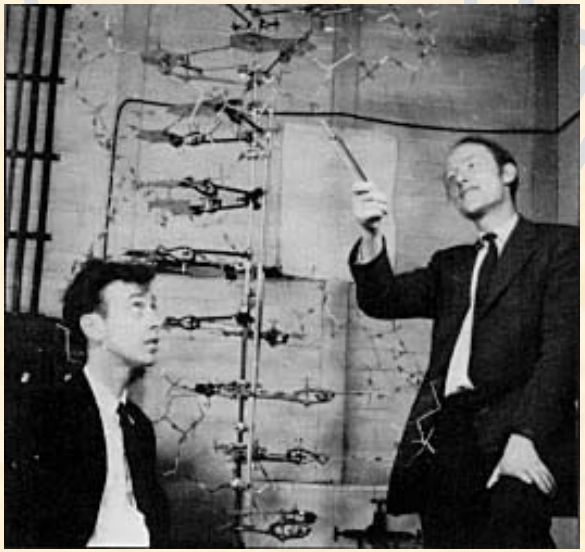
METABOLISM:

Structure and Metabolism of Nucleotide

USMAN SUMO FRIEND TAMBUNAN
ARLI ADITYA PARIKESIT
RIDO UTOMO



Nucleotide Function

- Building blocks for DNA and RNA
- Intracellular source of energy – Adenosine triphosphate (ATP)
- Second messengers – Involved in intracellular signaling (e.g. cyclic adenosine monophosphate [cAMP])
- Intracellular signaling switches (e.g. G-proteins)

Structure of a Nucleotide

- Despite the complexity and diversity of life the structure of DNA is dependent on only 4 different nucleotides
- Diversity is dependent on the nucleotide sequence

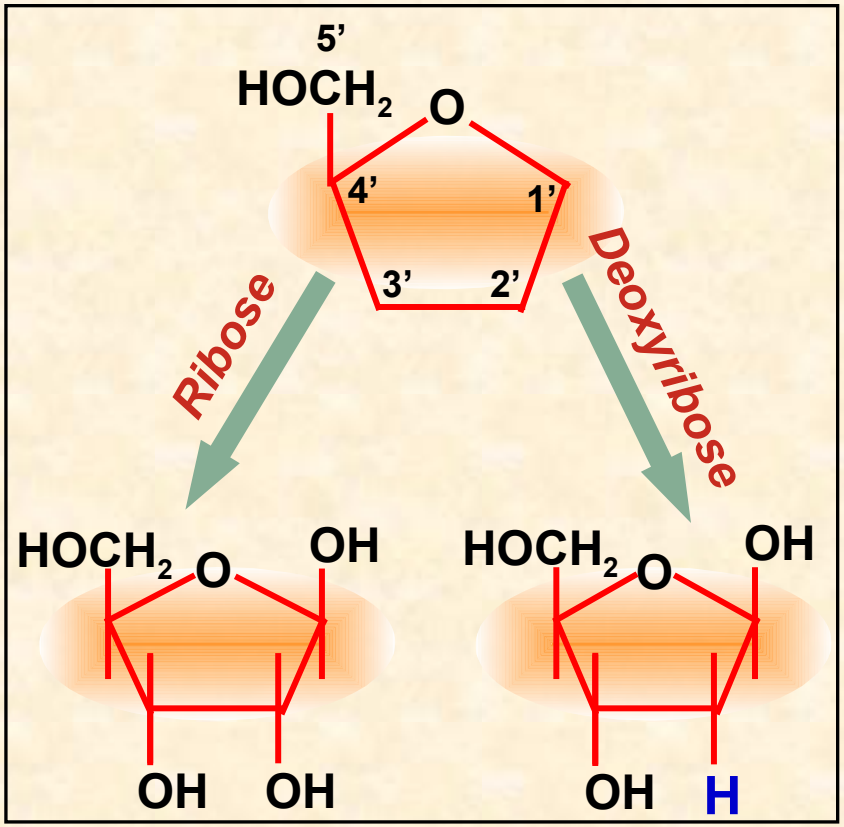
All nucleotides are 2 ring structures composed of:

5-carbon sugar :	β-D-ribose (RNA) β-D-deoxyribose (DNA)
Base	Purine Pyrimidine
Phosphate group	A nucleotide **WITHOUT** a phosphate group is a **NUCLEOSIDE**

Structure of a Nucleotide: **Sugar**

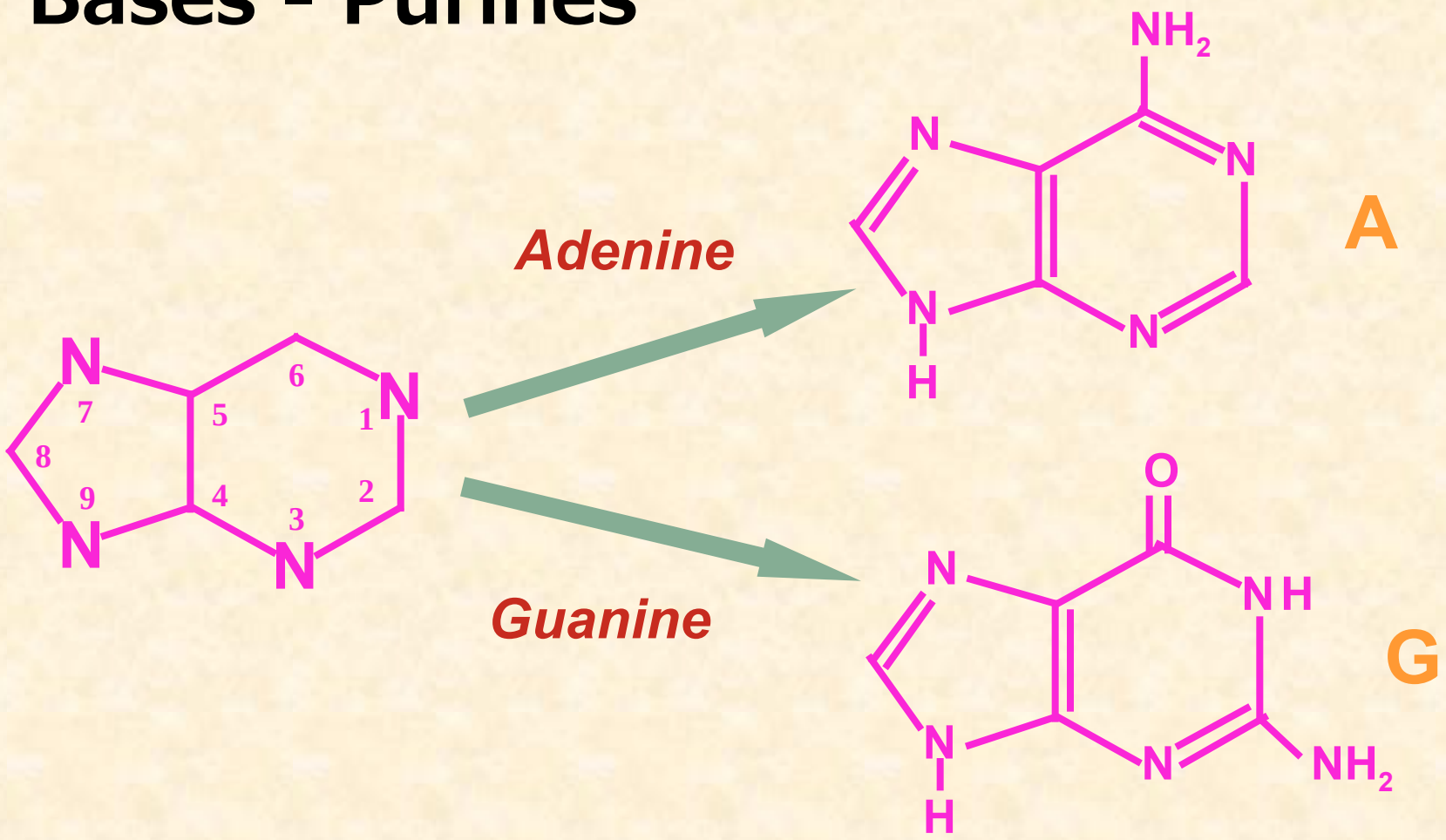
A nucleotide is made of 3 components:

- A Pentose sugar
- This is a 5 carbon sugar
- The sugar in DNA is deoxyribose (lacks a 2' –OH group)
- The sugar in RNA is ribose



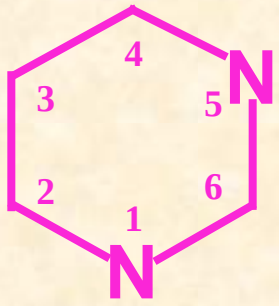
Structure of a Nucleotide:_

Bases - Purines



Nucleotide Structure – 2

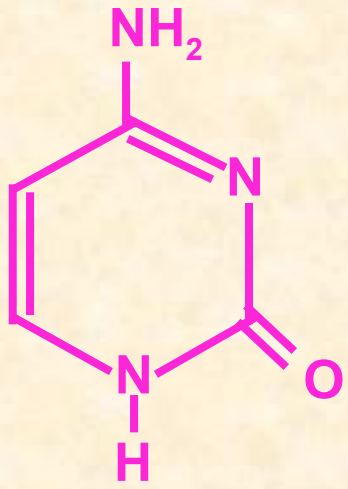
Bases – Pyrimidines



Thymine

Sytosine

T



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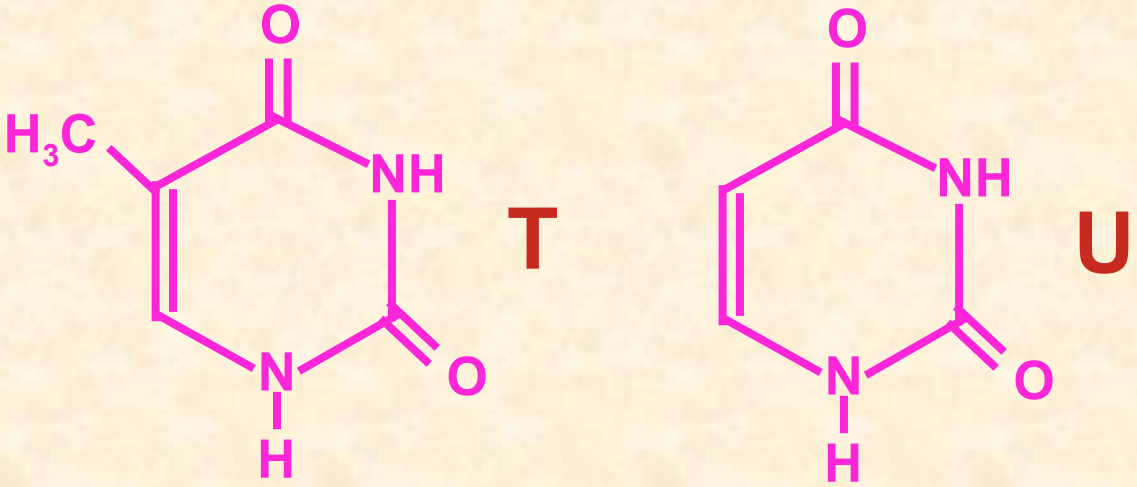
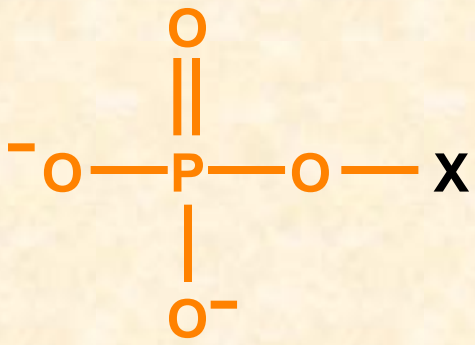
Nucleotide Structure: Bases – Pyrimidines

- Thymine is found ONLY in DNA.
- In RNA, thymine is replaced by uracil
- Uracil and Thymine are structurally similar



Phosphate Groups

- Phosphate groups are what makes a nucleoside a nucleotide
- Phosphate groups are essential for nucleotide polymerization

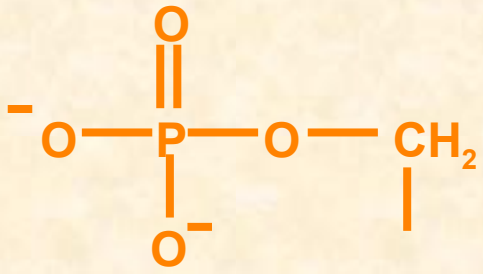


Basic structure

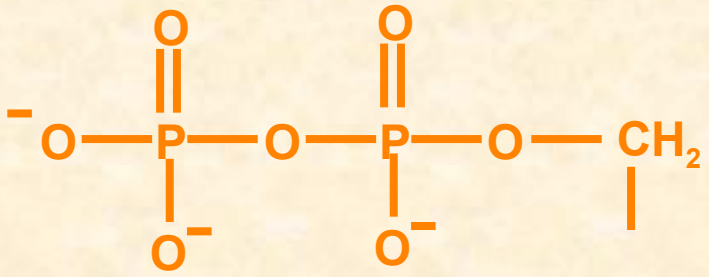
Phosphate Groups

Number of phosphate groups determines nomenclature

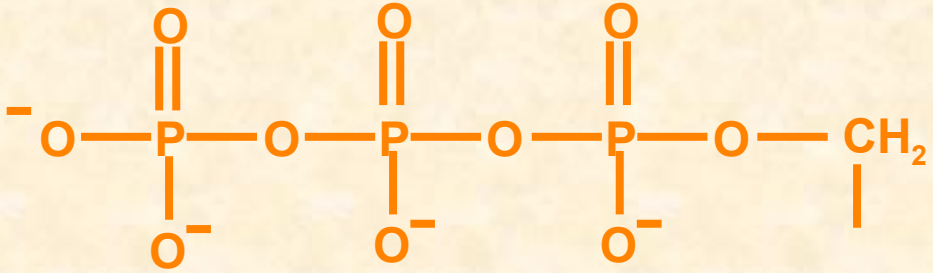
Monophosphate



Diphosphate

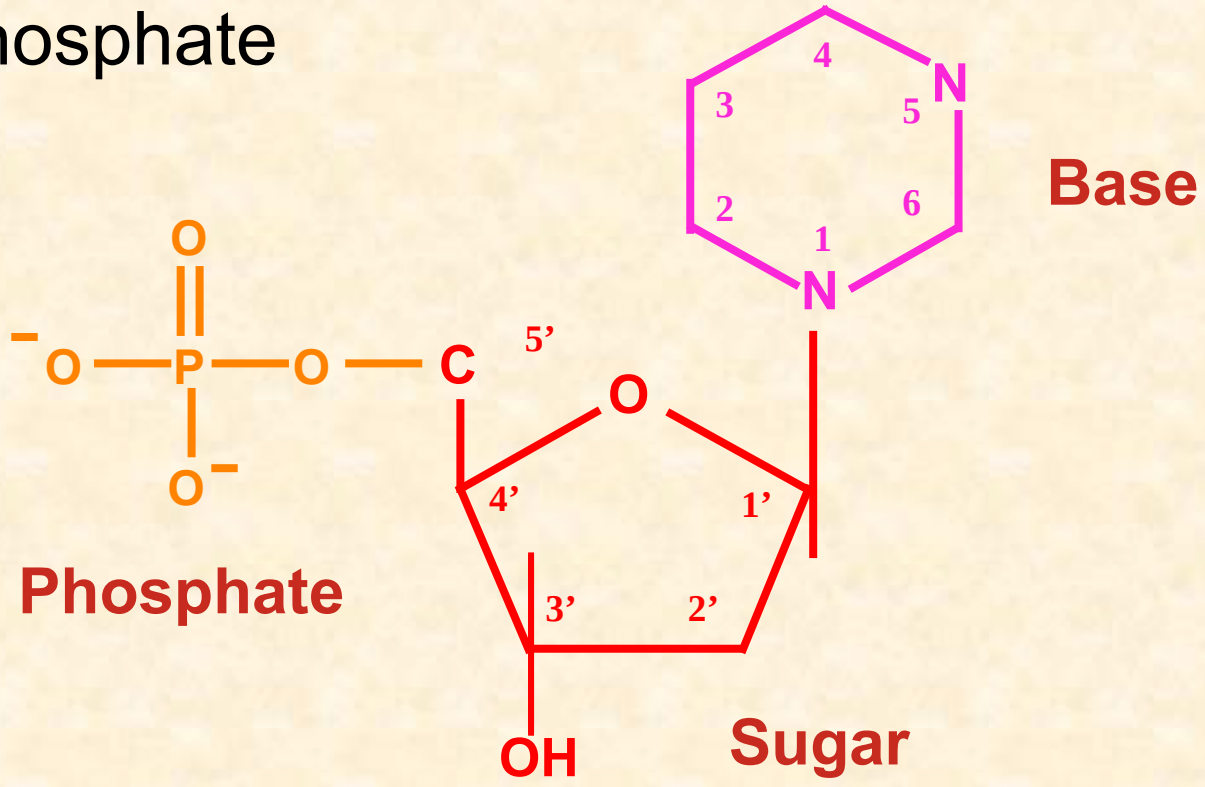


Triphosphate

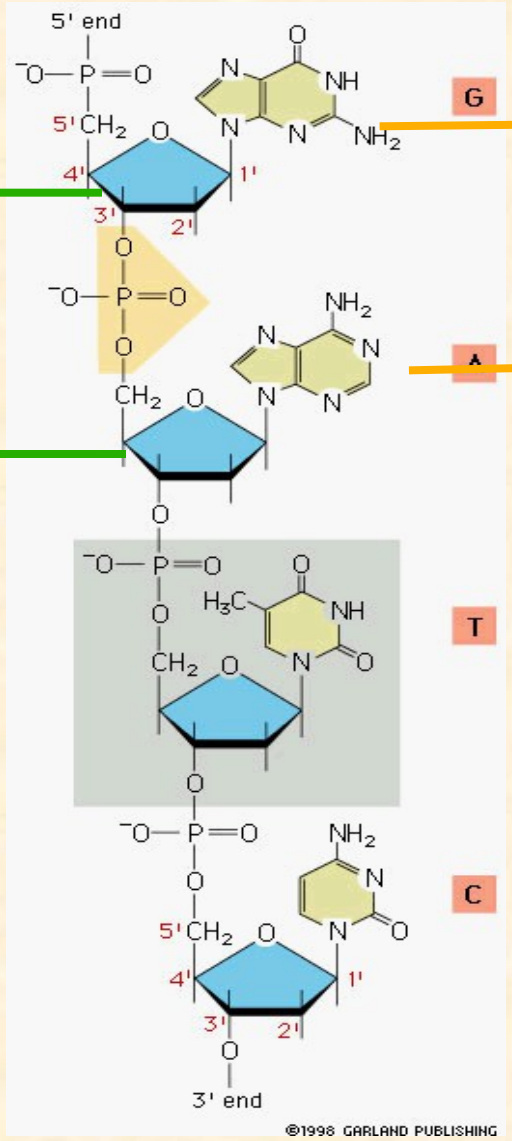


Base–Sugar–PO_4^{2-}

Monophosphate



Nucleic Acid Structure Polymerization



Sugar Phosphate "backbone"

Nucleotide

Nucleic Acid Structure:

"Base Pairing"

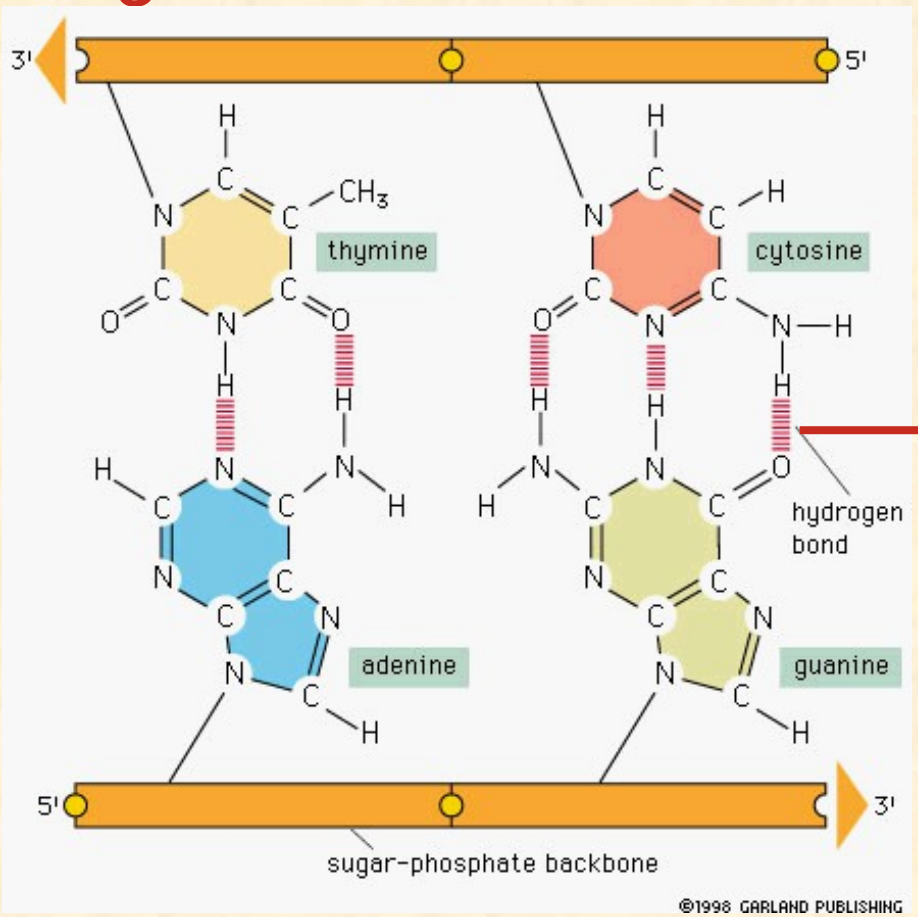
- RNA [normally] exists as a single stranded polymer
- DNA exists as a double stranded polymer
- DNA double strand is created by hydrogen bonds between nucleotides
- Nucleotides always bind to complementary nucleotides

A ⟷ T **(2 H-bonds)**

G ⟷ C **(3 H-bonds)**

Nucleic Acid Structure

"Base Pairing"



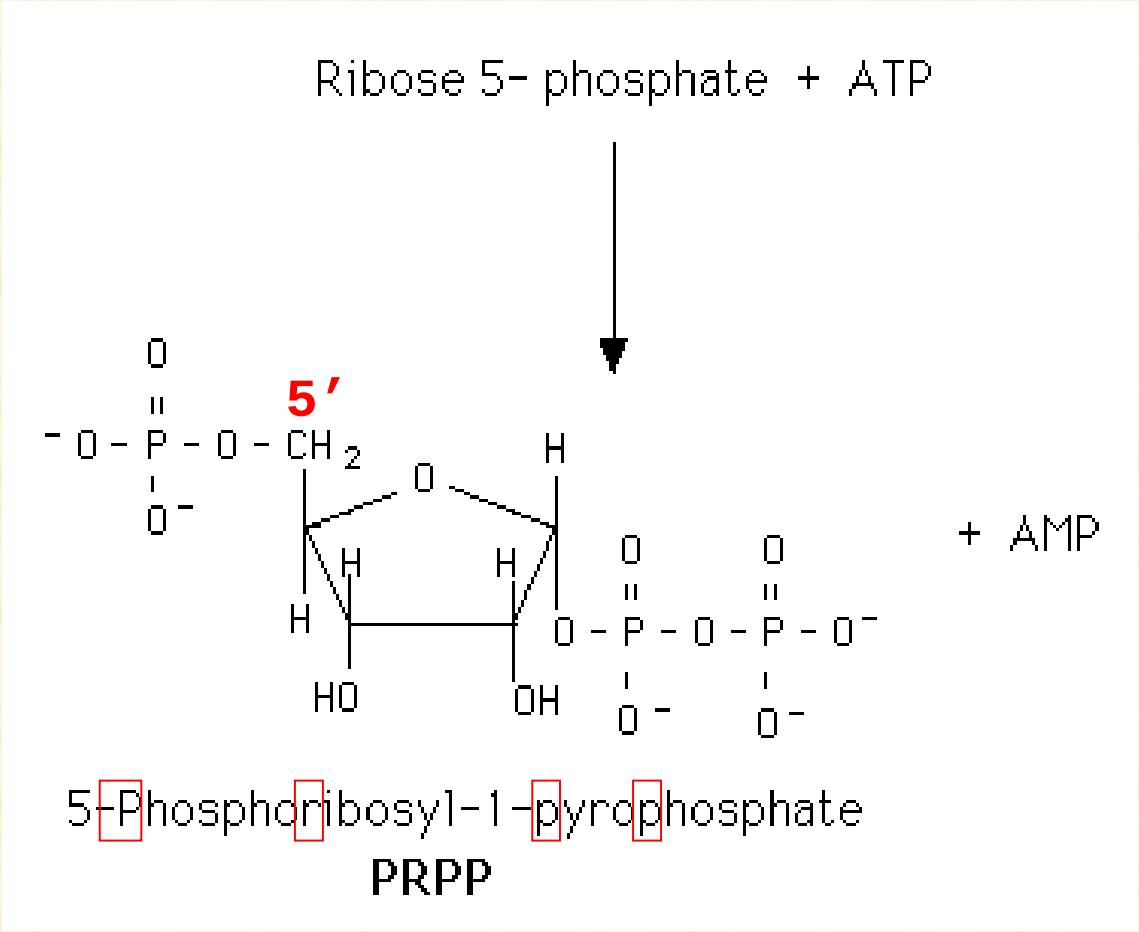
hydrogen bonds

Synthesis Pathways

For both purines and pyrimidines there are two means of synthesis (often regulate one another)

- de novo (from bits and parts)
- salvage (recycle from pre-existing nucleotides)

Many Steps Require an Activated Ribose Sugar (PRPP)

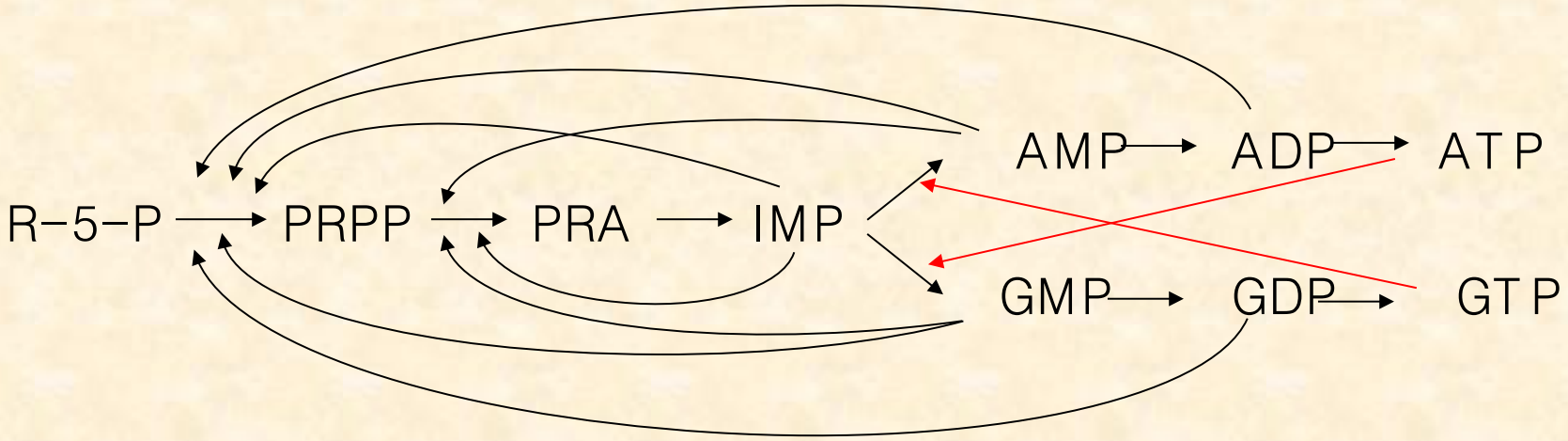


de novo Synthesis

- Committed step: This is the point of no return
- Occurs early in the biosynthetic pathway
- Often regulated by final product (feedback inhibition)

Purine Biosynthesis (de novo)

Feedback inhibitors: AMP, ADP, GMP, GDP, IMP



PRA: 5-phosphoribosyl-1-amine . activation inhibition

Salvage Pathway for Purines

Hypoxanthine + PRPP ⇌ IMP + PP_i

Guanine + PRPP ⇌ GMP + PP_i

Hypoxanthineguanosylphosphoribosyl transferase

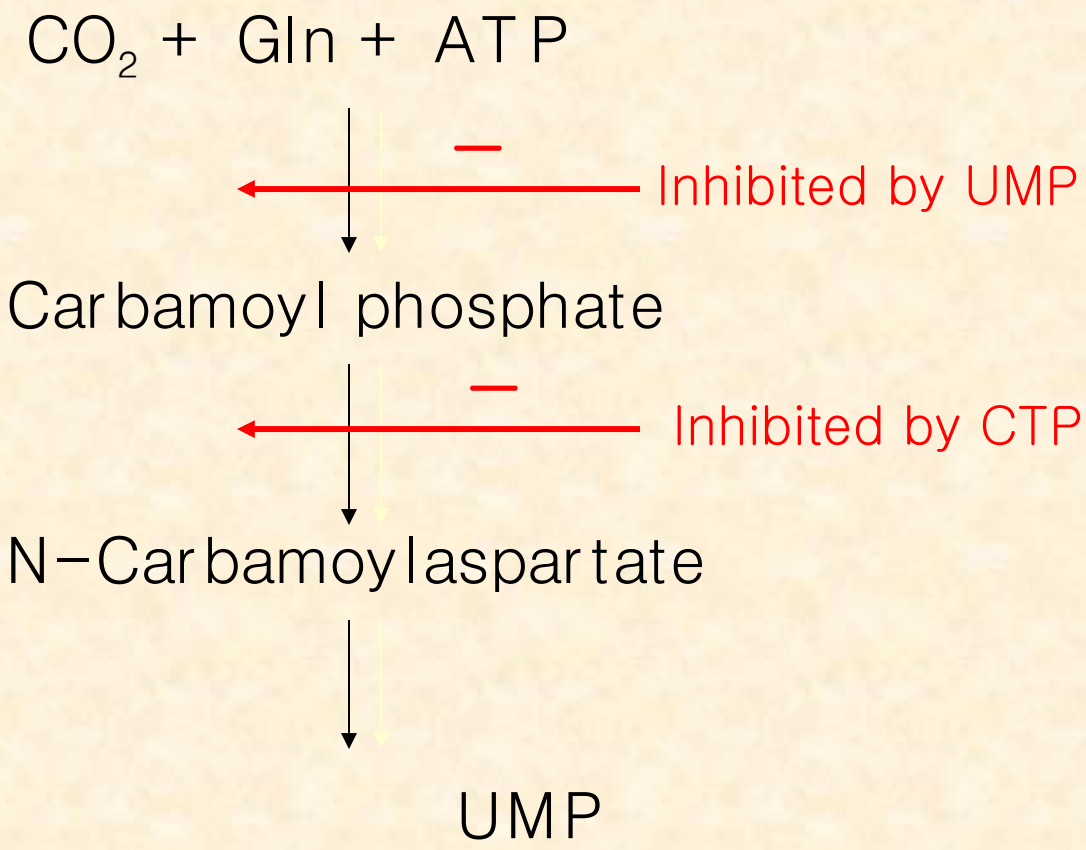
(HGPRTase)

Adenine + PRPP ⇌ AMP + PPi

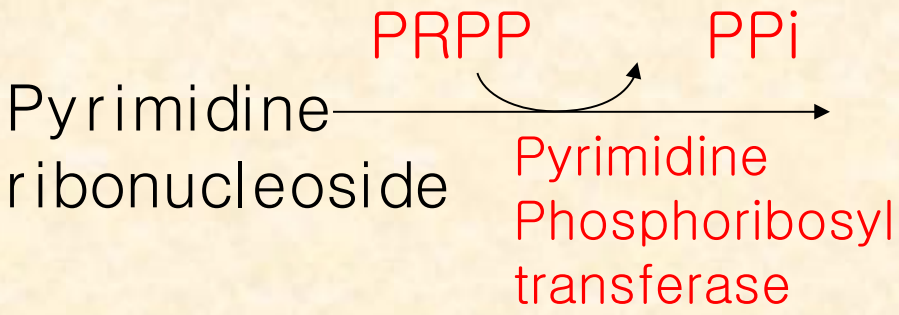
Adeninephosphoribosyl transferase

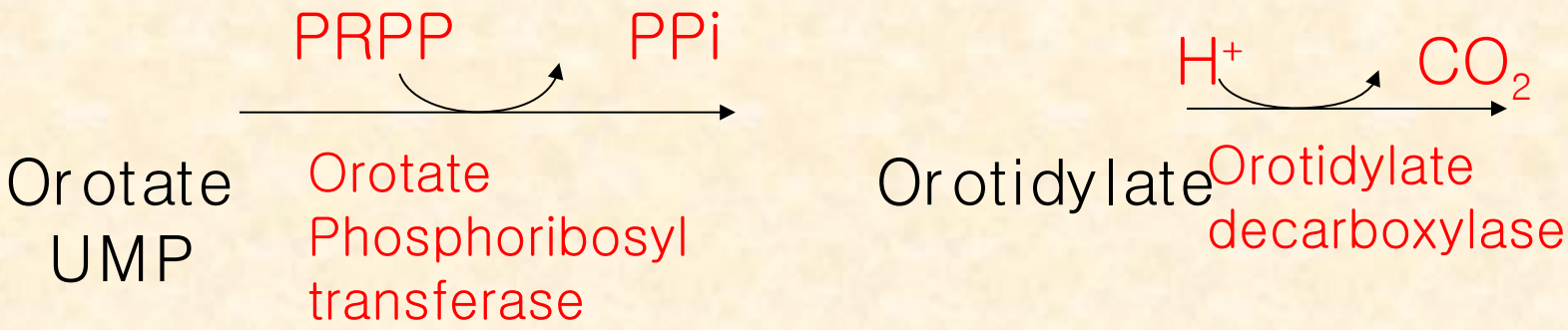
(APRTase)

Regulation of pyrimidine nucleotide synthesis



Salvage pathway for pyrimidine nucleotide biosynthesis





Conclusion

- Nucleotides are composed of 5-carbon sugar, Base, and Phosphate group
- For both purines and pyrimidines there are two means of synthesis:

- ❑ de novo
- ❑ salvage

References

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