Chapter 13 Biosynthesis of amino acids, nucleotides, and related molecules

4. Biosynthesis and degradation of nucleotides

◎ Nucleotides roles

- Precursor of DNA and RNA
- Essential carrier of chemical energy (ATP, GTP)
- Components of the cofactors (NAD, FAD, SAM, coenzyme A)

◎ **Biosynthetic pathways : De novo pathways, Salvage pathways**

1) De novo purine synthesis begins with PRPP

* The formation of PRPP : ***Ribose phosphate pyrophosphokinase***

  Ribose-5-Ⓟ + ATP 5-phosphoribosyl-1-pyrophosphate + AMP

2) Purine nucleotide biosynthesis is regulated by feedback control

* Purine (A, G)생합성에 엽산(folate)이 관여한다.

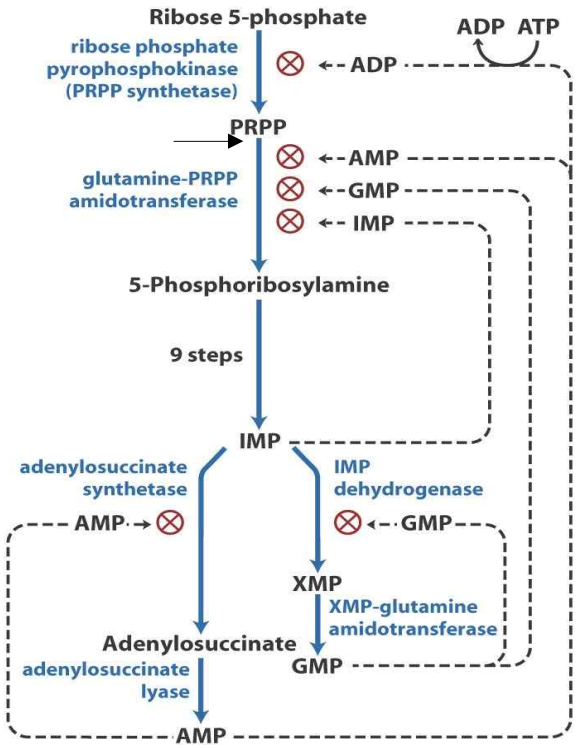


Fig. Regulation mechanism in the biosynthesis of adenine and guanine nucleotides in *E. coli*

3) Pyrimidine nucleotides are made from **aspartate and ribose-5-phosphate**

* The common pyrimidine nucleotides are cytidine 5′-monophosphate (CMP: cytidylate) and uridine 5′-monophophate (UMP; uridylate)

4) Pyrimidine nucleotides biosynthesis is regulated by feed back inhibition

5) Nucleotide monophosphates are converted to nucleoside triphosphates

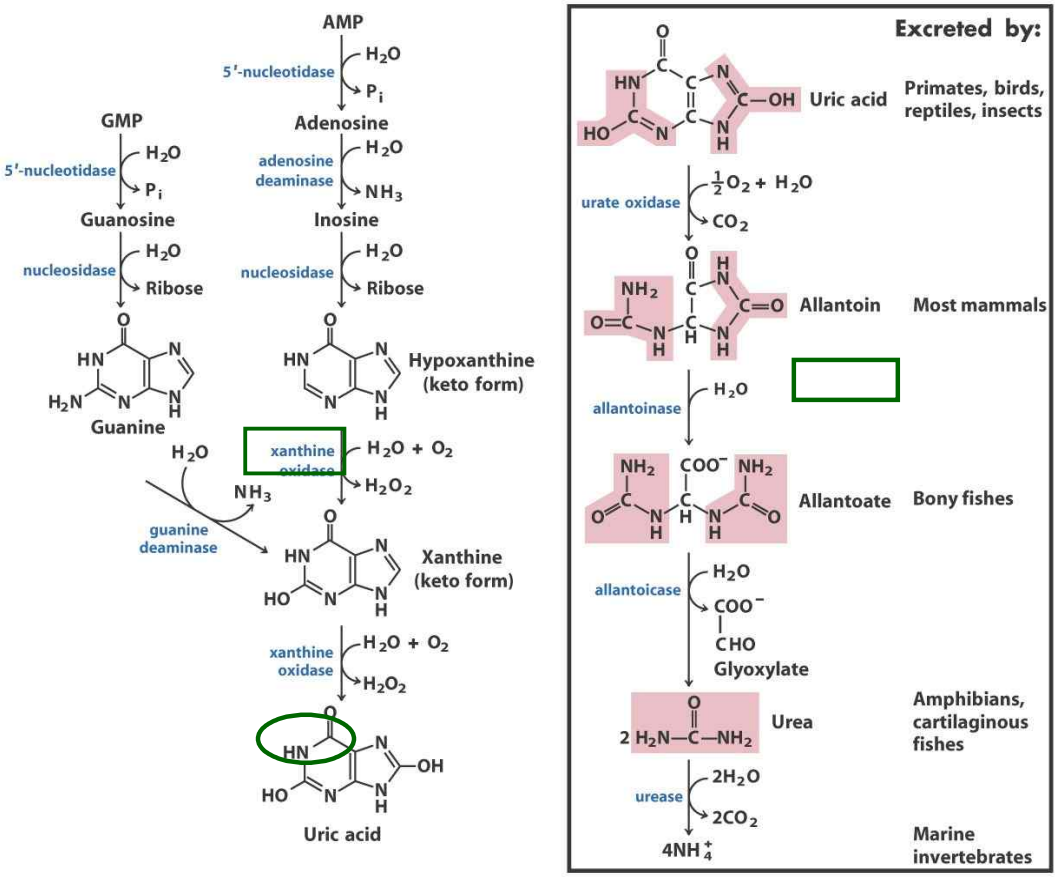
① ATP + AMP 2ADP

adenylate kinase

② The ADP so formed is then phosphorylated to ATP by glycolytic enzymes or through ~~oxidative~~ phosphorylation

6) Thymidylate is derived from dCTP and dUMP

7) Degradation of purines and pyrimidines leads to uric acid and urea, respectively



◎ Purine nucleotide 염기는 분해하여 요산(uric acid) 만든다.

◎ Pyrimidine은 간에서 분해되어 β-알라닌과 β-아미노이소부티르산 생성

- Uracil → β-alanine + NH_3, CO_2
- Thymine → β-aminobutyric acid + NH_3, CO_2

8) Purine and pyrimidine bases are recycled by salvage pathways

① Adenine phosphoribosyltransferase

- Adenine + PRPP AMP + PPi

② Hypoxanthine-guanine phosphoribosyltransferase (HGPRT)

: Guanine and hypoxanthine are salvaged

- Hypoxanthine + PRPP IMP + PPi

- Guanine + PRPP GMP + PPi

◎ 레쉬-나이한 증후군(Lesch-Nyhan syndrome) :

- HGPRT의 결핍은 심각한 임상적 질병을 유발
- 신경계통에 심각한 이상 : 정신지체, 경련성 마비, 공격적인 행동, 신체자해행위

9) Excess uric acid causes gout (과량의 요산은 통풍을 유발)

: 체액에 과량의 요산이 축적되어 연골조직에 요산염이 축적되어 통풍성 관절염 통증 유발 (엄지발가락의 관절이 특히 민감)

*** 원인 : 요산배설과정 손상 및 요산이 과도하게 생산되어** 요산의 축적

* 치료제 : Allopurinol (an inhibitor of xanthine oxidase)

* **Many chemotherapeutic agents** target enzymes in the nucleotide biosynthetic pathways

◎ Adenosine deaminase deficiency (ADA)

- leads to **severe immunodeficiency diseases** in humans
- B-cell, T-cell 생성부족
- AIDS, 빈혈, 백혈병 등 유발

* 중증합병면역 결핍증 (Severe combined immunideficiency syndrome, SCID) 환자의 30% 정도는 ADA 결핍증으로 고통을 받고 있다

5. Porphrin biosynthesis

* Porphrin : tetra pyrrole 이 methine bridge로 연결된 것

* Mg^{++} : chlorophyll

* Fe^{++} : hemoglobin, myoglobin, cytochrome

*** Precursor : Succinyl-CoA, glycine**

* Heme is the source of bile pigments

6. Alkaloid : 염기성질소 함유

* 코카인 : 중추신경자극

* 아트로핀(atropine) : 근육 이완제

* Codeine, morphine : 아편