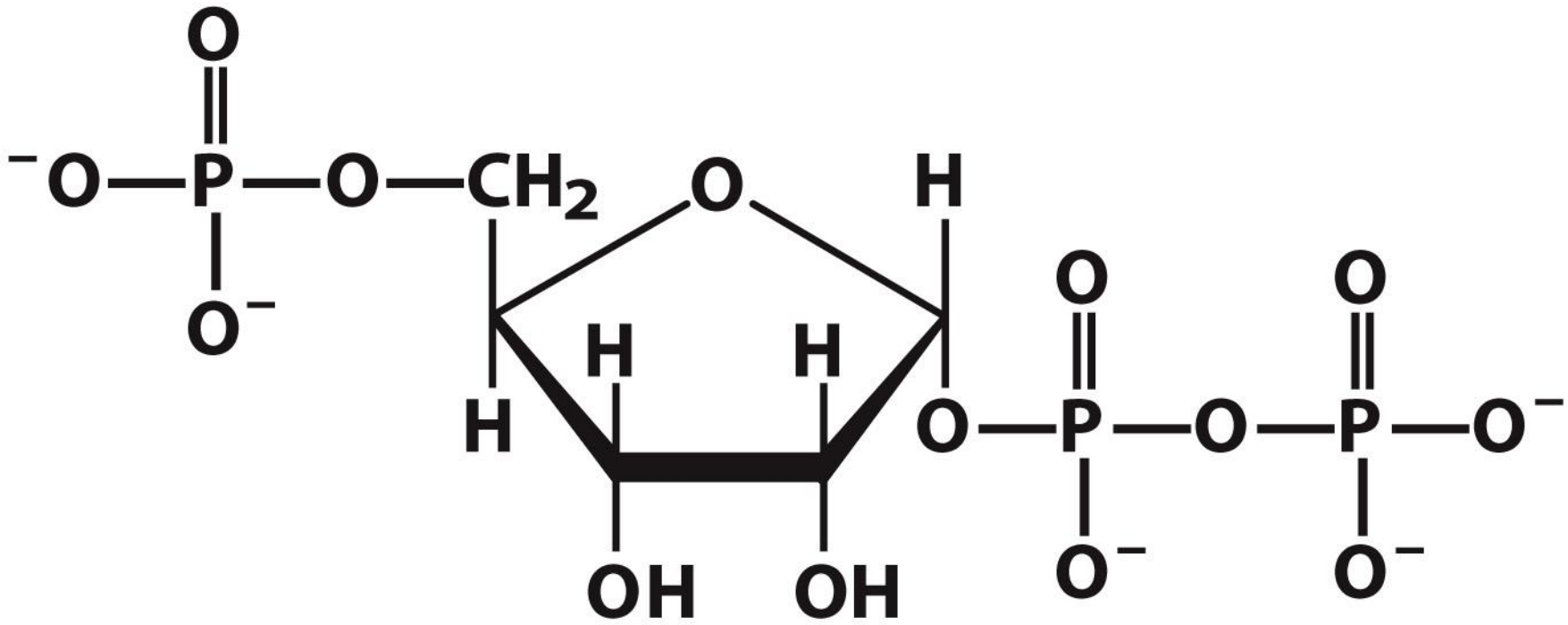
1 of 2

In all nucleoside monophosphates, the sugar and phosphate come from PRPP

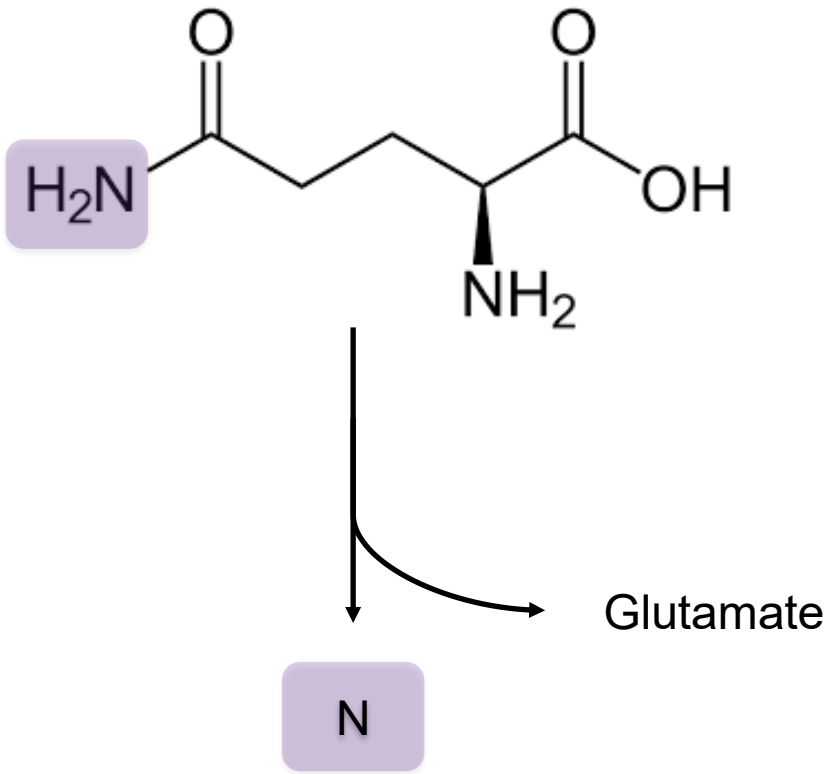


Unnumbered 22 p870a
Lehninger Principles of Biochemistry, Seventh Edition

5-phosphoribosyl-1-pyrophosphate

Glutamine and folate are other common players in purine and pyrimidine synthesis

Glutamine: Nitrogen donor

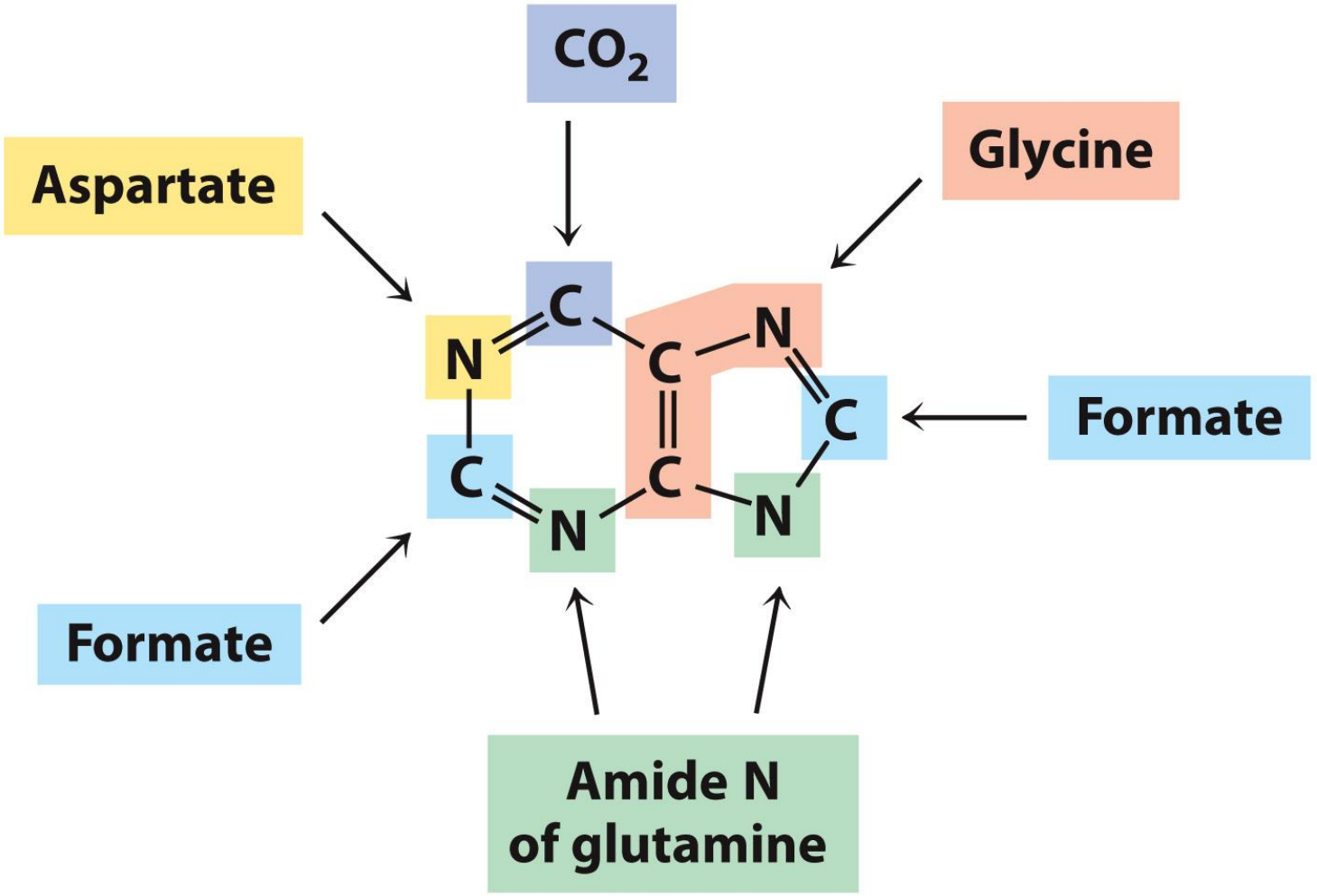


Folate: 1-Carbon Carrier

Vitamin B9

N^{10} formyl THF
N-N methylene THF

Purine biosynthesis requires components from many sources

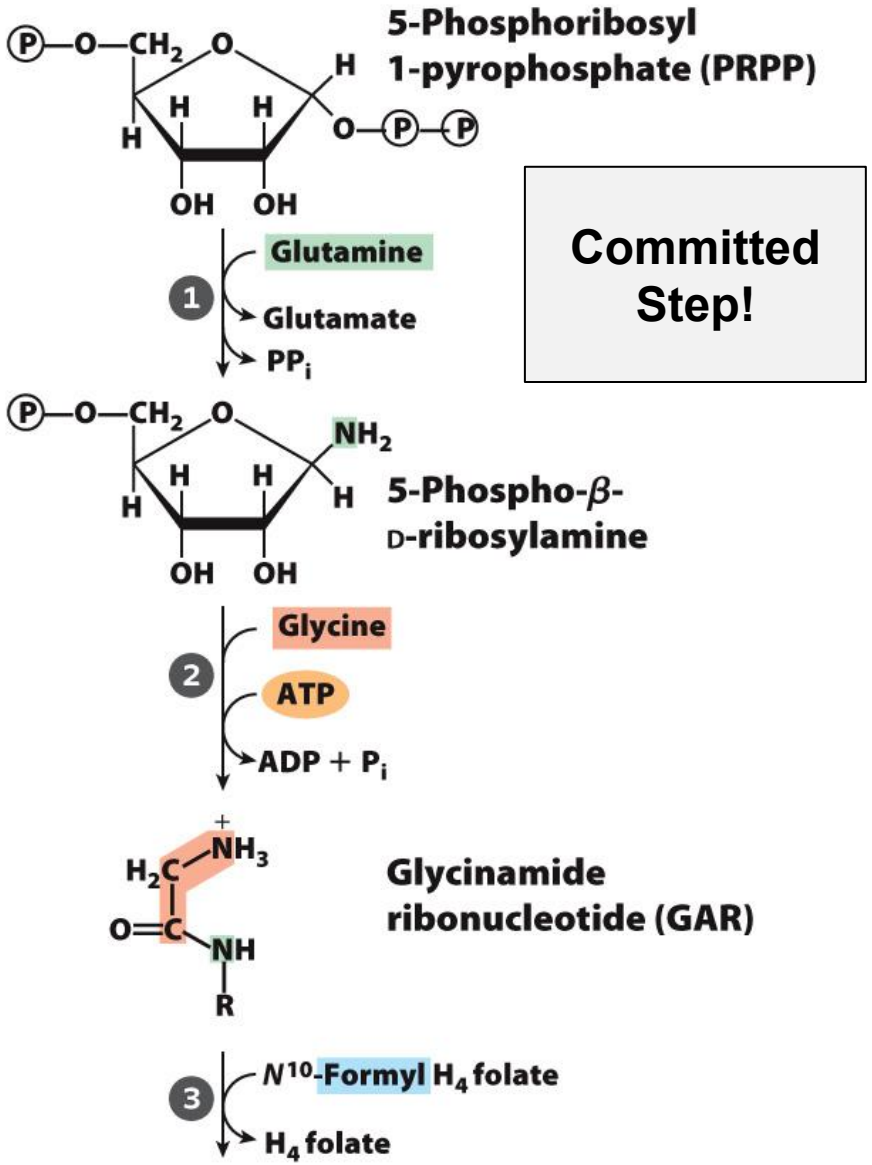


Built directly onto PRPP

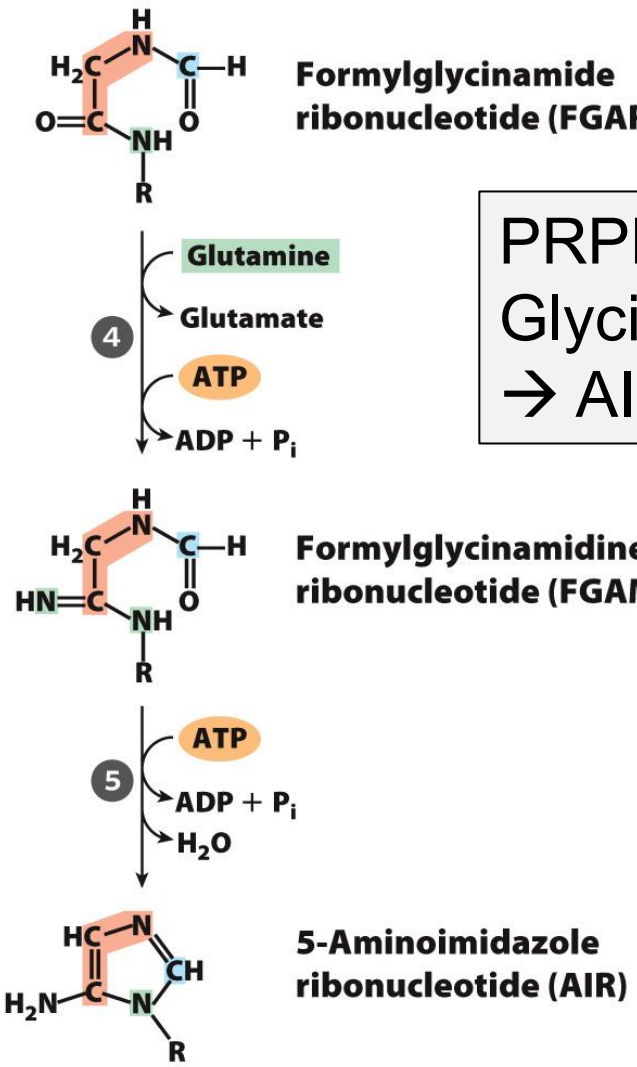
1. 5-membered ring
2. 6-membered ring

Lehninger: Figure 22-34

Part I: Generating the 5-membered ring



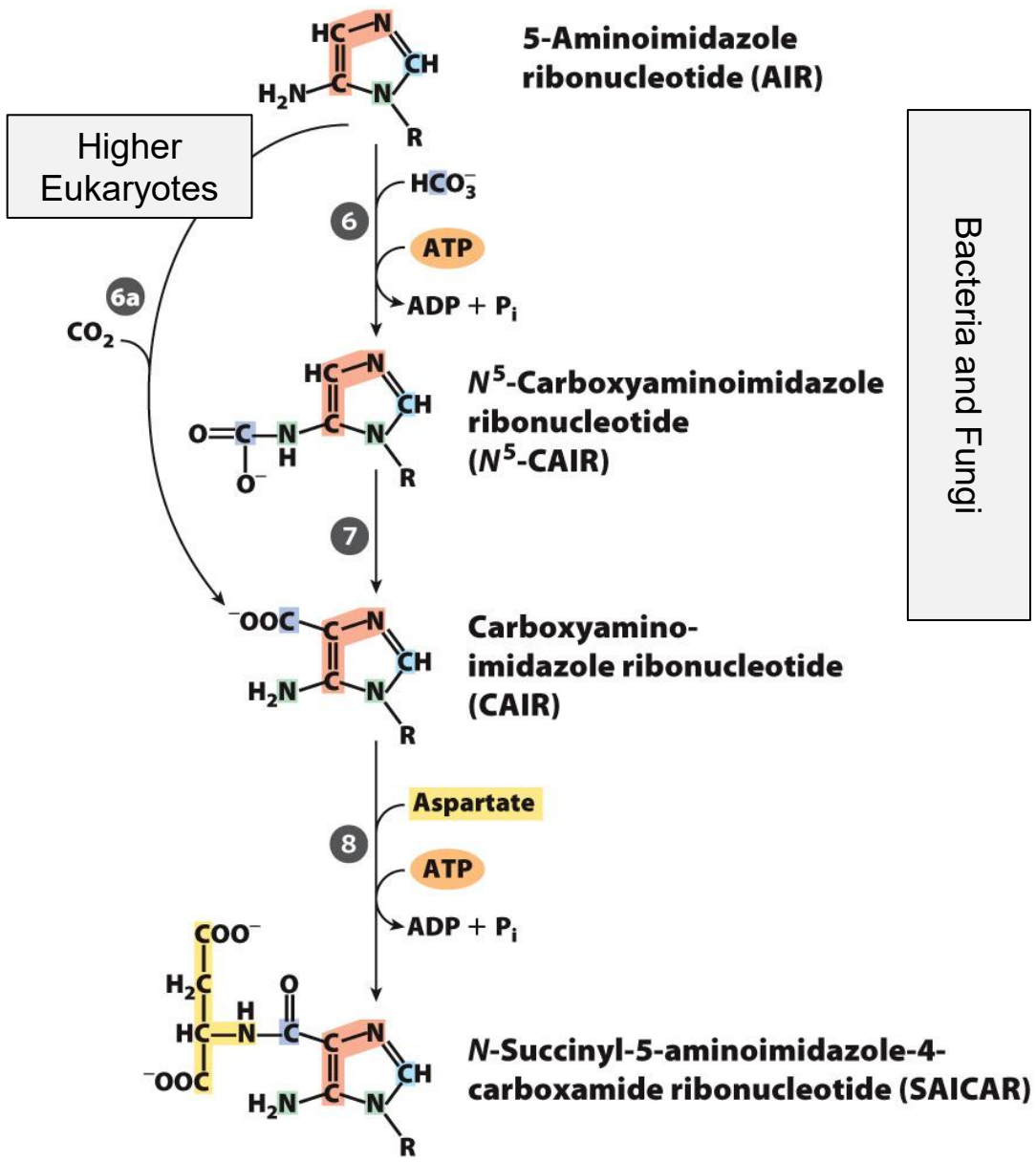
Committed Step!

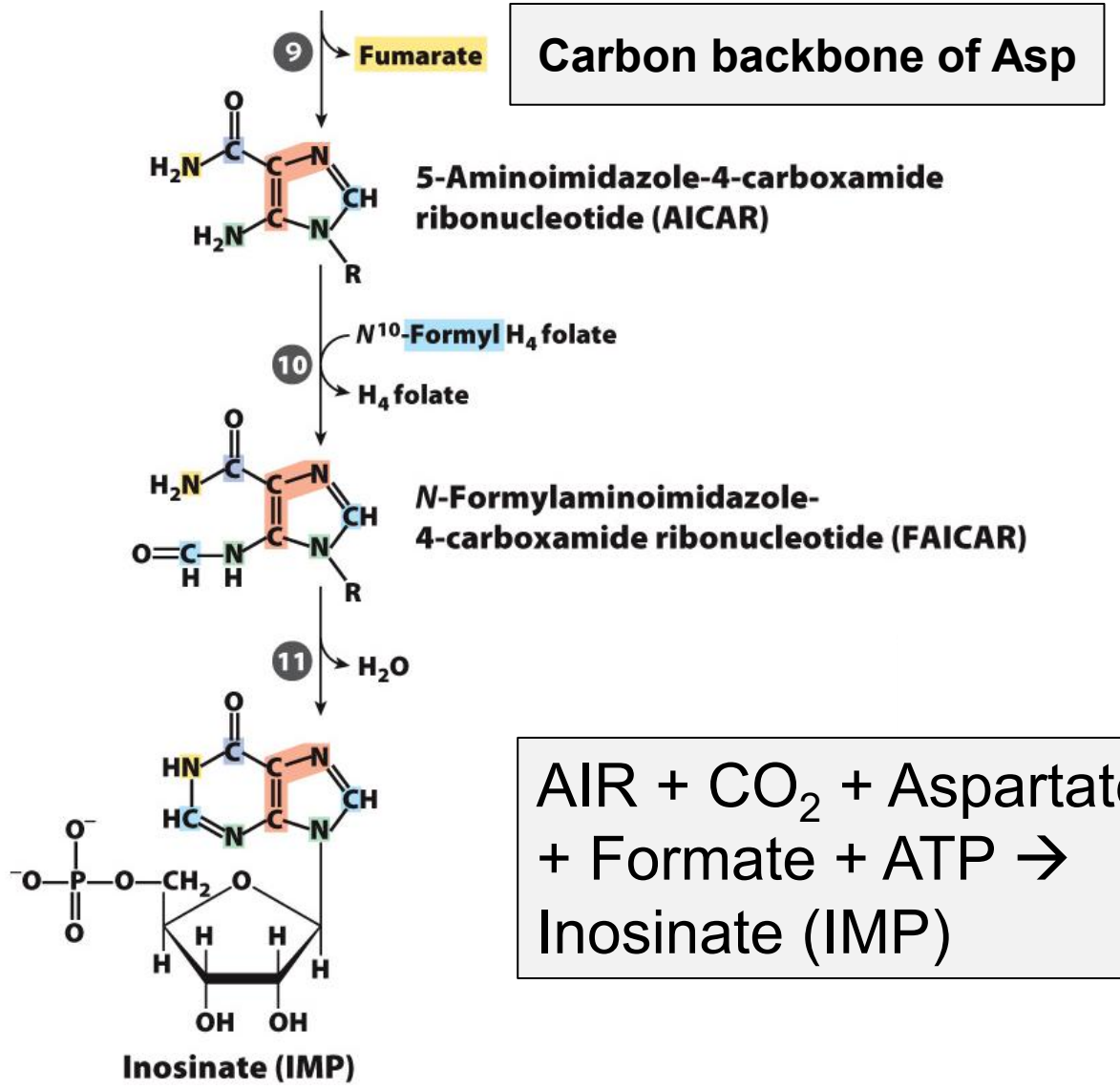


PRPP + 2 Glutamine + Glycine + Formate + 3 ATP → AIR

Lehninger: Figure 22-35

Part II: Generating the 6-membered ring





Carbon backbone of Asp

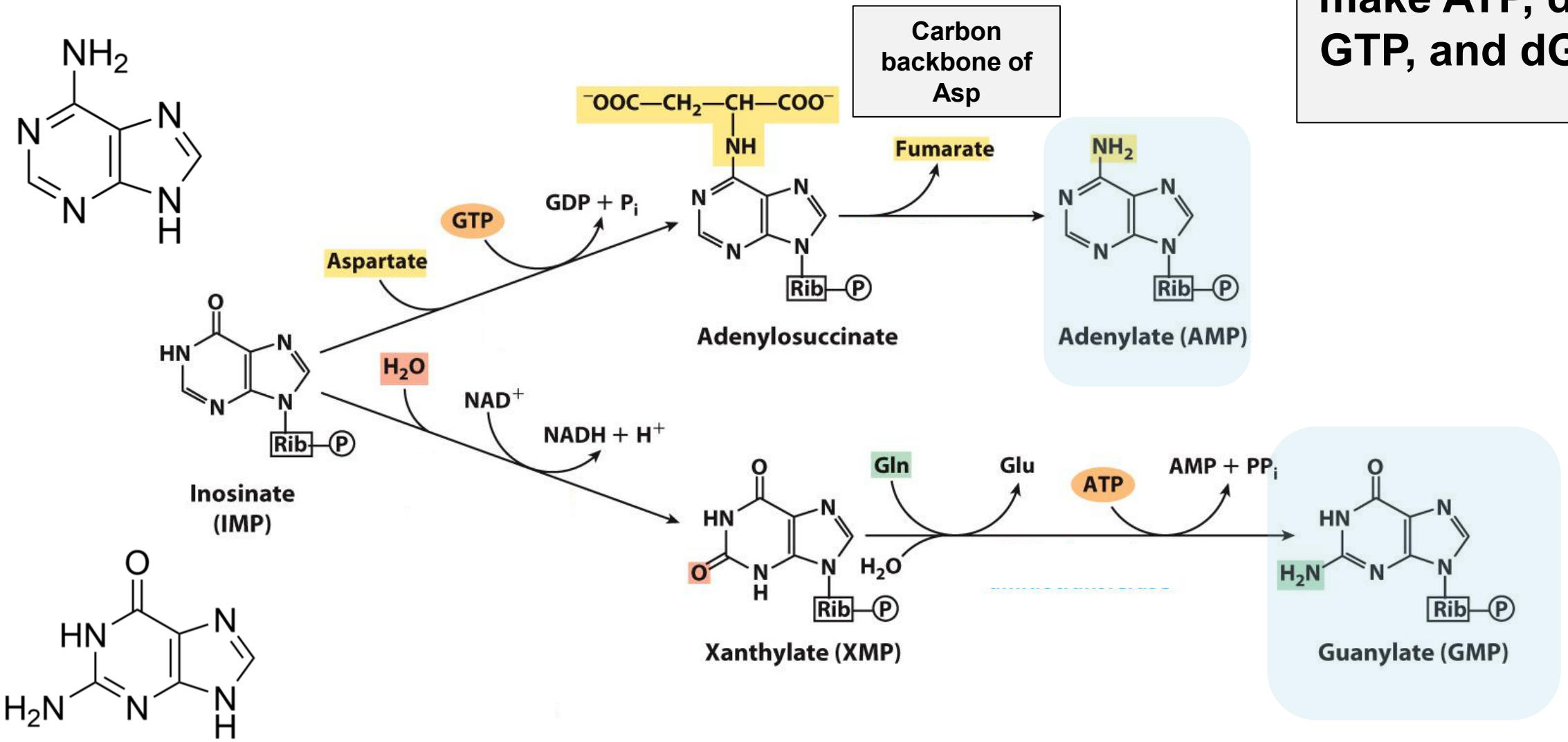
AIR + CO_2 + Aspartate + Formate + ATP → Inosinate (IMP)

Inosine –
our precursor to AMP and GMP

Lehninger: Figure 22-35

Part III: Making AMP or GMP

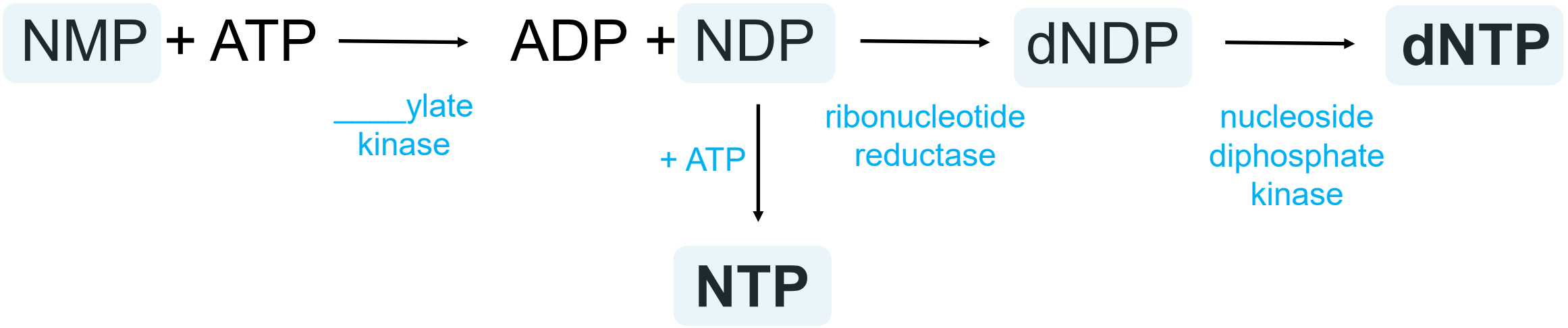
But how do we make ATP, dATP, GTP, and dGTP?



Lehninger: Figure 22-36

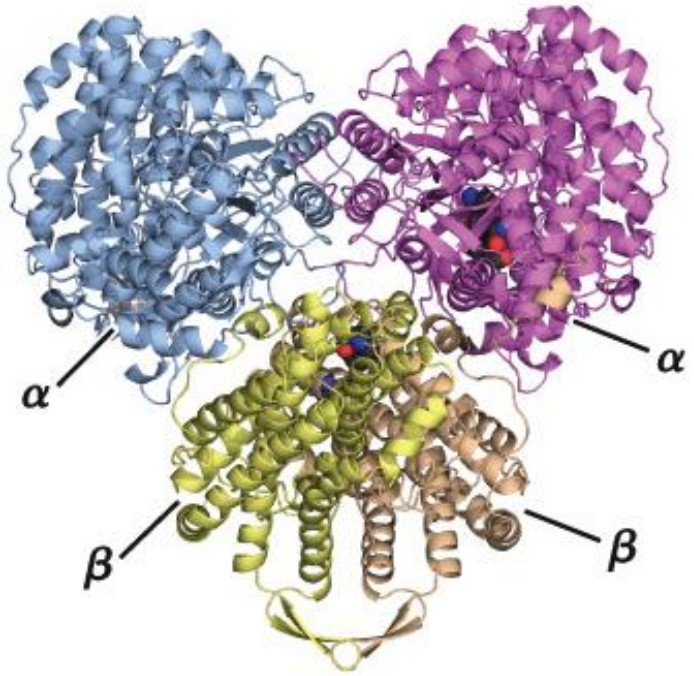
Part IV: Creating triphosphates and deoxy triphosphates

Deoxynucleotides can only be formed from ribonucleoside diphosphates



Ribonucleotide reductase is a heterotetramer

NDP ⟶ dNDP



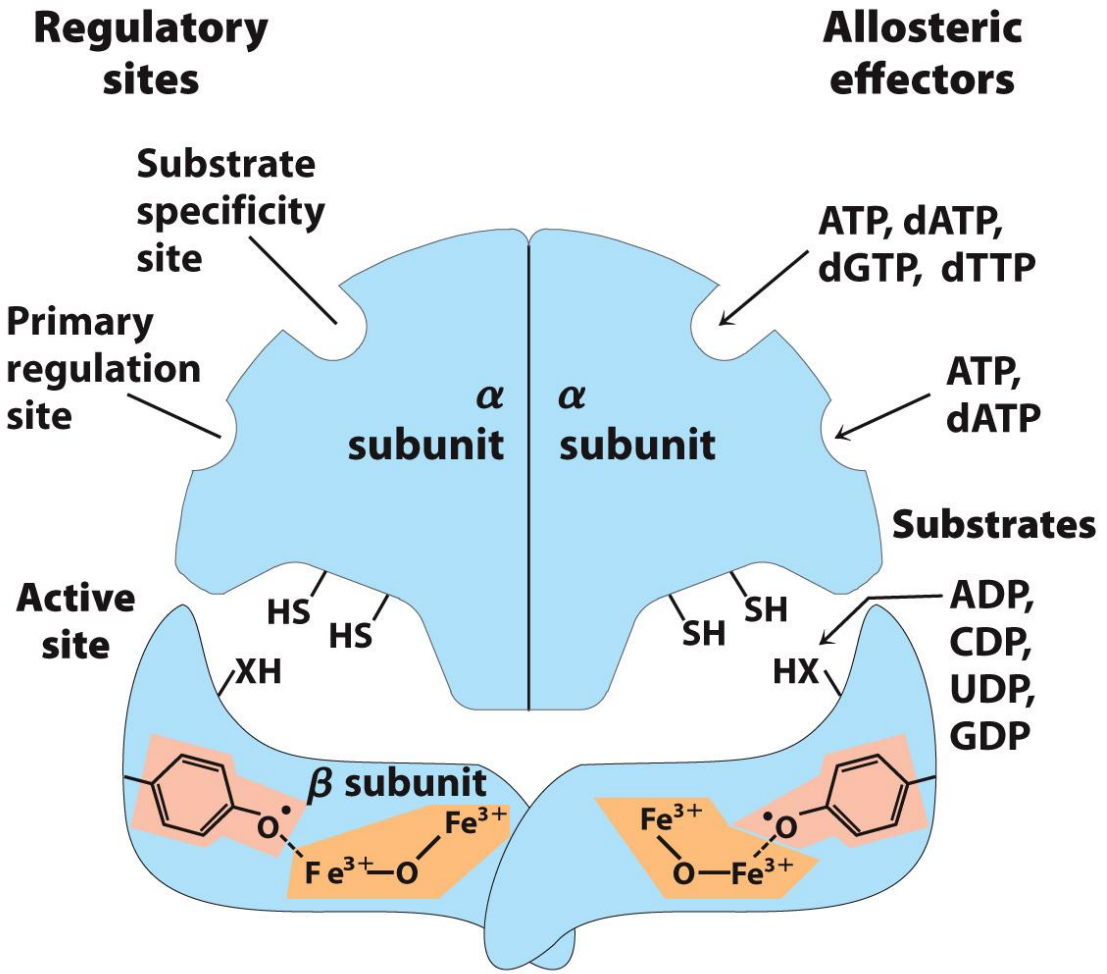


Figure 22-42a
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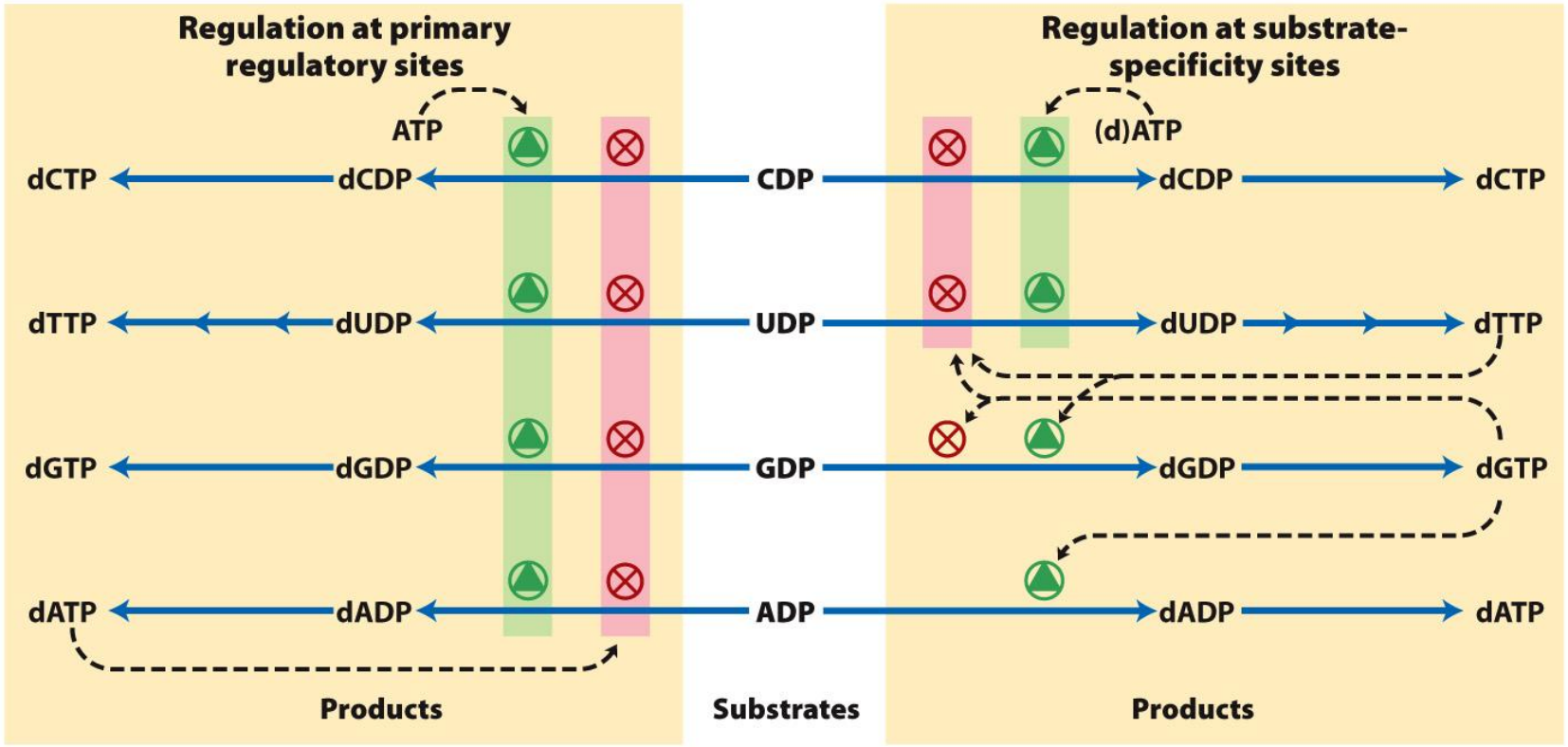
Ribonucleotide reductase ensures that we have balanced pool of dNTPs

Overall Activity



Substrate Specificity

Figure 22-44
Lehninger Principles of Biochemistry, Seventh Edition

Close

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During purine biosynthesis, the six-membered ring is synthesized first.

Scan the QR or use link to join

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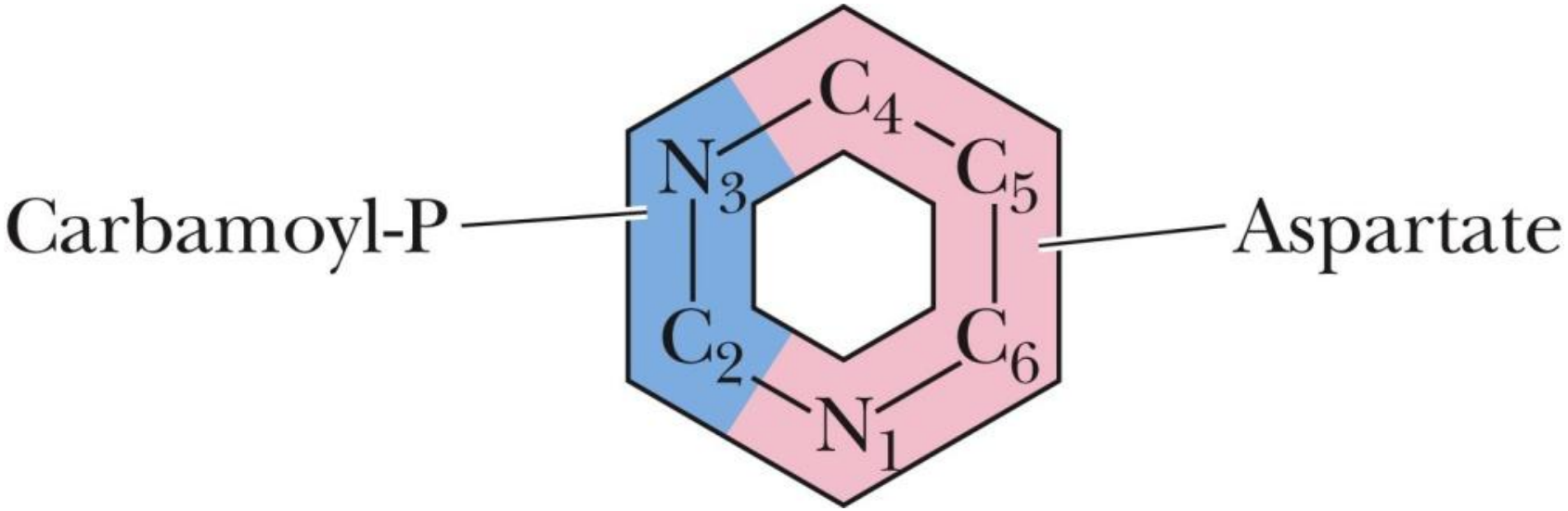
Copy link

False

Treemap Bar

1 of 2

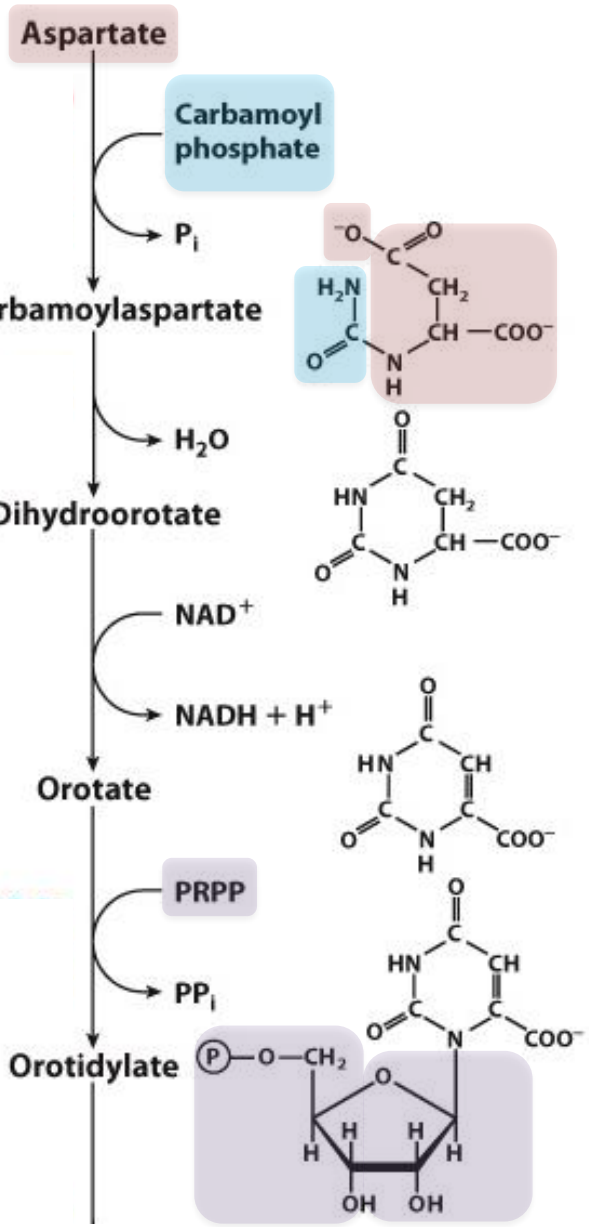
Pyrimidine biosynthesis only requires input from two precursor molecules

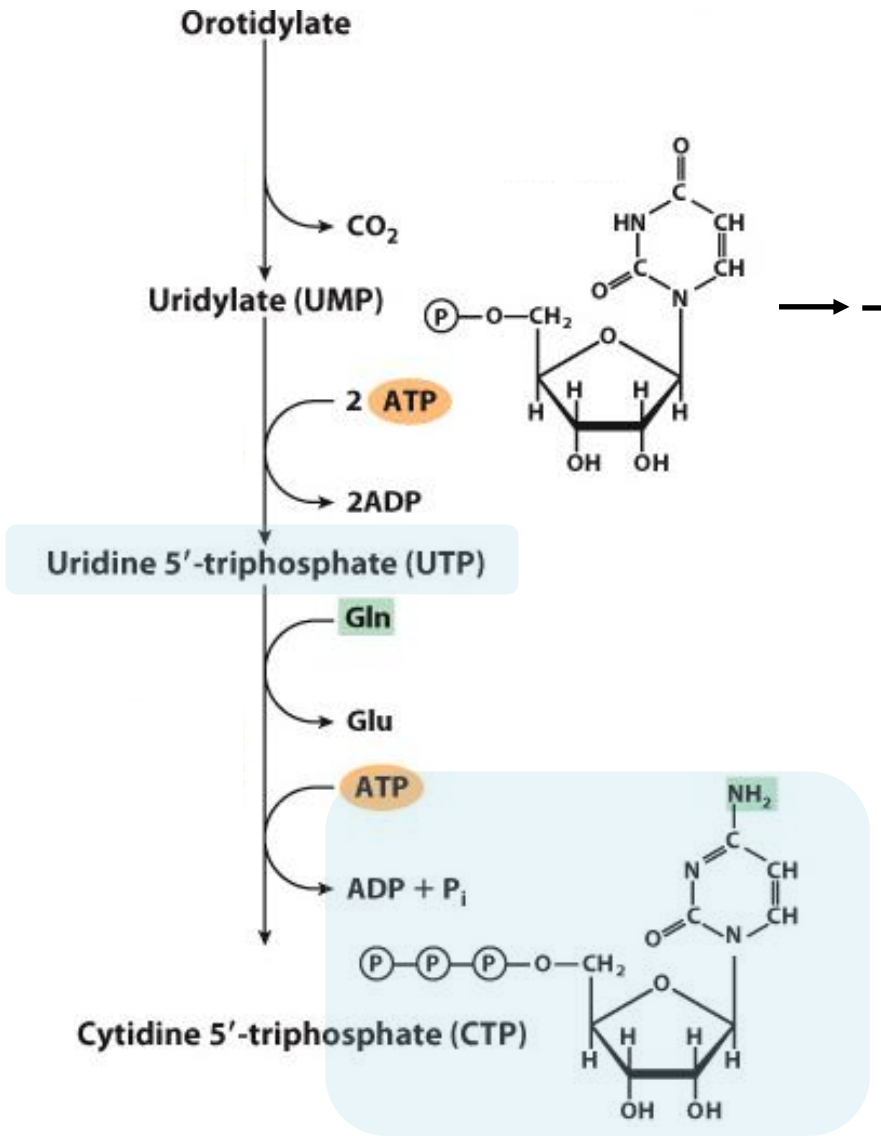


Base is built first, then condensed with PRPP

UTP and CTP synthesis are closely linked

Comm... Step!

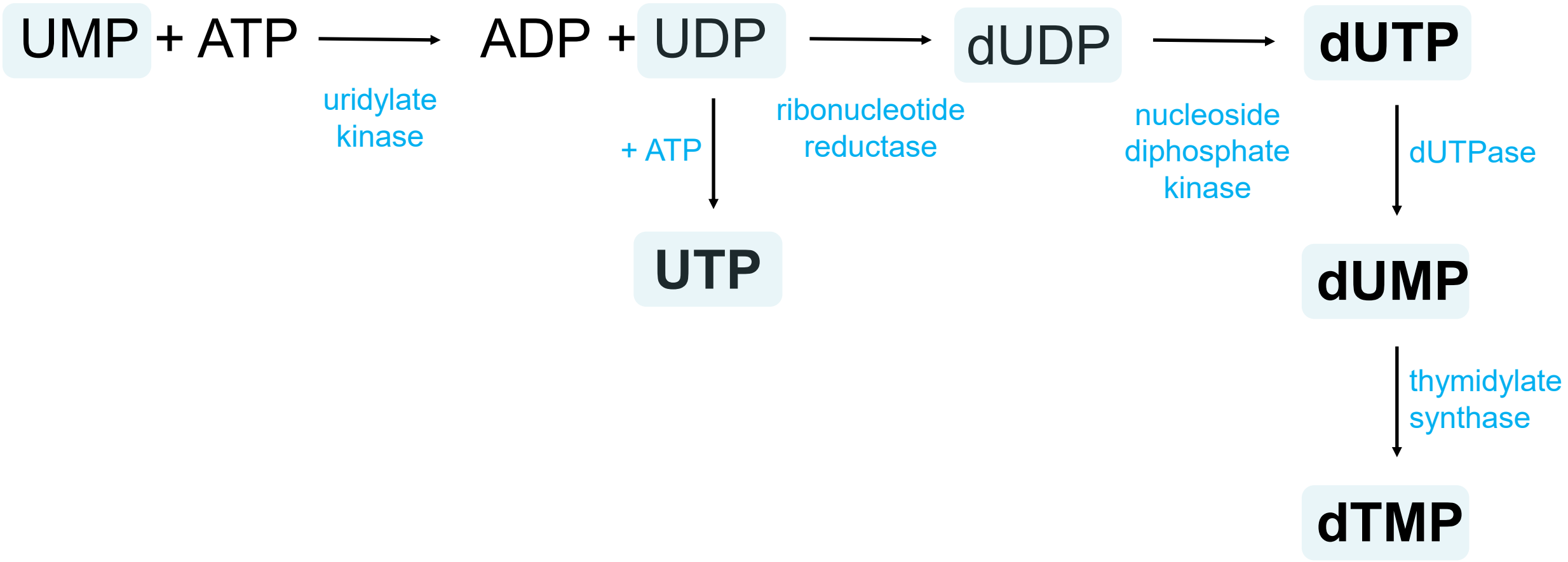




dUMP

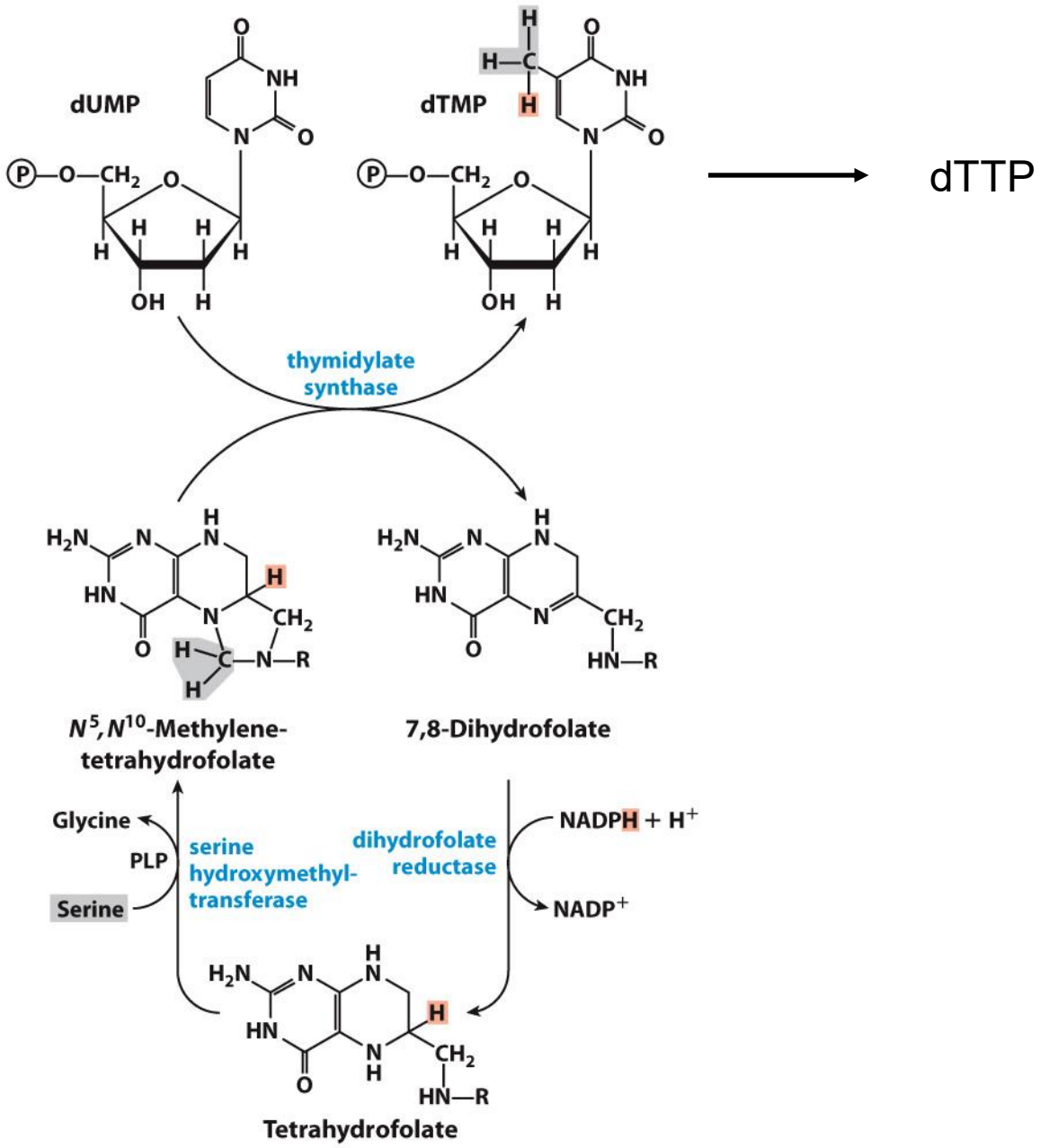
Lehninger: Figure 22-38

We cannot allow dUTP to accumulate in the cell



Lehninger: Figure 22-47

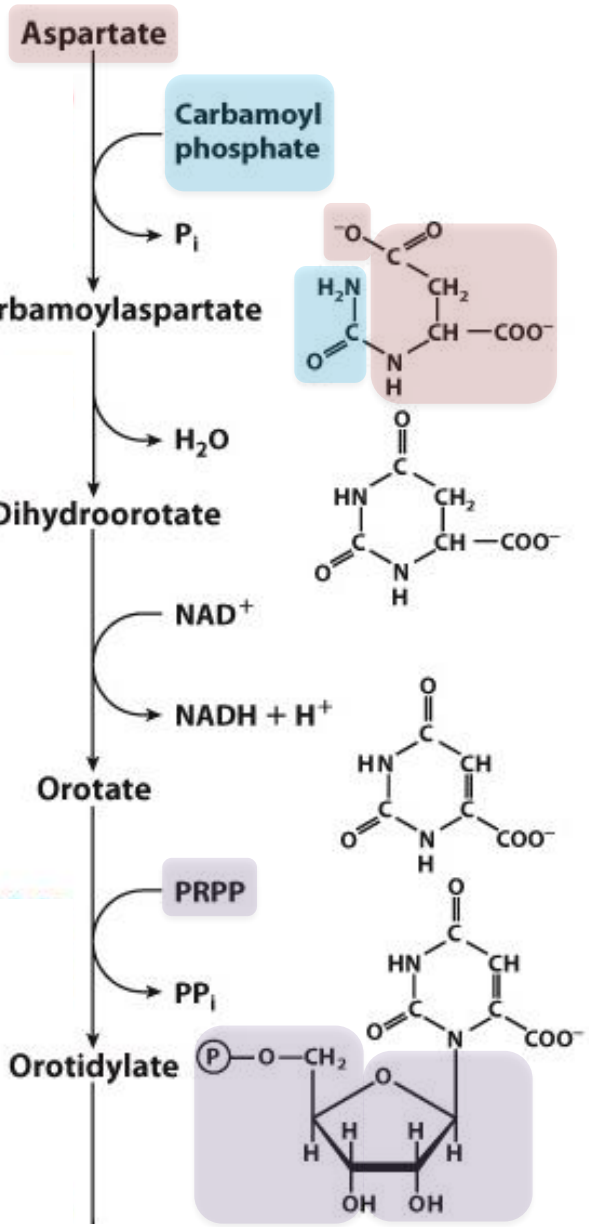
dTMP is synthesized from dUMP

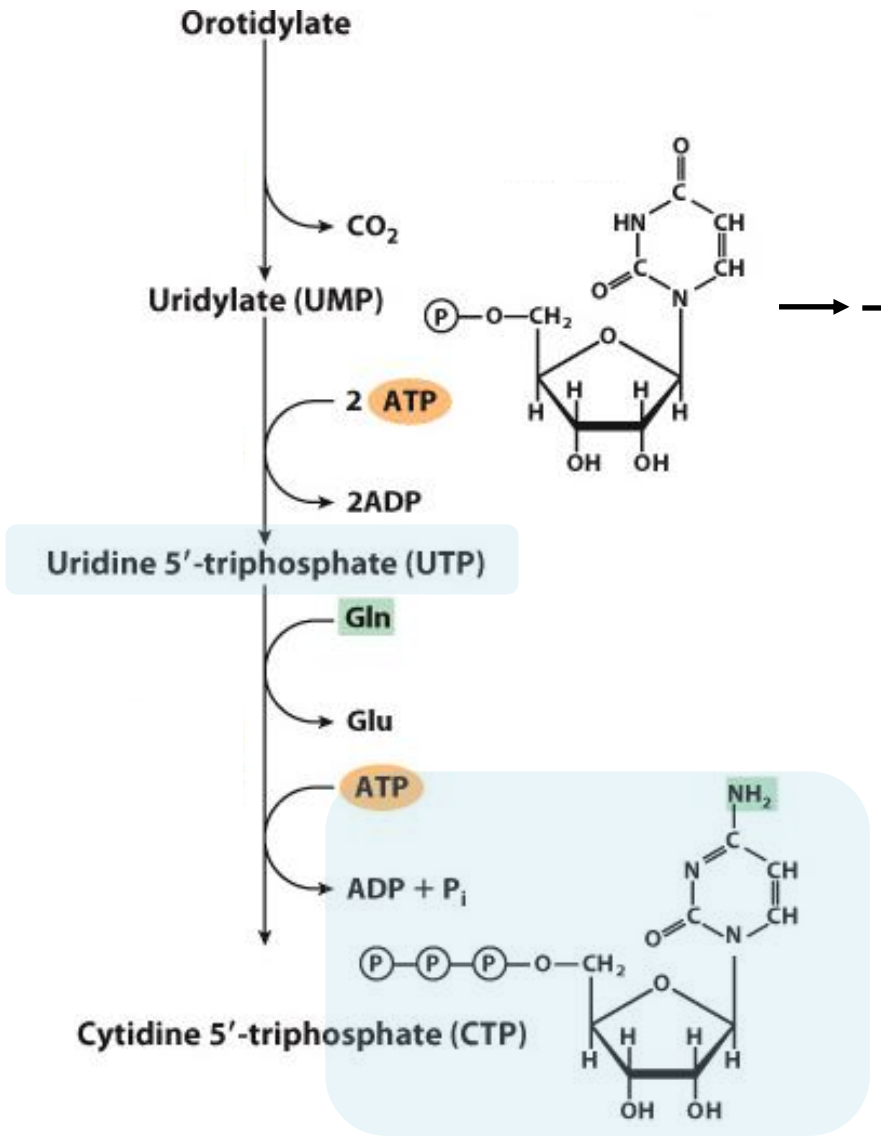


Lehninger: Figure 22-47

UTP and CTP synthesis are closely linked

Comm... Step!





dUMP

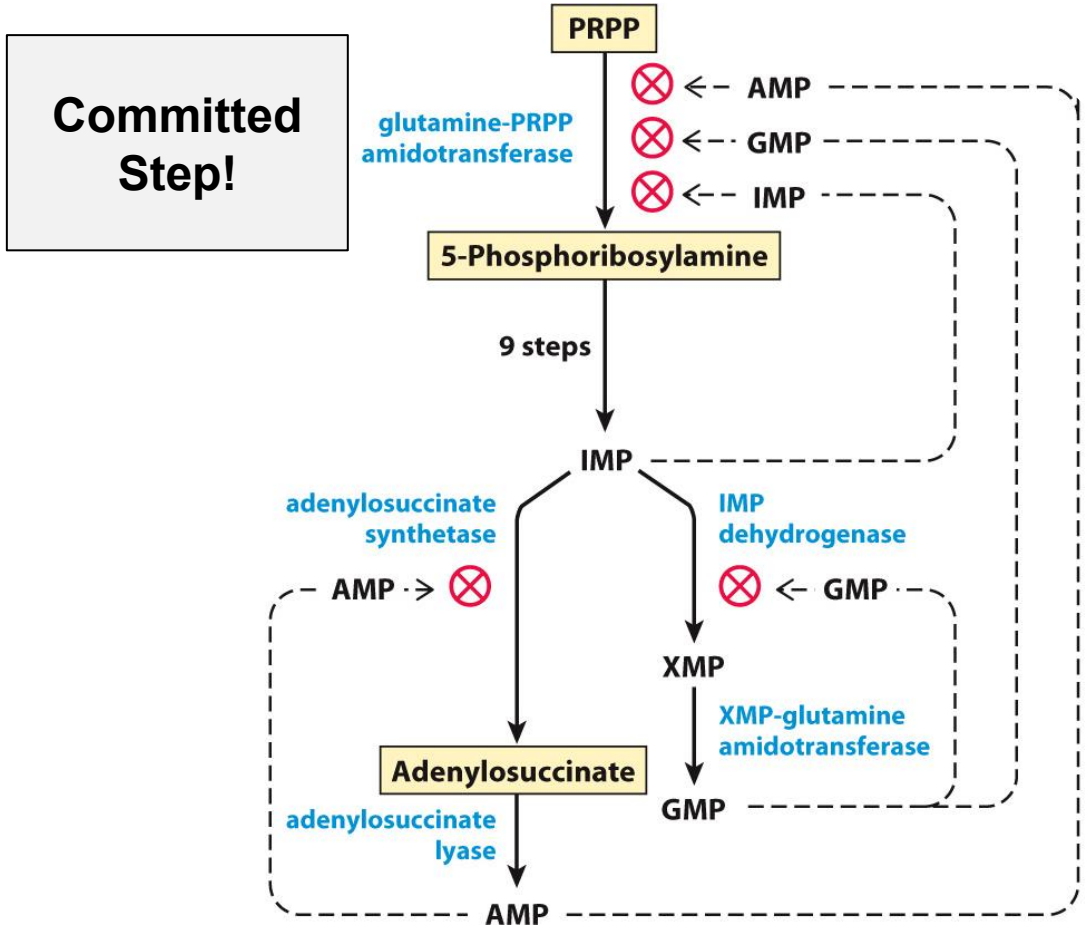
Lehninger: Figure 22-38

Making dCTP

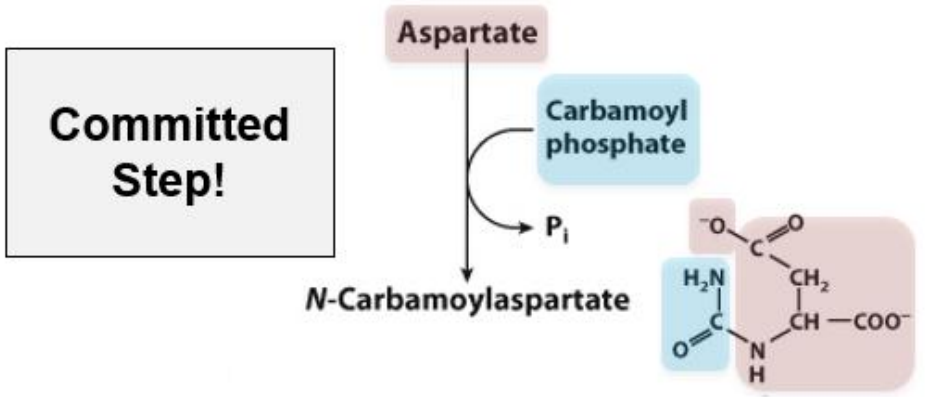

CMP + ATP
cytidylate kinase
ADP + CDP
ribonucleotide reductase
dCDP
nucleoside diphosphate kinase
dCTP

Feedback inhibition is an important regulator of nucleotide synthesis

Purines



Pyrimidines



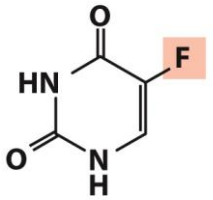
Aspartate transcarbamoylase is inhibited by CTP

Lehninger: Figure 22-37

Nucleotide biosynthesis pathways are attractive pharmaceutical targets

Nucleotide Analogs

Chemotherapeutic



Fluorouracil

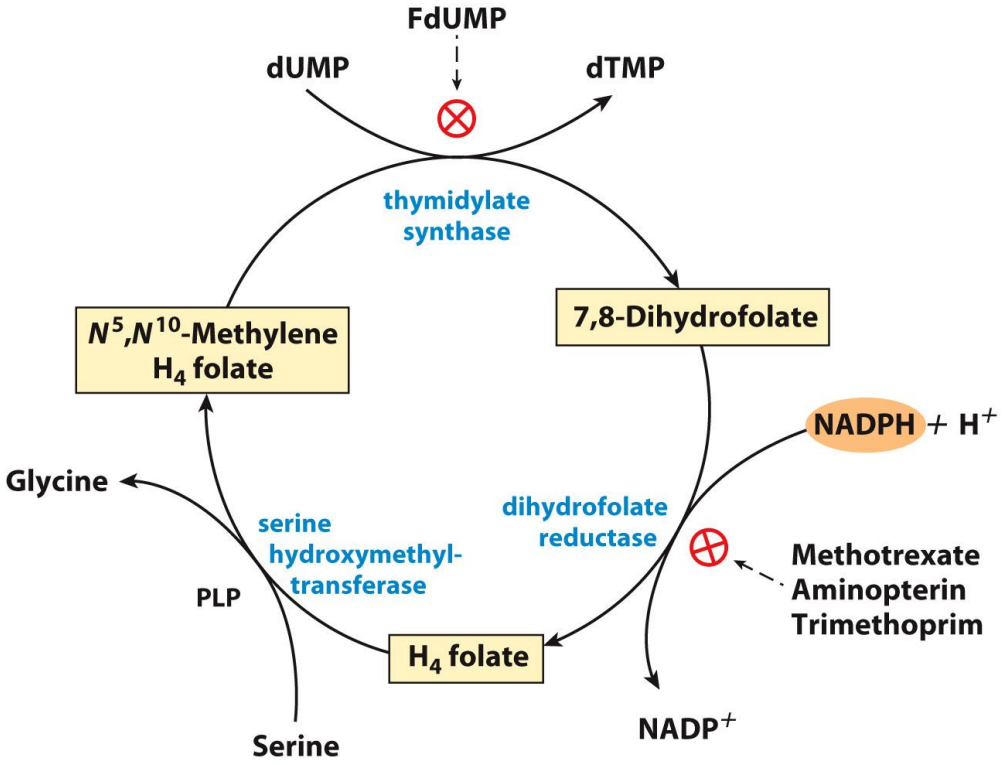


Figure 22-52a
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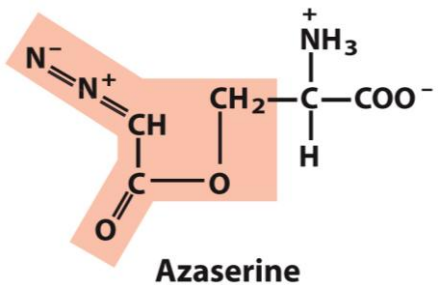
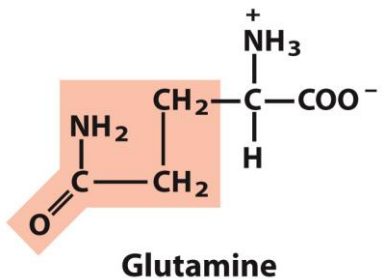
Glutamine Analogs



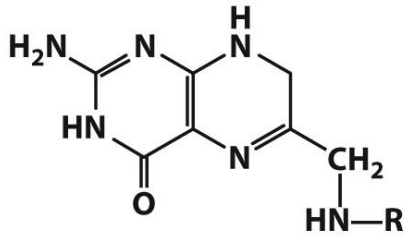
Azaserine

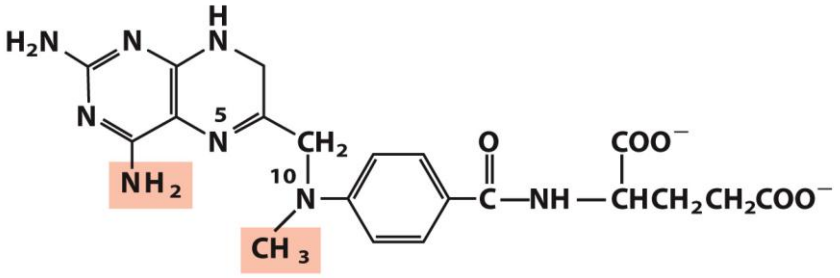
Antibiotic



Glutamine

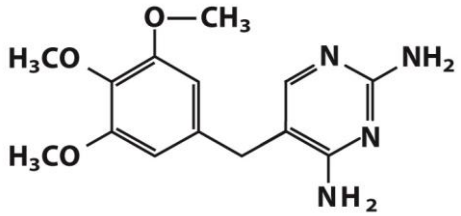
Folate Analogs





Methotrexate

Chemotherapeutic



Trimethoprim

Antibiotic

Figure 22-52b

Close

0 response submitted

Which of the following about pyrimidine biosynthesis is true?

Scan the QR or use link to join

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Copy link

The ring is directly onto

Aspartate nscarbamoylase is feedback hibited by CTP

Asparagine is a key nitrogen donor during ring formation

Treemap Bar

1 of 2