

*Faculté de Médecine Paris7*

*Biochimie & Biologie Moléculaire PCEM2*

## **BASES PURIQUES / BASES PYRIMIDIQUES**

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**Département de Génétique, Hôpital Robert Debré**

## BASES AZOTEES

Bases azotées

Nucléotides

Bases modifiées

## BIOSYNTHESE DES NUCLEOTIDES

Biosynthèse *de novo* des pyrimidines

Biosynthèse *de novo* des purines

Inhibiteurs pharmacologiques

- anticancéreux
- antiretroviraux

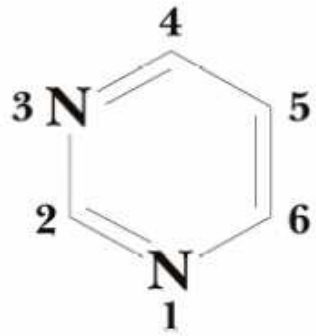
## CATABOLISME/RECYCLAGE DES NUCLEOTIDES

Catabolisme des pyrimidines

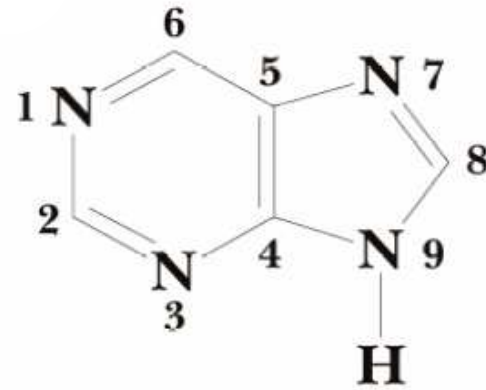
Catabolisme des purines

Pathologies : la goutte

# LES BASES AZOTEES



pyrimidine

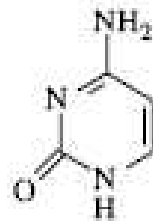


purine

# LES BASES AZOTEES

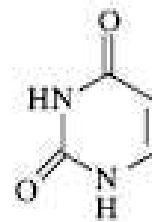


pyrimidine



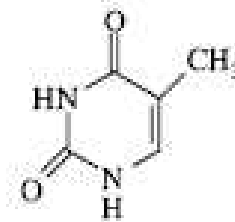
cytosine

2-oxy-4-aminopyrimidine



uracile

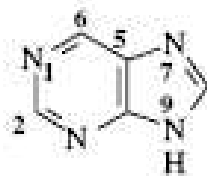
2,4-dioxyrimidine



thymine

5-méthyl-2,4-dioxyrimidine

bases pyrimidiques



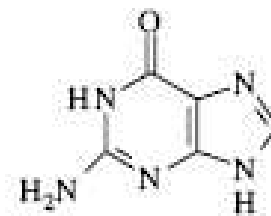
purine

imidazopyrimidine



adénine

6-aminopurine



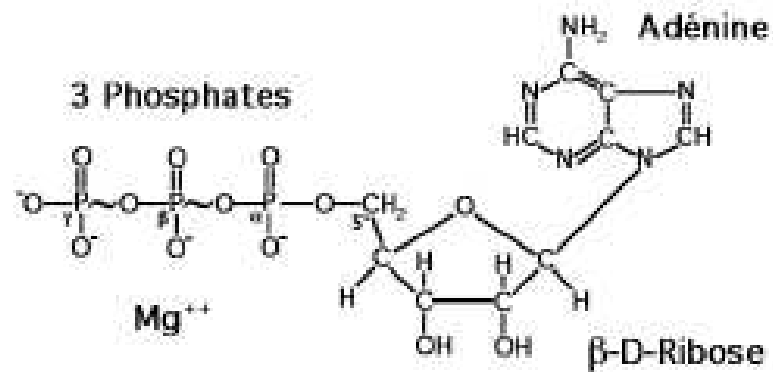
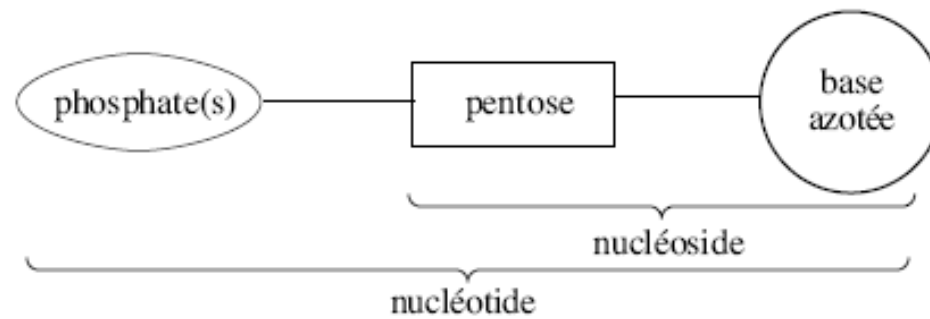
guanine

2-amino-6-oxyurine

bases puriques

# LES NUCLEOTIDES

# NUCLEOTIDES

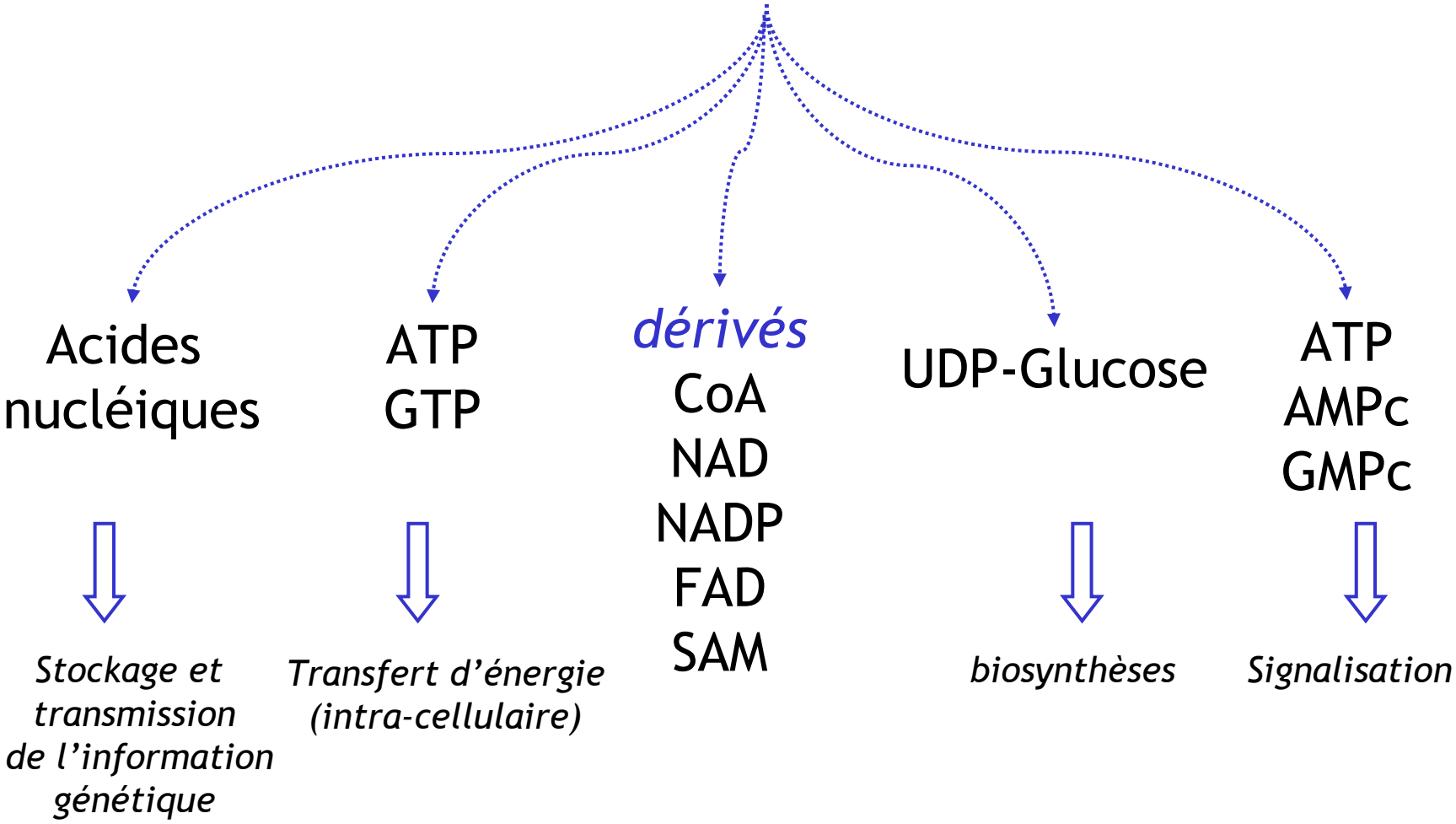


**Adénosine Tri Phosphate**

# NUCLEOTIDES

Bases	Nucléosides	Nucléosides 5'-mono, di, triphosphates	Unités nucléotidiques des acides nucléiques
A = Adénine	(désoxy-) adénosine	AMP, ADP, ATP dAMP, dADP, dATP	(d-) adénylate
G = Guanine	(désoxy-) guanosine	GMP, GDP, GTP dGMP, dGDP, dGTP	(d-) guanylate
C = Cytosine	(désoxy-) cytidine	CMP, CDP, CTP dCMP, dCDP, dCTP	(d-) cytidylate
U = Uracile	uridine	UMP, UDP, UTP	uridylate
T = Thymine	désoxy- thymidine	dTMP, dTDP, dTTP	d-thymidylate

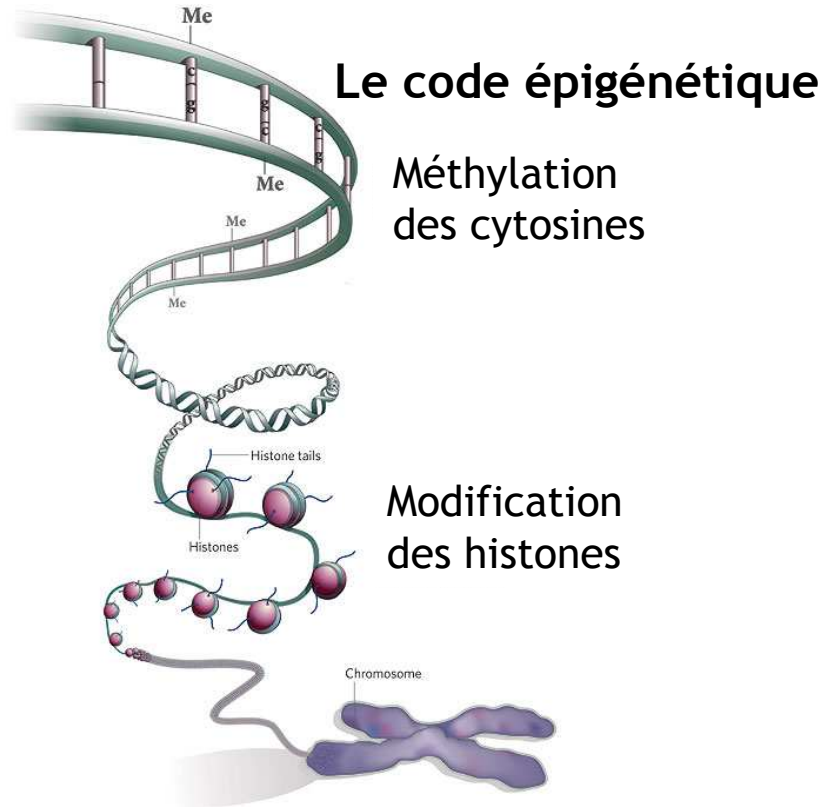
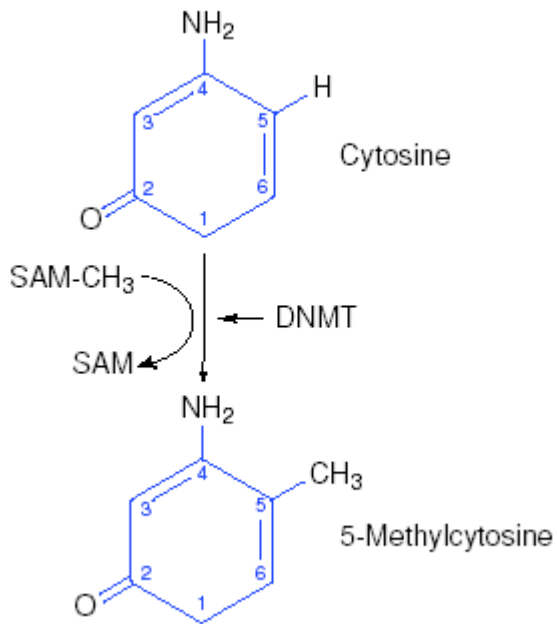
# NUCLEOTIDES





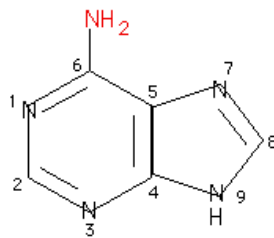
# BASES MODIFIEES

## 5-Methylcytosine

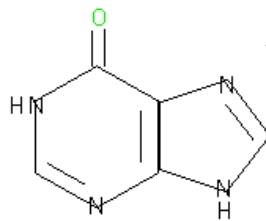


# BASES MODIFIEES

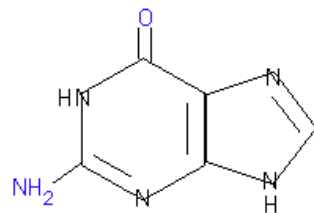
## L'ARN de transfert (ARnt)



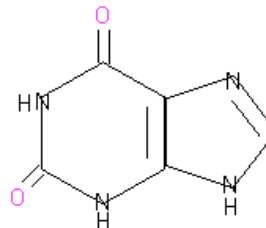
Adenine



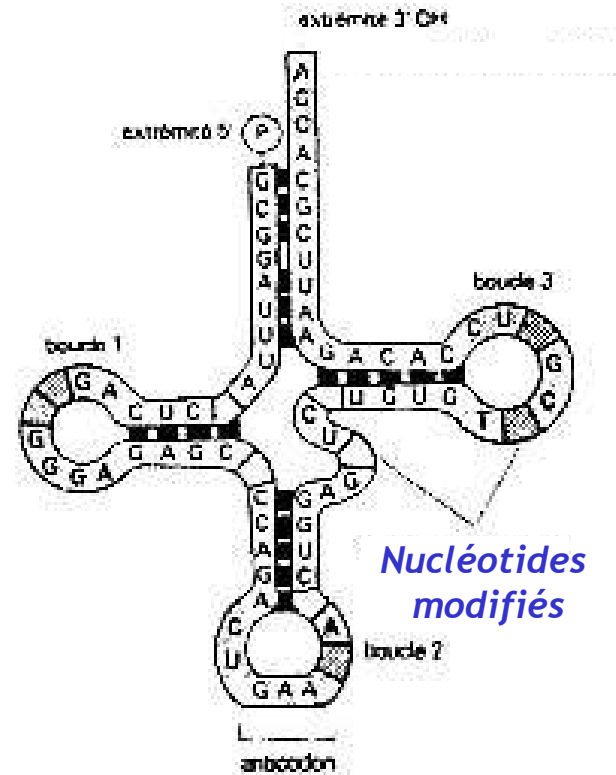
Hypoxanthine



Guanine



Xanthine



# BASES MODIFIEES

## Bromo-desoxyuridine (BrdU)

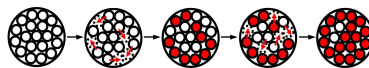
*Un outil pour mesurer l'index mitotique*

### *Exemple d'expérience :*

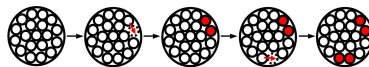
*Quel est le niveau de renouvellement des cellules  $\beta$  du pancréas (modèle souris) ?*

- Incubation en présence de BrdU
- Marquage par des Ac anti insuline et anti-BRDU

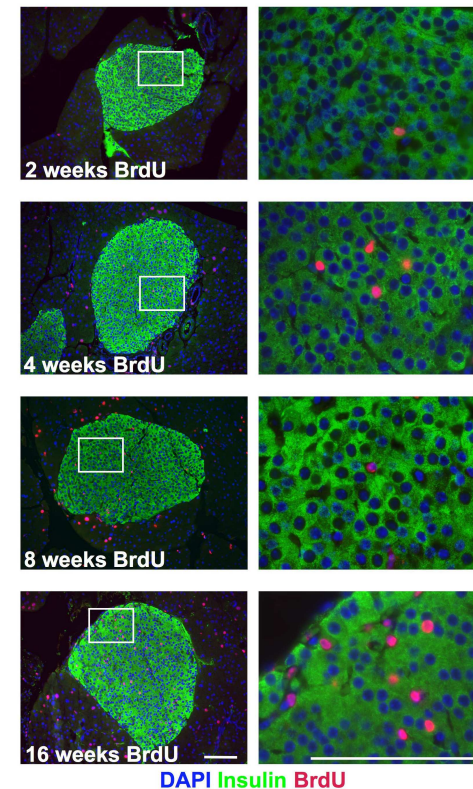
*Si renouvellement rapide*



*Si renouvellement lent*



→ *Les cellules  $\beta$  du pancréas de la souris adulte sont principalement en  $G_0$*

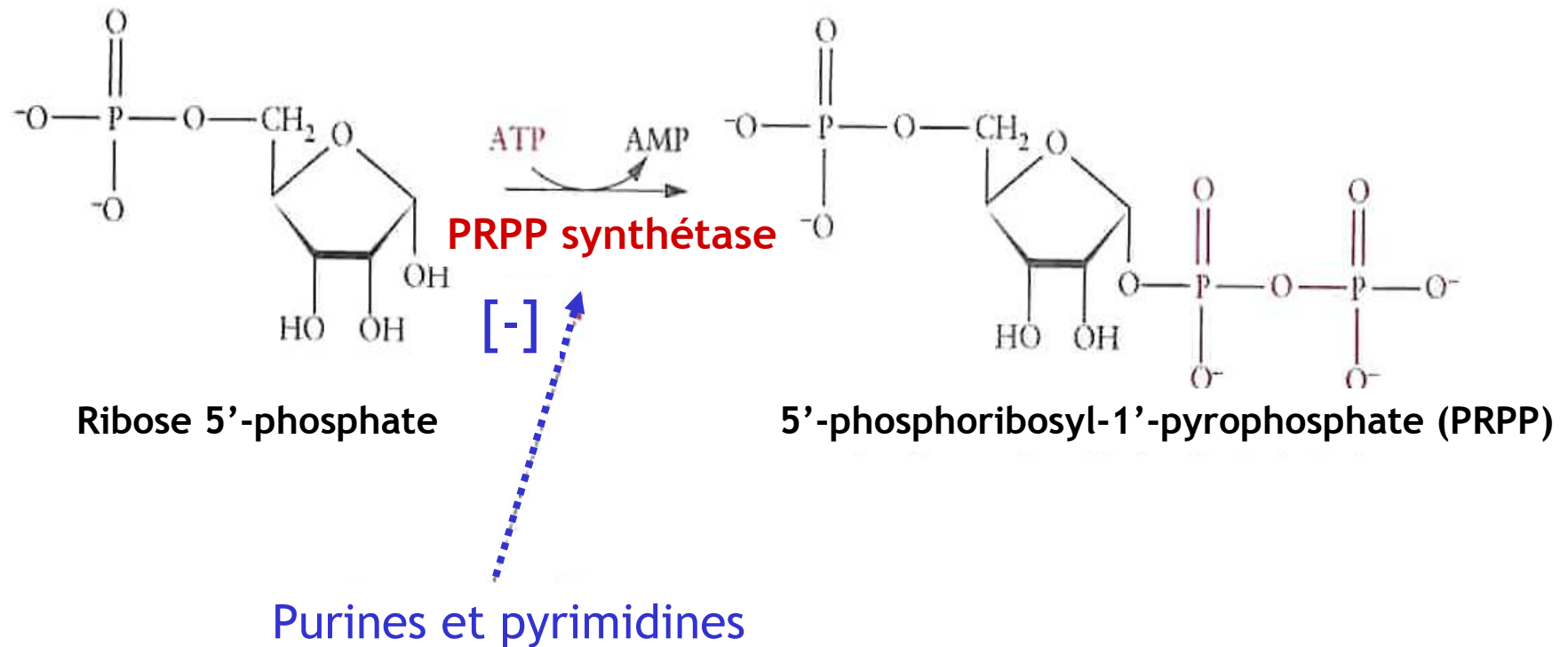


Histologie des cellules  $\beta$  du pancréas

# **BIOSYNTHESE *DE NOVO* DES NUCLEOTIDES**

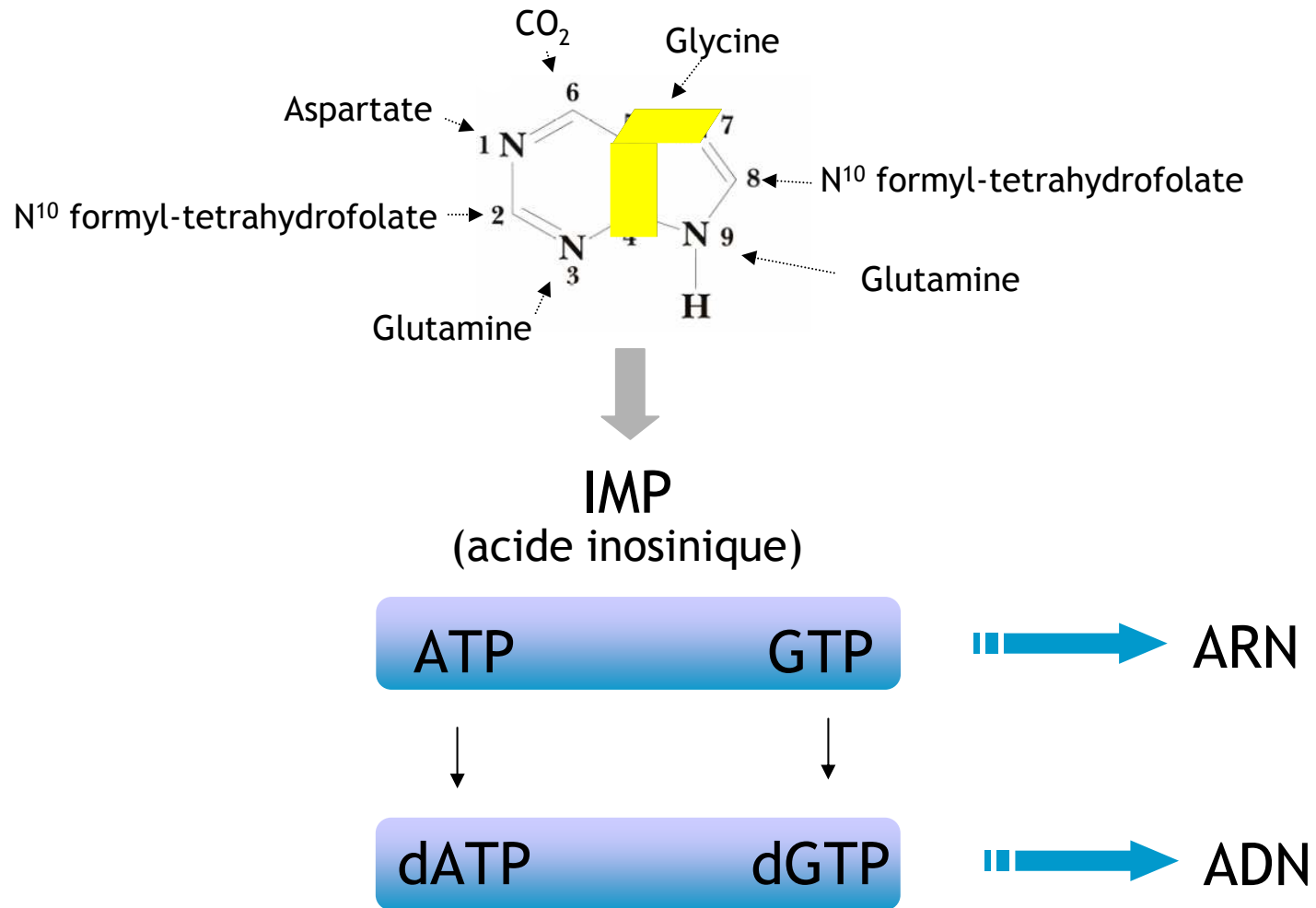
# SYNTHÈSE *DE NOVO* DES RIBONUCLEOTIDES PURIQUES ET PYRIMIDIQUES

## *Apport du ribose 5-Phosphate*



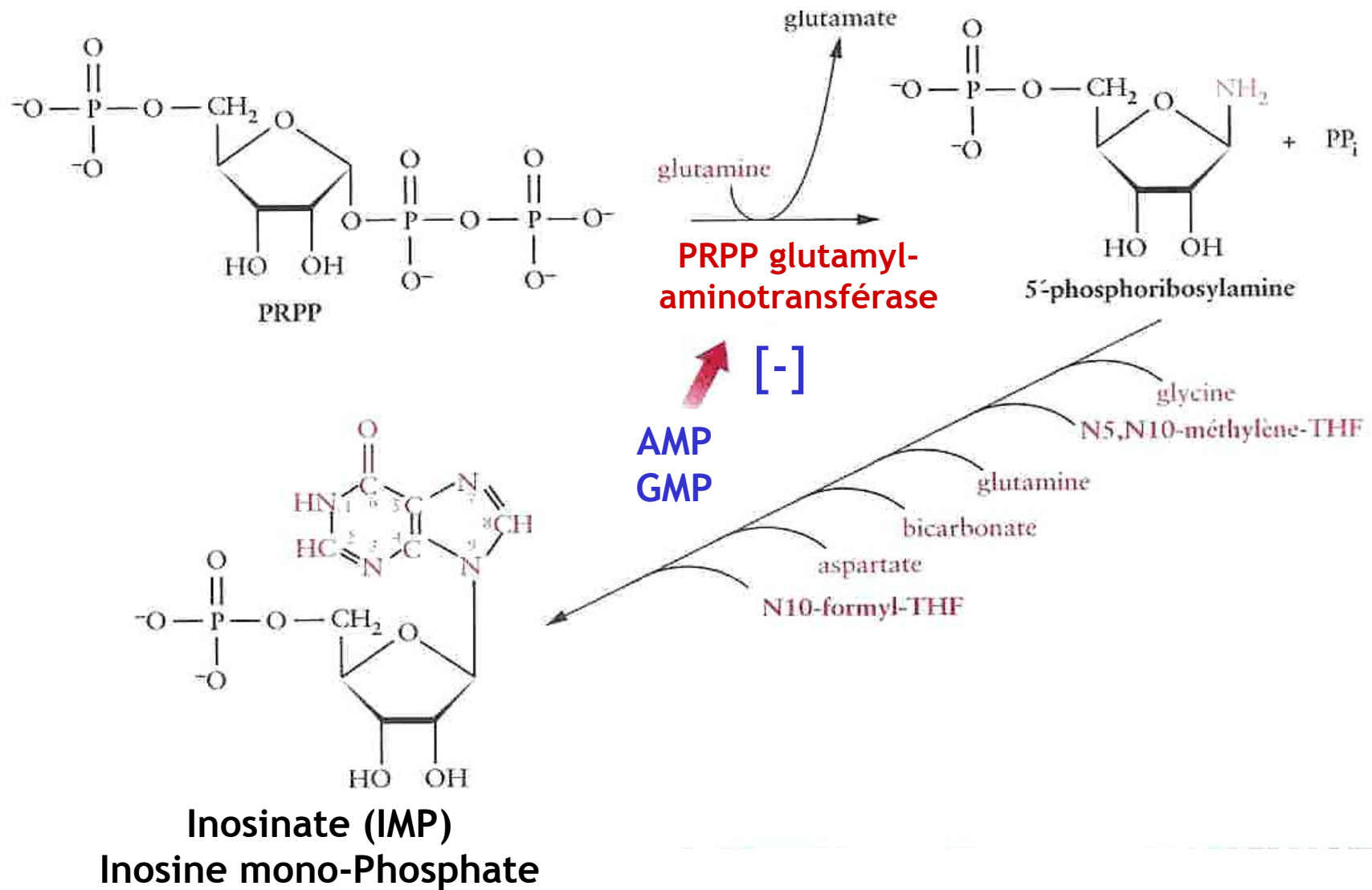
## **BIOSYNTHESE *DE NOVO* DES PURINES**

# SYNTHESE DE NOVO DES PURINES



# BIOSYNTHESE *DE NOVO* DES RIBONUCLEOTIDES PURIQUES (I)

## *Formation d'IMP*

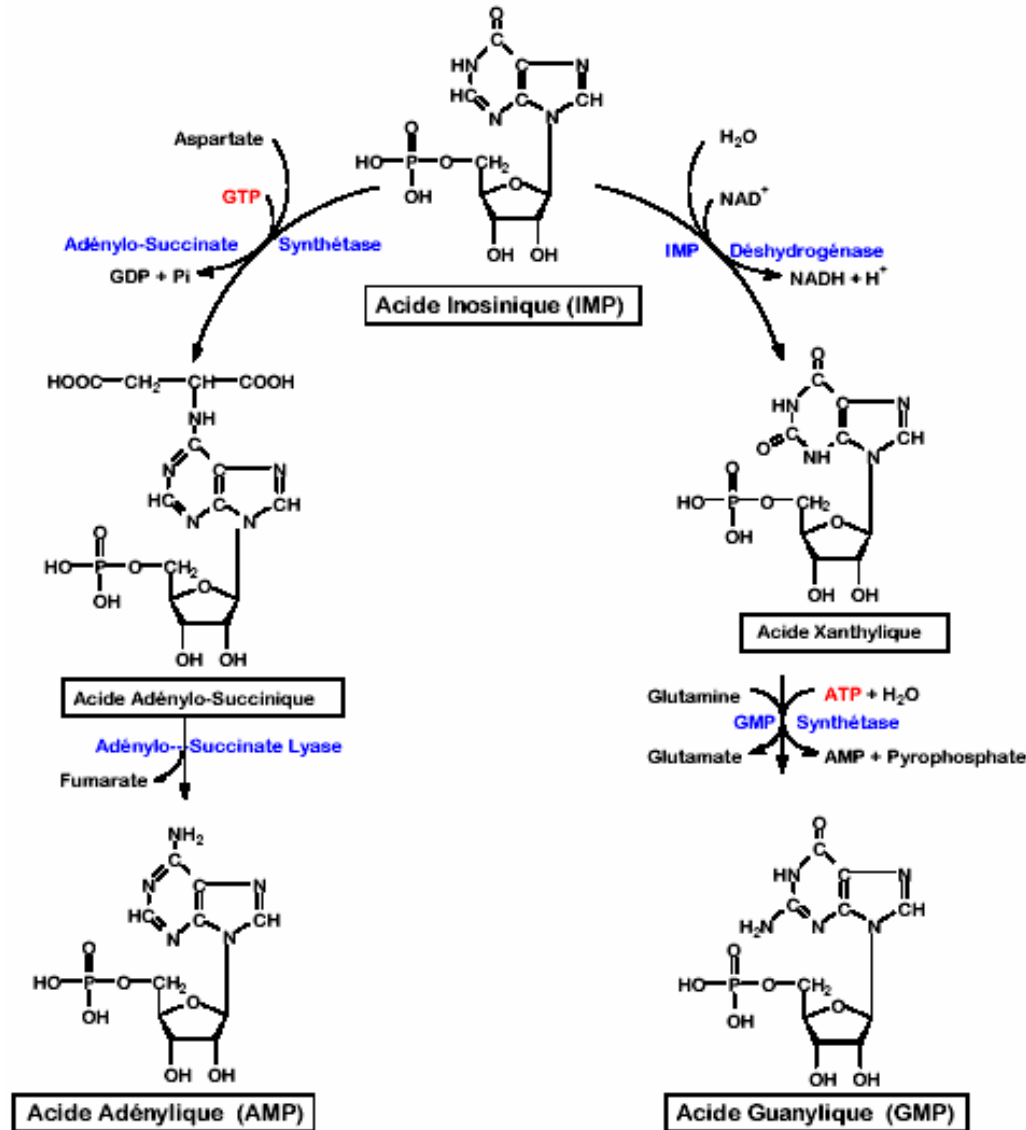




# BIOSYNTHESE *DE NOVO* DES RIBONUCLEOTIDES PURIQUES (II)

## *Transformation de l'IMP en AMP et GMP*

*Amination*



*Oxydation*

*Amination*

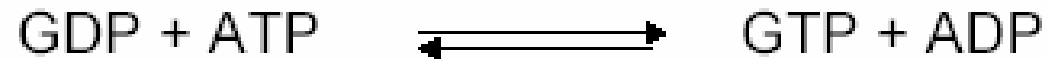
# BIOSYNTHESE *DE NOVO* DES RIBONUCLEOTIDES PURIQUES (III)

## *Phosphorylation des nucléosides mono-phosphate*

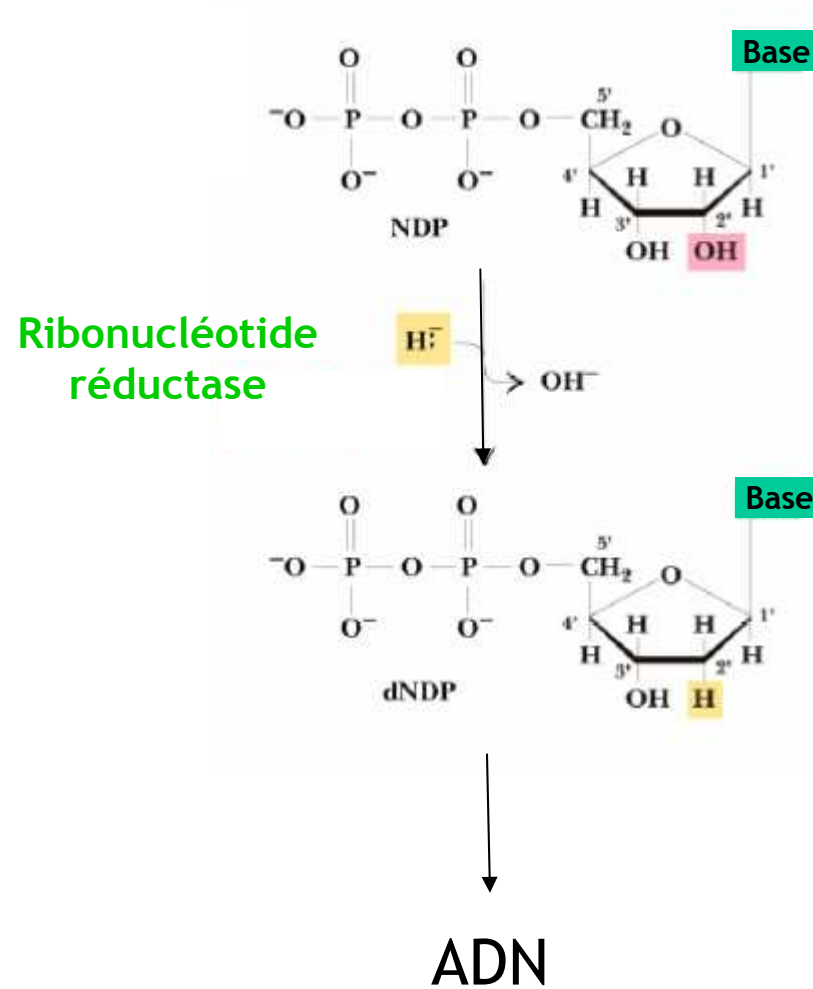
### Nucléosides 5' monophosphates kinases



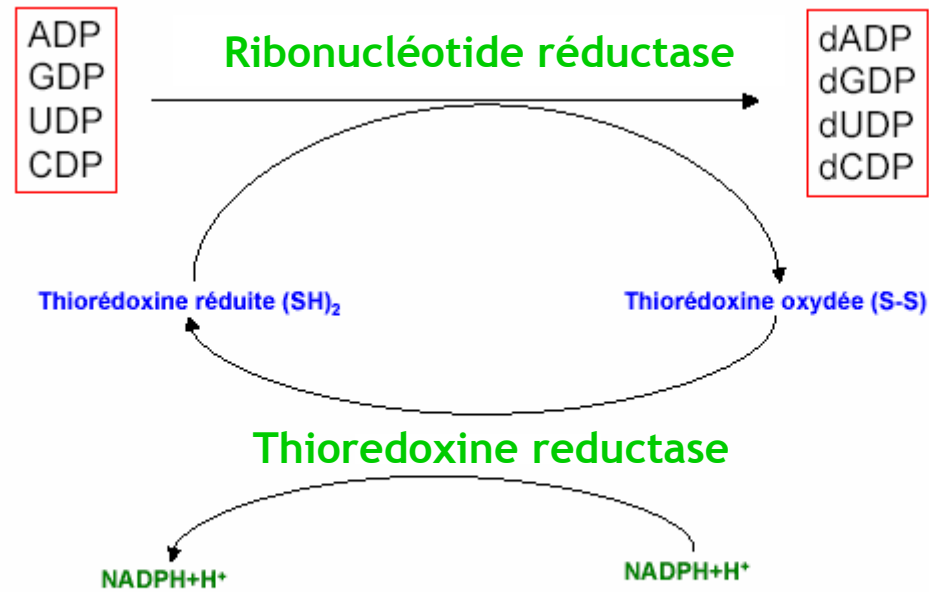
### Nucléosides 5' diphosphates kinases



# BIOSYNTHESE DES DESOXY-RIBONUCLEOTIDES



# BIOSYNTHESE DES DESOXY-RIBONUCLEOTIDES



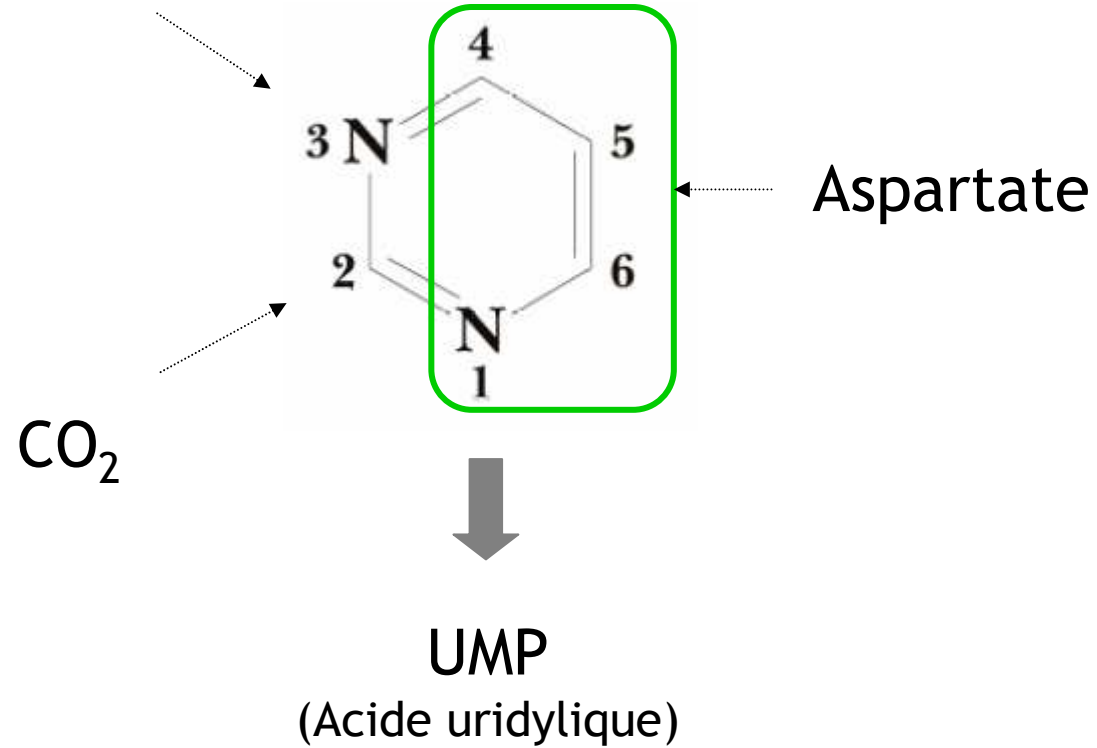
Un système de régulation permet une production équilibrée des 4 dNDP nécessaires à la synthèse de l'ADN

# **BIOSYNTHESE *DE NOVO* DES PYRIMIDINES**

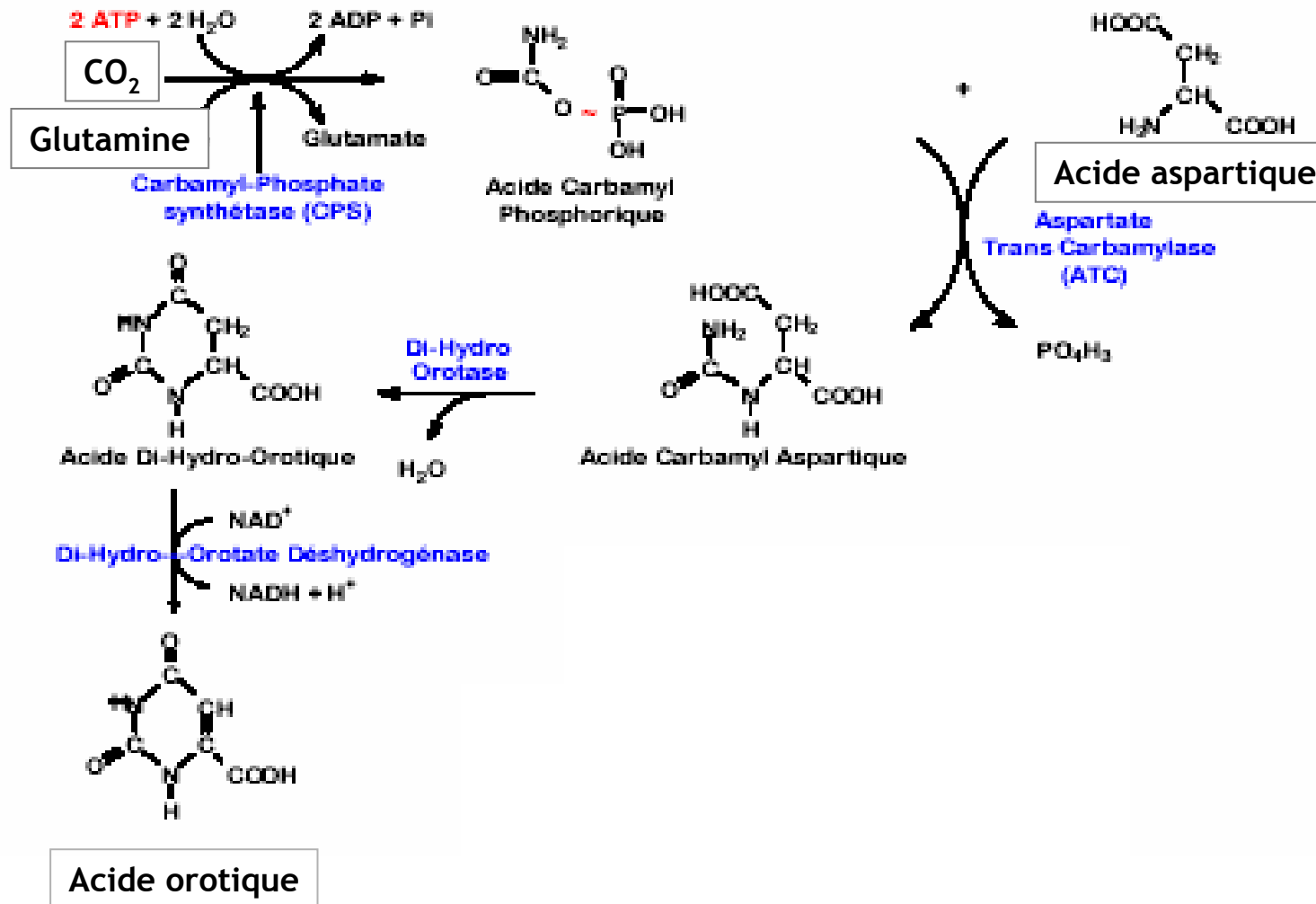
# BIOSYNTHESE *DE NOVO* DES PYRIMIDINES

## *Les précurseurs*

Glutamine

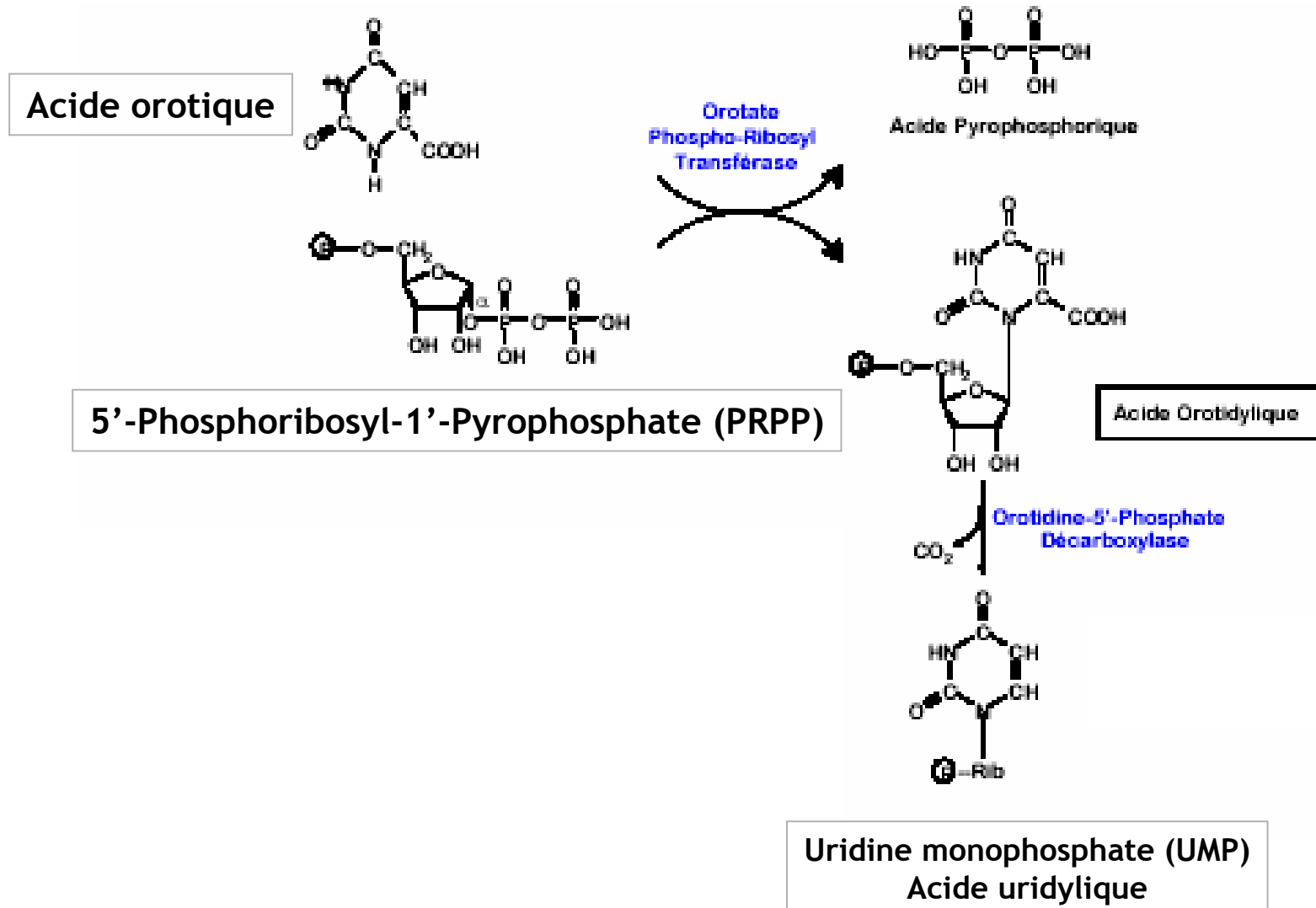


# BIOSYNTHESE *DE NOVO* DES PYRIMIDINES (I)



# BIOSYNTHESE *DE NOVO* DES PYRIMIDINES (II)

## *Production d'UMP*

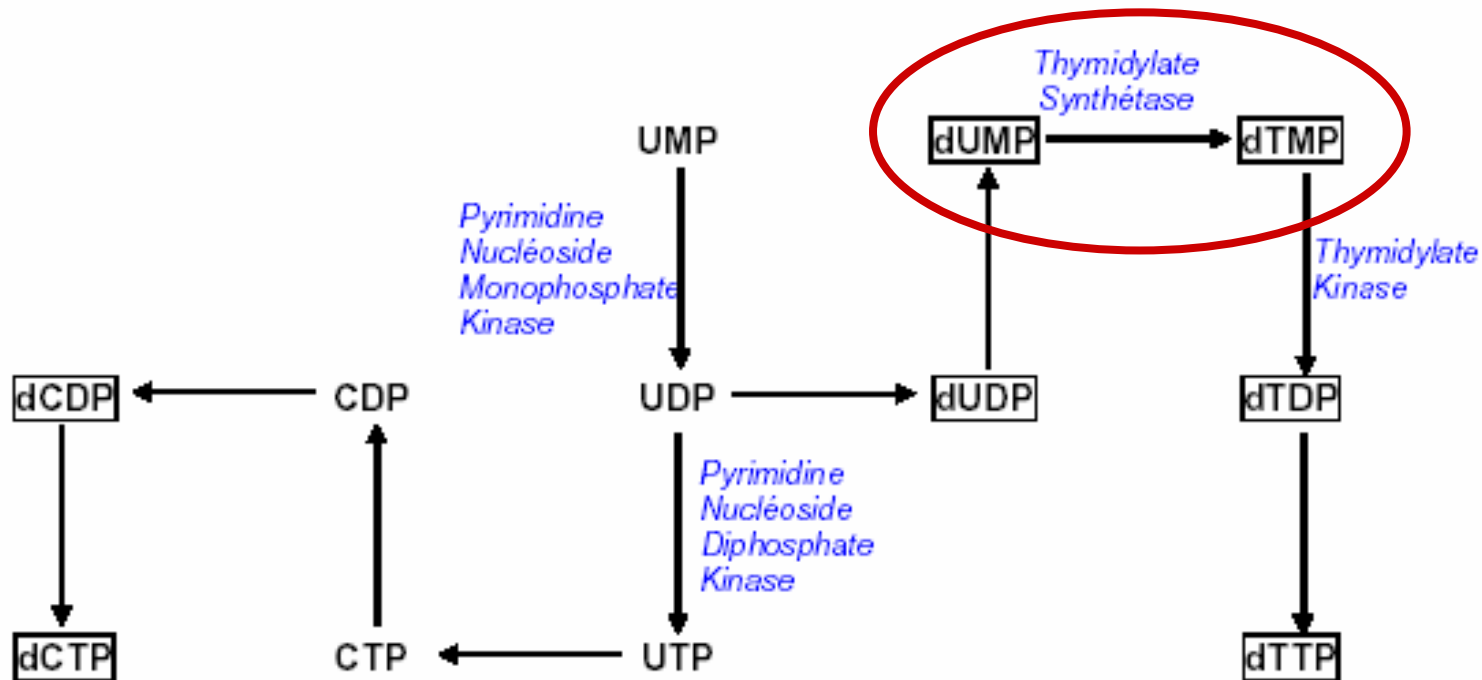




# BIOSYNTHESE *DE NOVO* DES PYRIMIDINES (III)

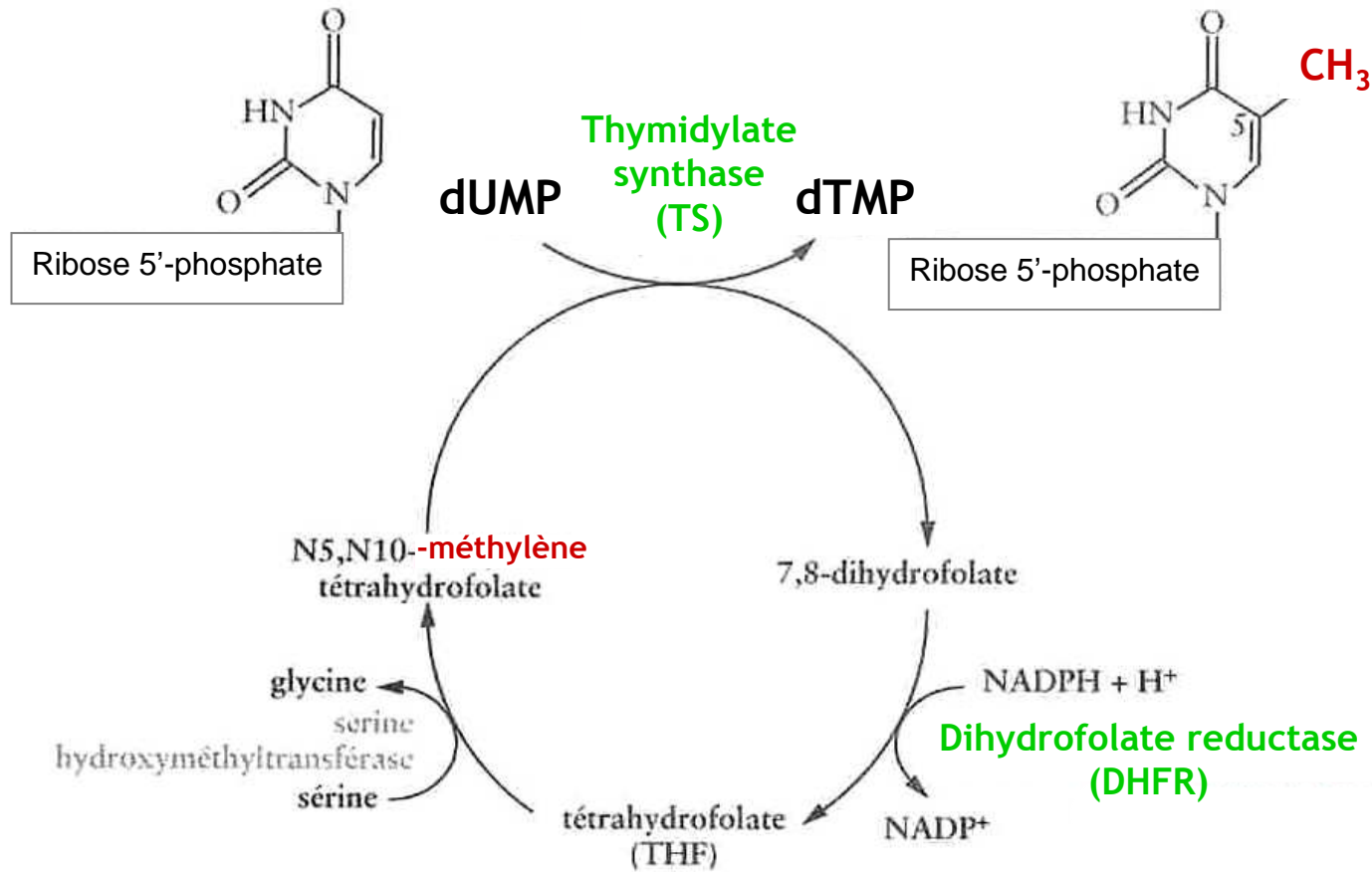
*Biosynthèse des desoxy-ribonucléotides*

*Phosphorylation des nucléosides mono-phosphate*



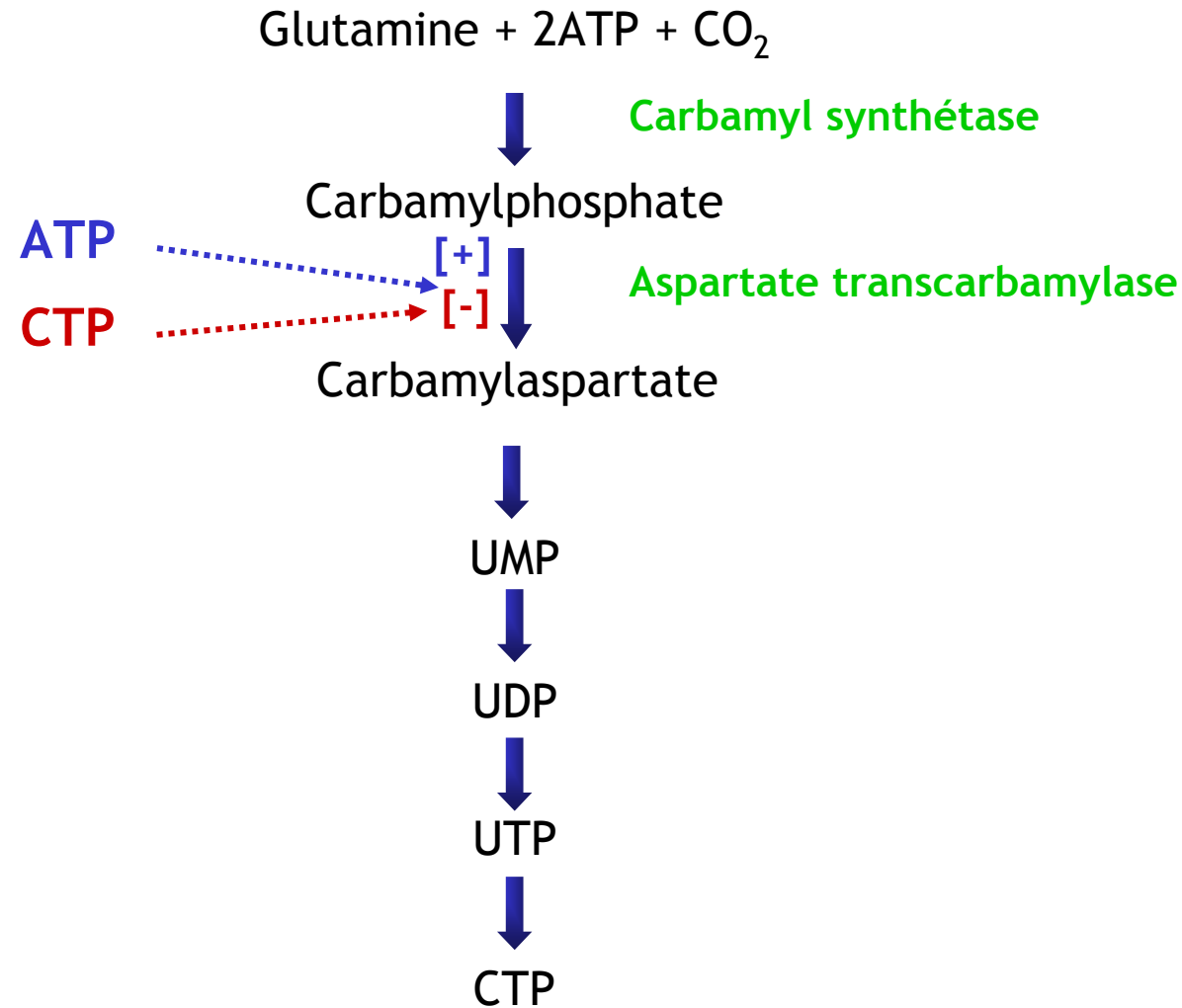
# BIOSYNTHESE DE LA (DEOXY)THYMIDINE

## *Méthylation du dUMP en dTMP*



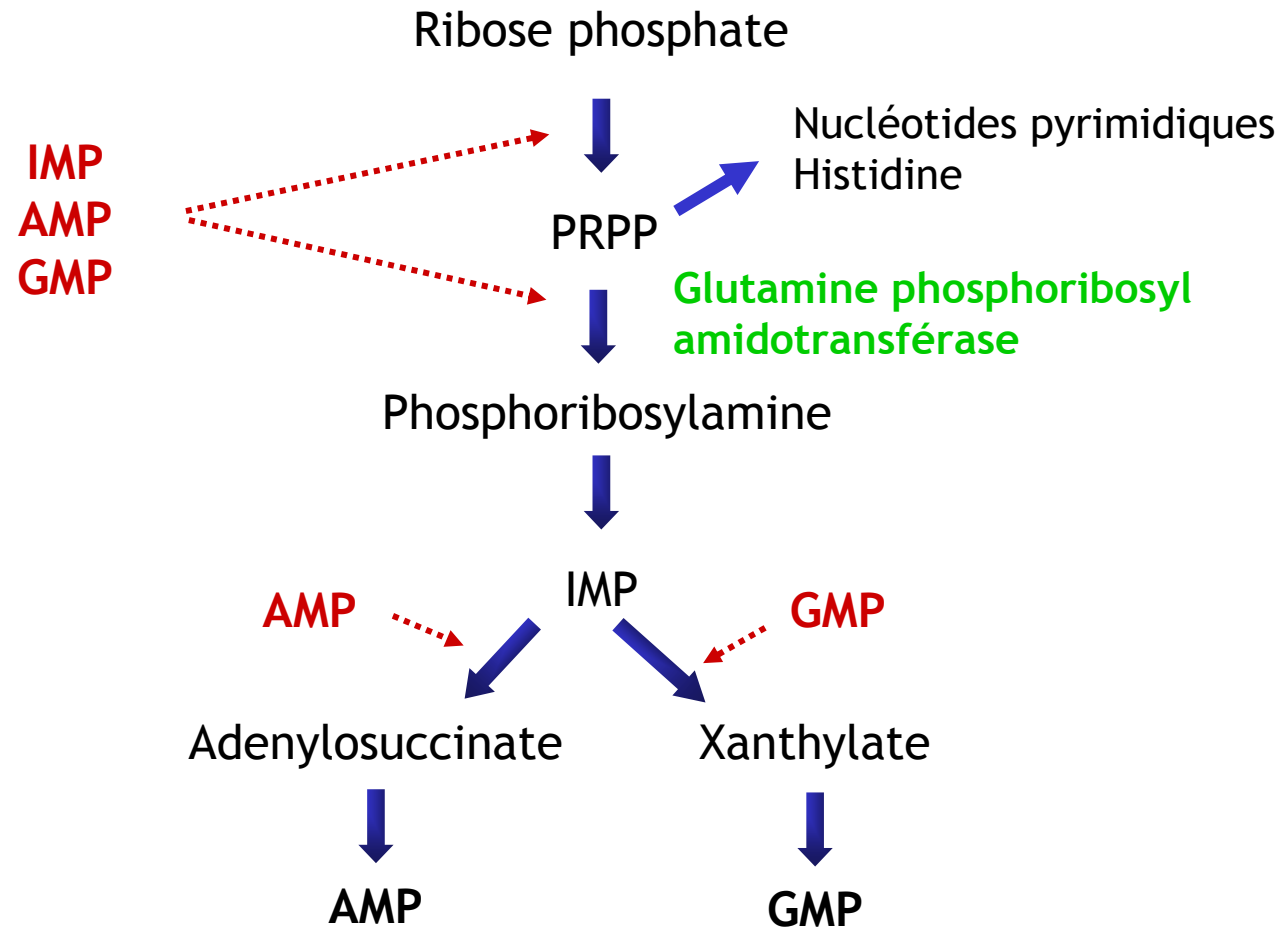
# REGULATION DE LA BIOSYNTHESE DES NUCLEOTIDES

## Nucléotides pyrimidiques

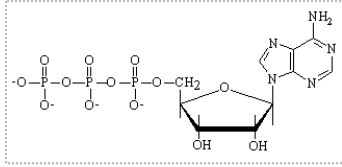


# REGULATION DE LA BIOSYNTHESE DES NUCLEOTIDES

## Nucléotides puriques



*Rétrocontrôles négatifs*

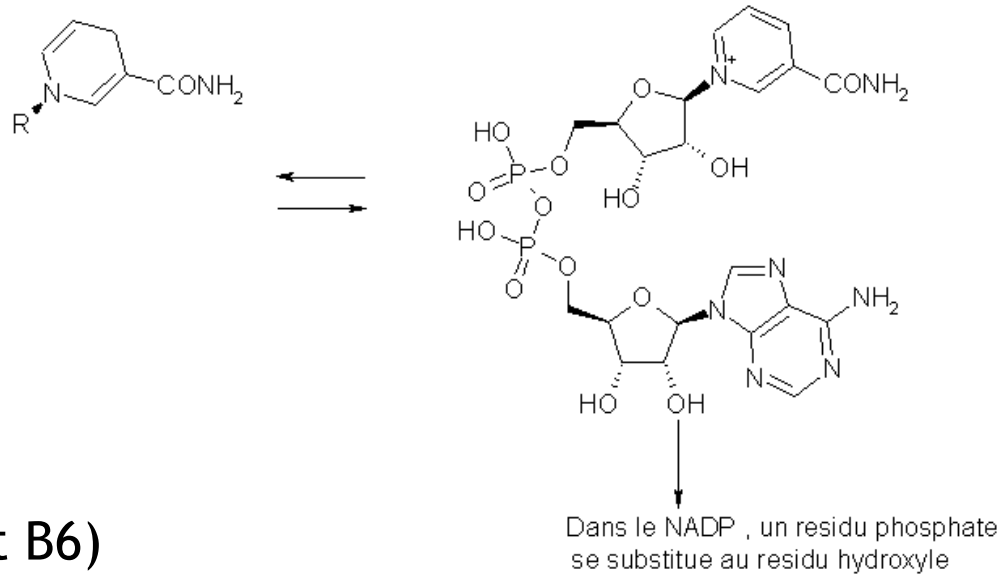


# COENZYMES D'OXYDO-REDUCTION

## NAD<sup>+</sup> ET NADP<sup>+</sup>

FORME REDUITE

FORME OXYDEE



*Précurseurs :*

ATP

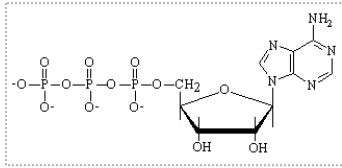
PRPP

Nicotinate (vit B6)

Glutamine (amide)

***Nicotinamide-Ribose-P-P-ribose-adénine***

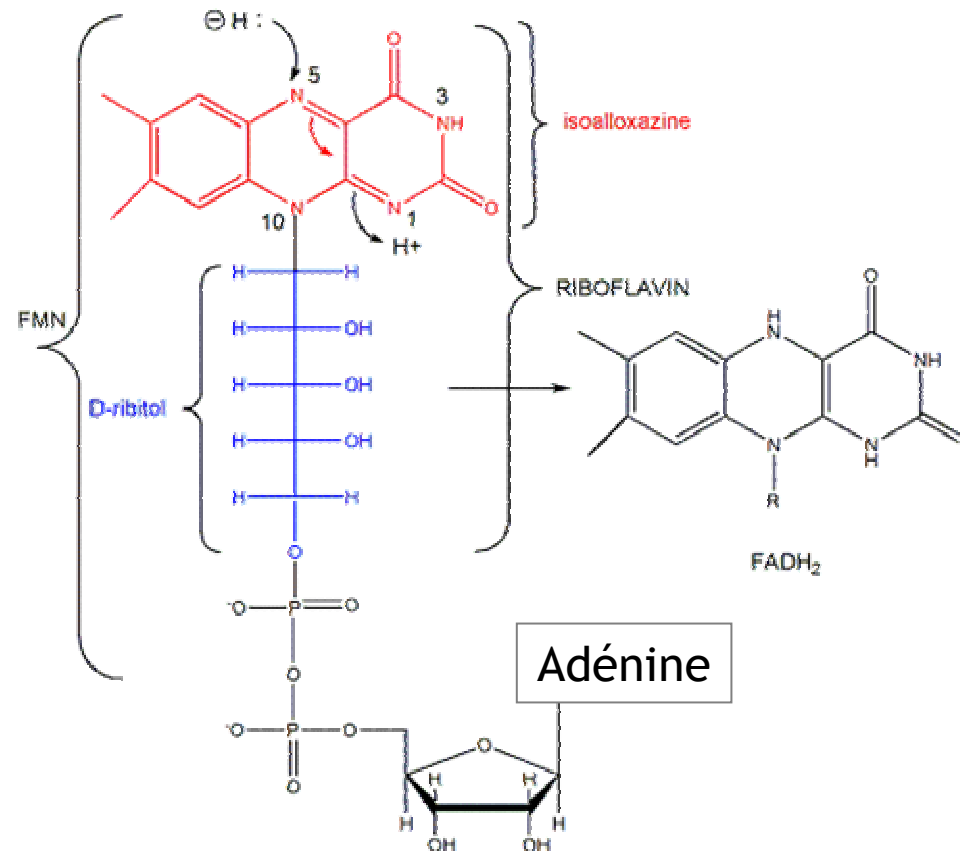
***NAD : Nicotinamide Adénine dinucléotide***



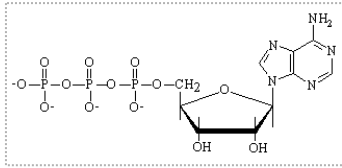
# COENZYMES D'OXYDO-REDUCTION

## FAD

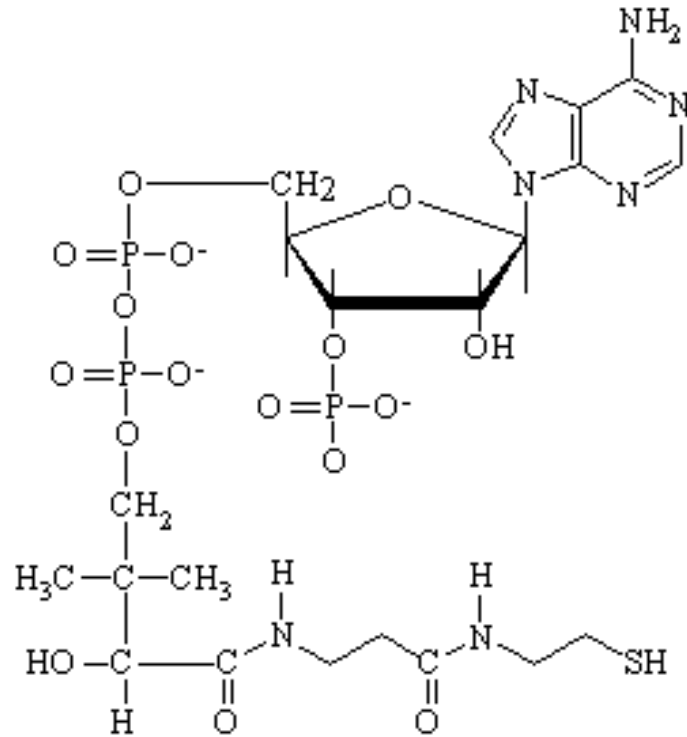
*Précurseurs :*  
 2 ATP  
 Riboflavine



*FAD : Flavine Adénine dinucléotide*



# COENZYME A



## **LES ANTIMETABOLITES**

**-Anticancéreux**

**-Antiviraux**

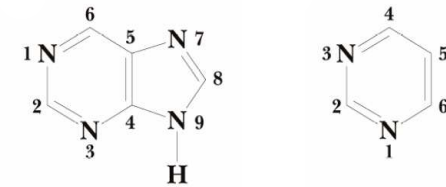
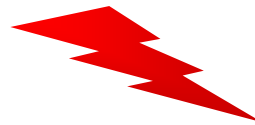


# LES ANTICANCEREUX

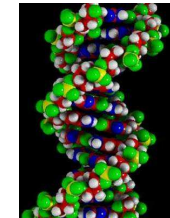
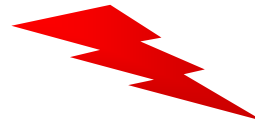
## *Action centrée sur l'ADN*

Action en amont

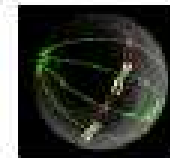
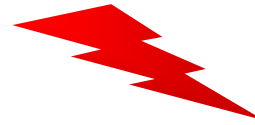
Antimétabolites



Action directe



Action en aval



# LES ANTIMETABOLITES

Anti-Pyrimidiques

5-fluorouracile(5-FU)  
Cytarabine

Anti-Puriques

6-Mercaptopurine (6-MP)

Anti-Folates

Méthotrexate (MTX)

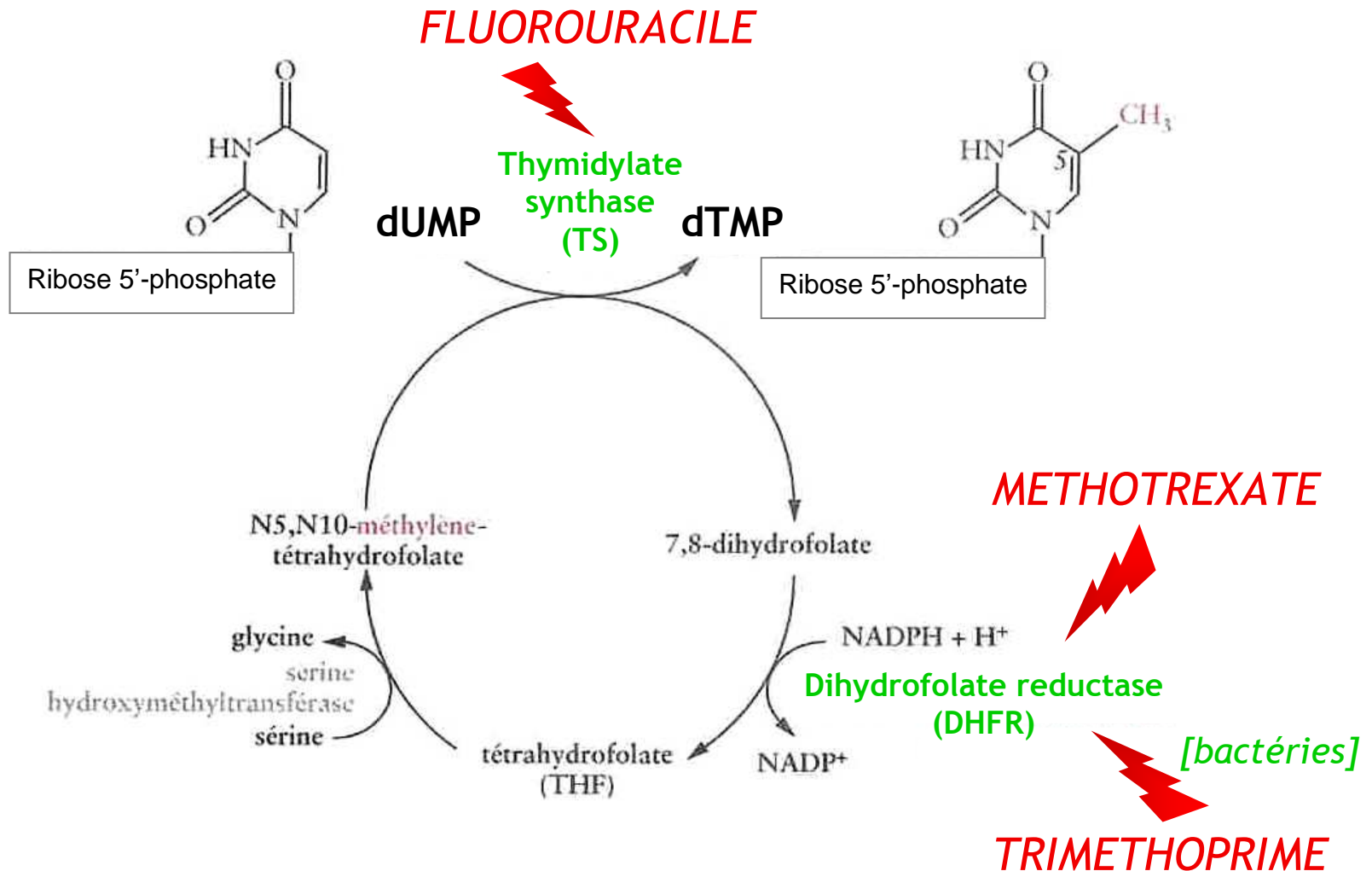
Anti ribonucléotide réductase

Hydroxycarbamide

# ACTION DES ANTIMETABOLITES

## BIOSYNTHESE DE LA (DEOXY)THYMIDINE

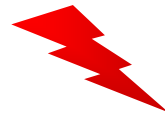
### *Méthylation du dUMP en dTMP*



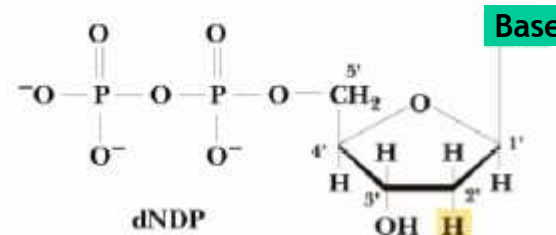
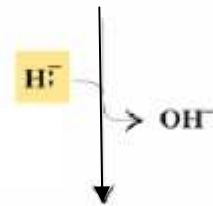
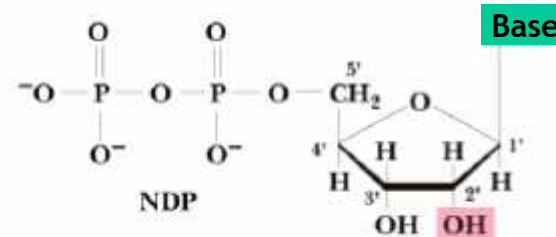
# ACTION DES ANTIMETABOLITES

## BIOSYNTHESE DES DESOXY-RIBONUCLEOTIDES

**HYDROXYCARBAMIDE**  
(Hydroxyurée)

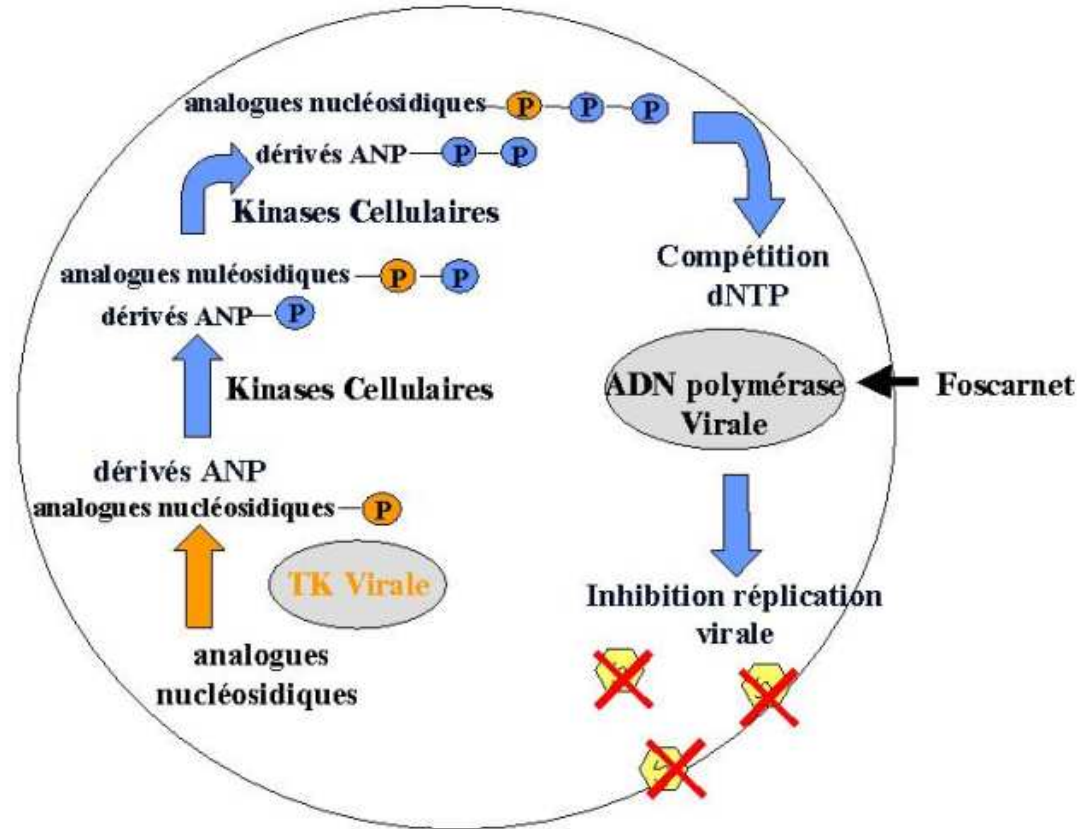
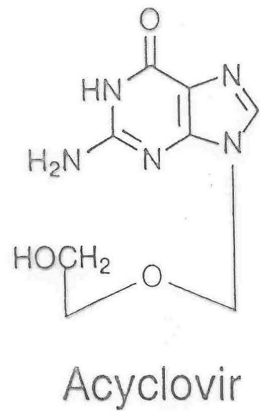


Ribonucléotide  
réductase



ADN

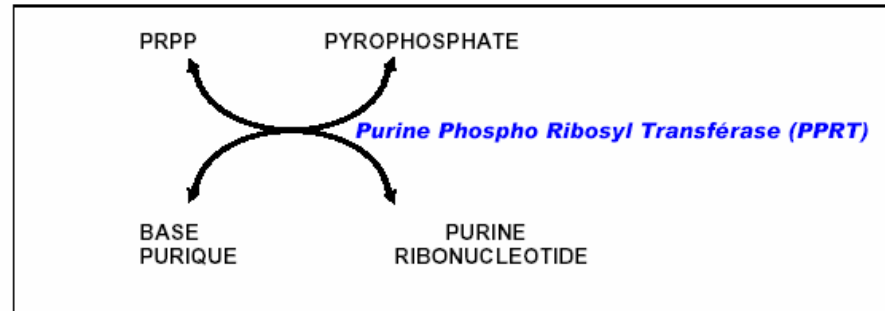
# ANTI RETROVIRAUX



# CATABOLISME/RECYCLAGE DES PURINES

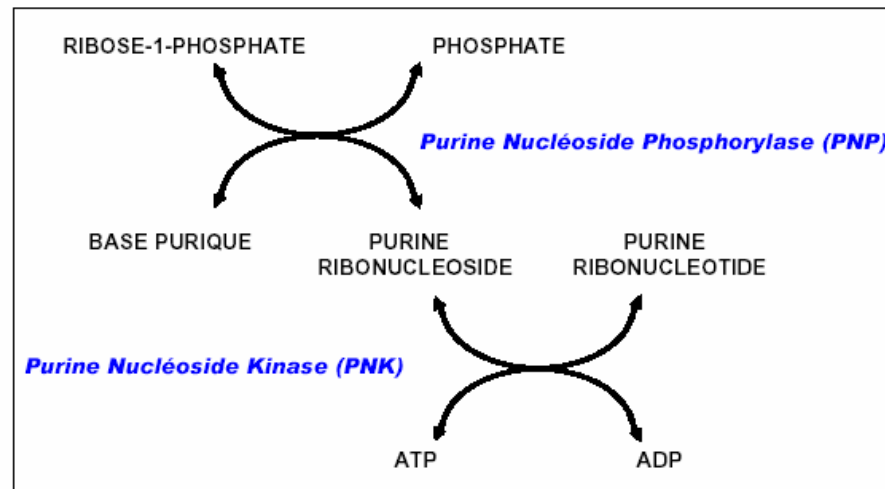
# VOIES DE RECYCLAGE (ou voies d'épargne)

## LA VOIE D'EPARGNE EN UN TEMPS

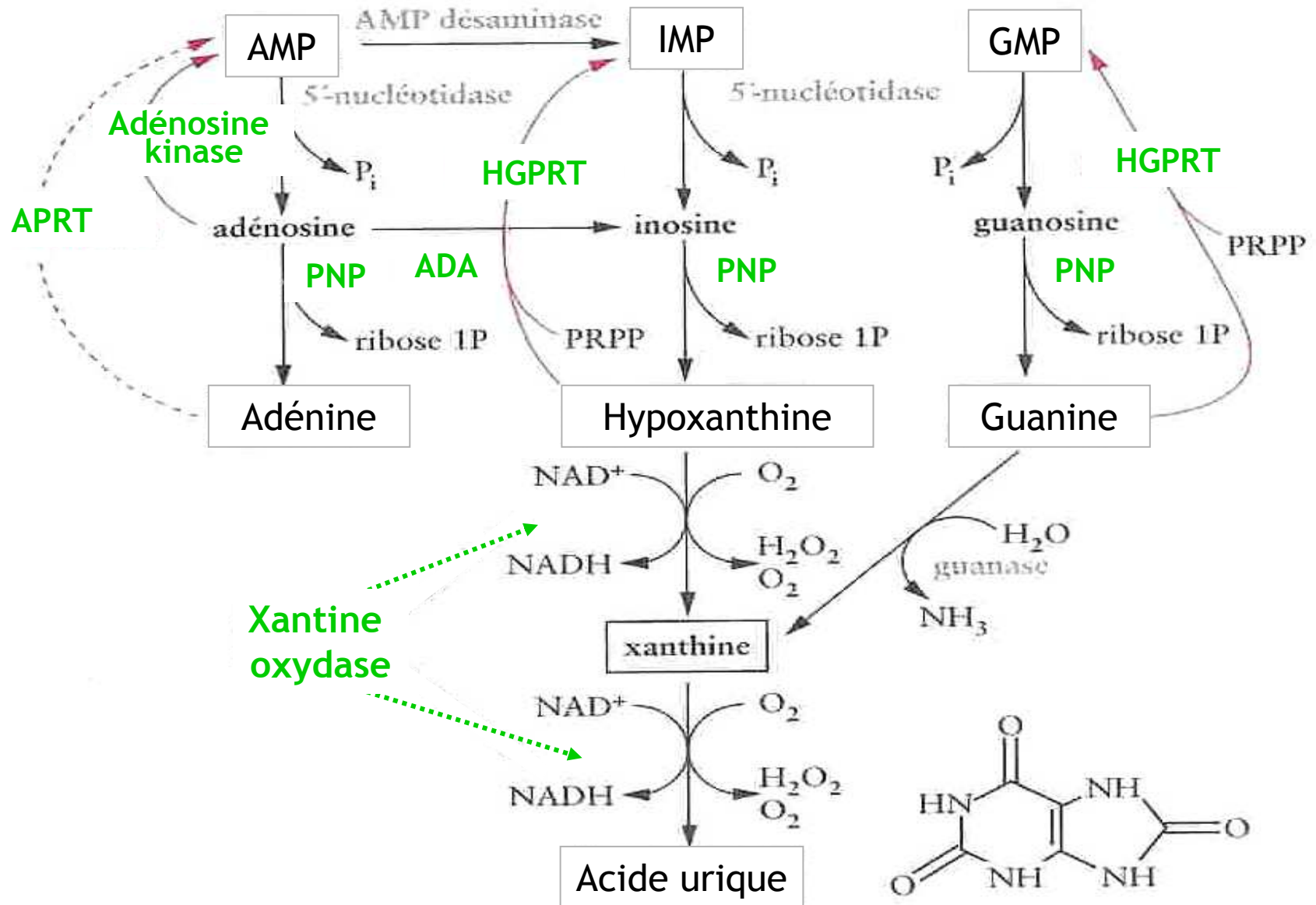


APRT  
HGPRT

## LA VOIE D'EPARGNE EN DEUX TEMPS



# DEGRADATION ET RECUPERATION DES BASES PURIQUES

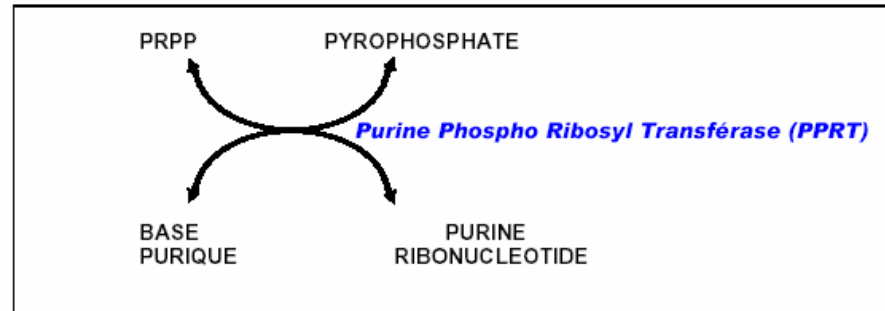




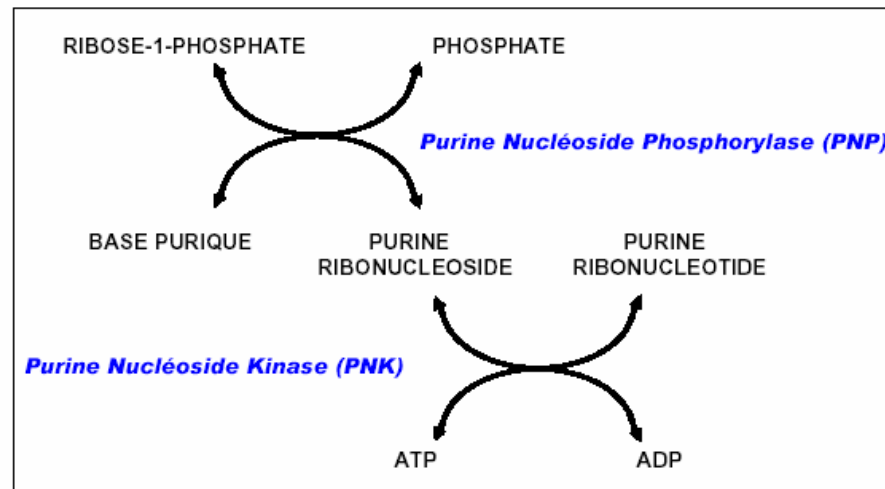
# CATABOLISME/RECYCLAGE DES PYRIMIDINES

# VOIES DE RECYCLAGE (ou voies d'épargne)

## LA VOIE D'EPARGNE EN UN TEMPS

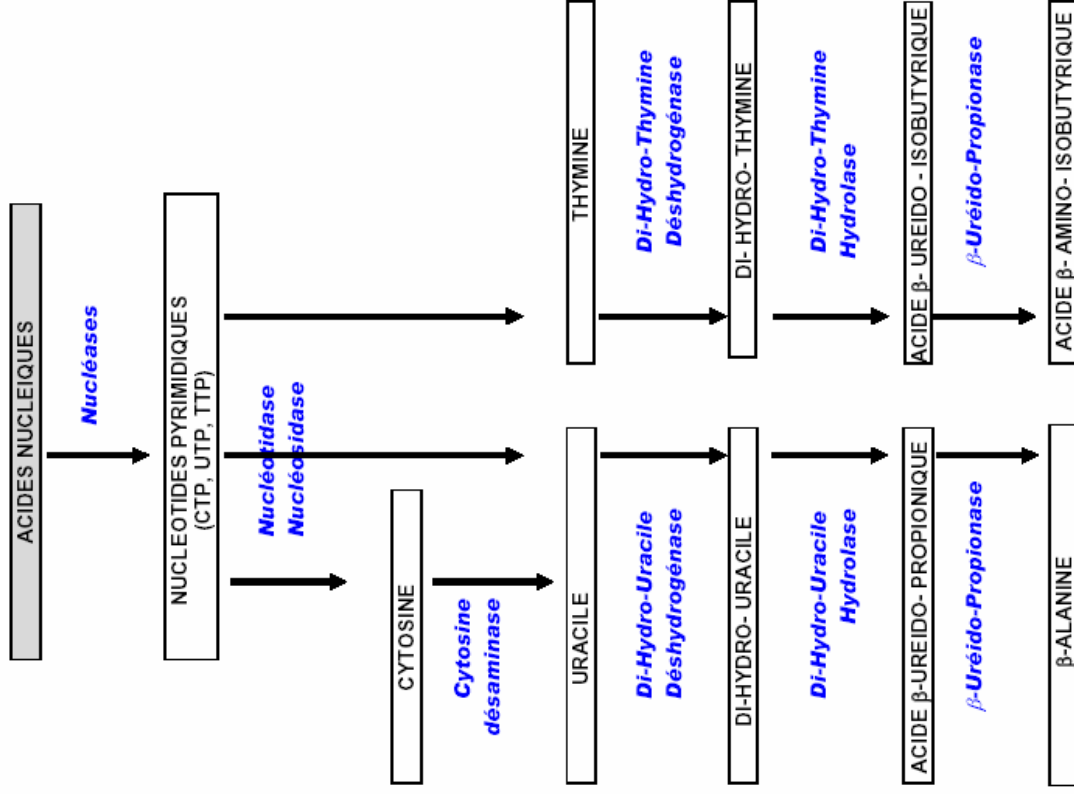


## LA VOIE D'EPARGNE EN DEUX TEMPS



# CATABOLISME DES NUCLEOTIDES PYRIMIDIQUES

Schéma général

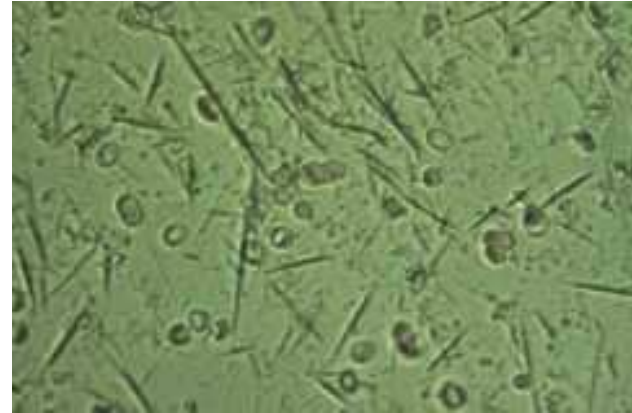


# LA GOUTTE

# URICEMIE

Normales : 150-400  $\mu$ moles/l (urate>>acide urique)

# LA GOUTTE



*Ponction articulaire (état frais)*

# DEGRADATION DES BASES PURIQUES

