Dezazma Pazhuh
Intelligent Science, Real Impact
www.dezazma.com

Nucleotide Metabolism

Dr. Hadi Ansarihadipour

Clinical Biochemist, Ph.D.

Arak University of Medical Sciences

Nucleotides:

Building Blocks of DNA and RNA

1. Nucleobase: A,G,C,T or U
2. Pentose: Ribose or deoxyribose
3. Phosphate group

Nucleotide Synthesis

1. **Salvage Pathway** (obtain from diet)
2. ***De novo* Pathway** (synthesis in cells)

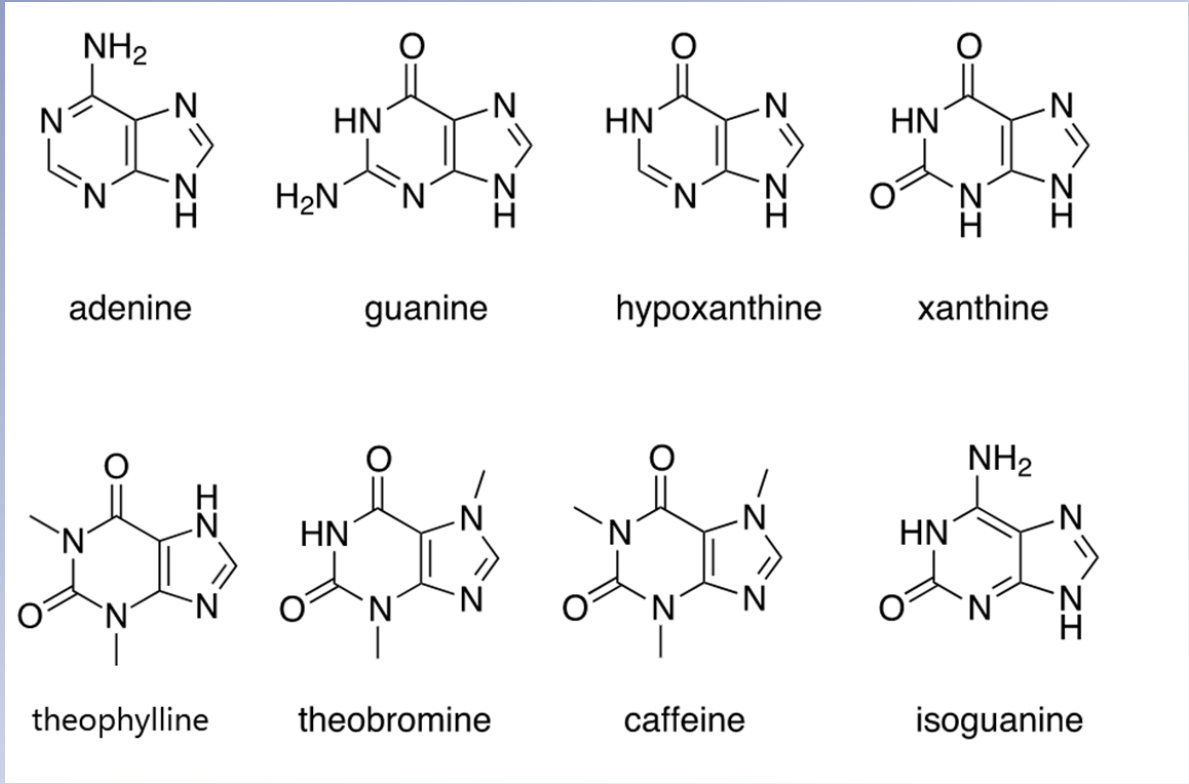
Dezazma Pazhuh
Intelligent Science, Real Impact
www.dezazma.com

Salvage Pathway

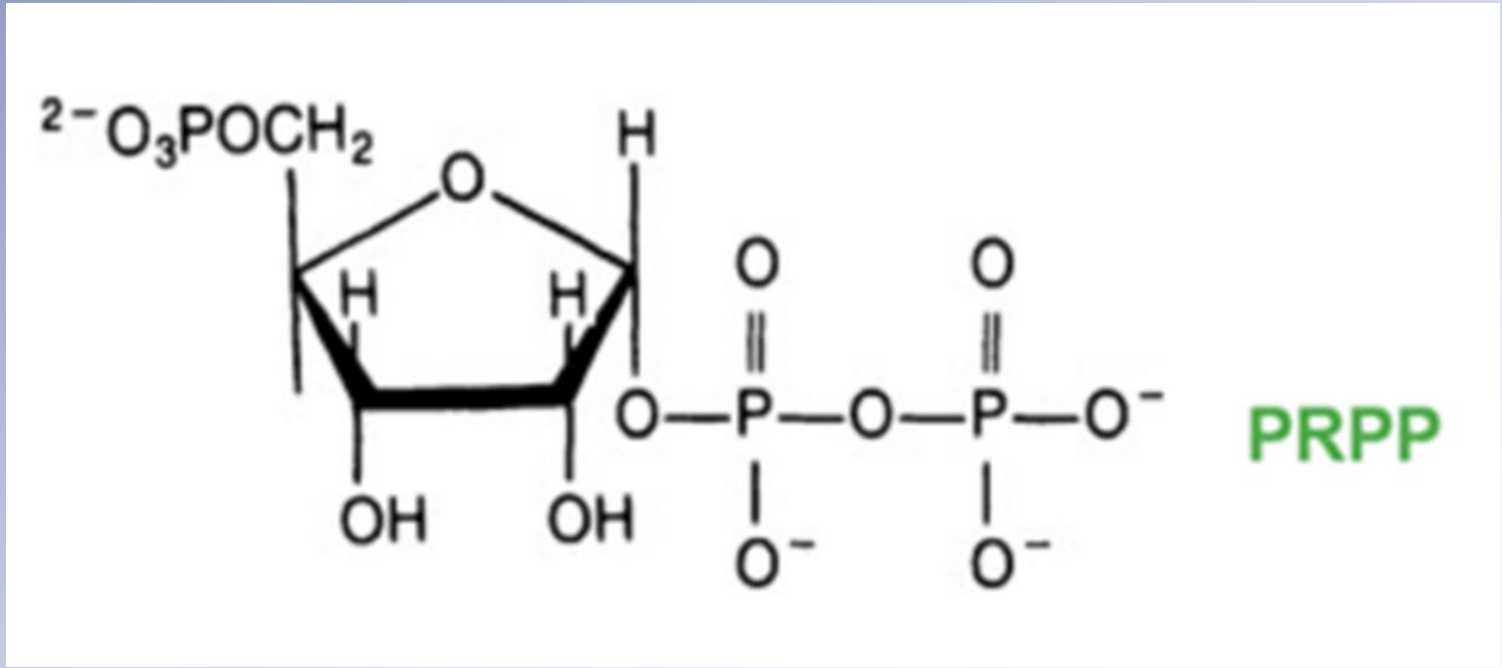
(Dietary nucleotides)

Dezazma Pazhuh
Intelligent Science, Real Impact
www.dezazma.com

Notable dietary purines

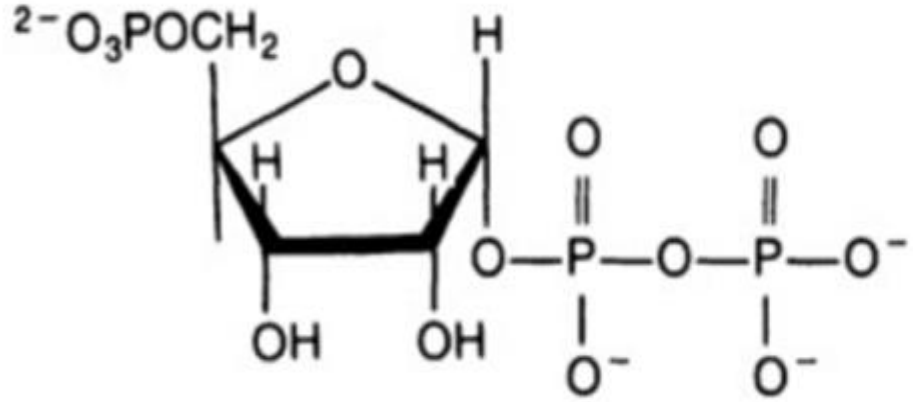


PRPP:
Phosphoribosyl Pyrophosphate



Pentose Phosphate Pathway

Ribose 5 phosphate



ATP → PRPP Synthetase

PRPP

APRTase:

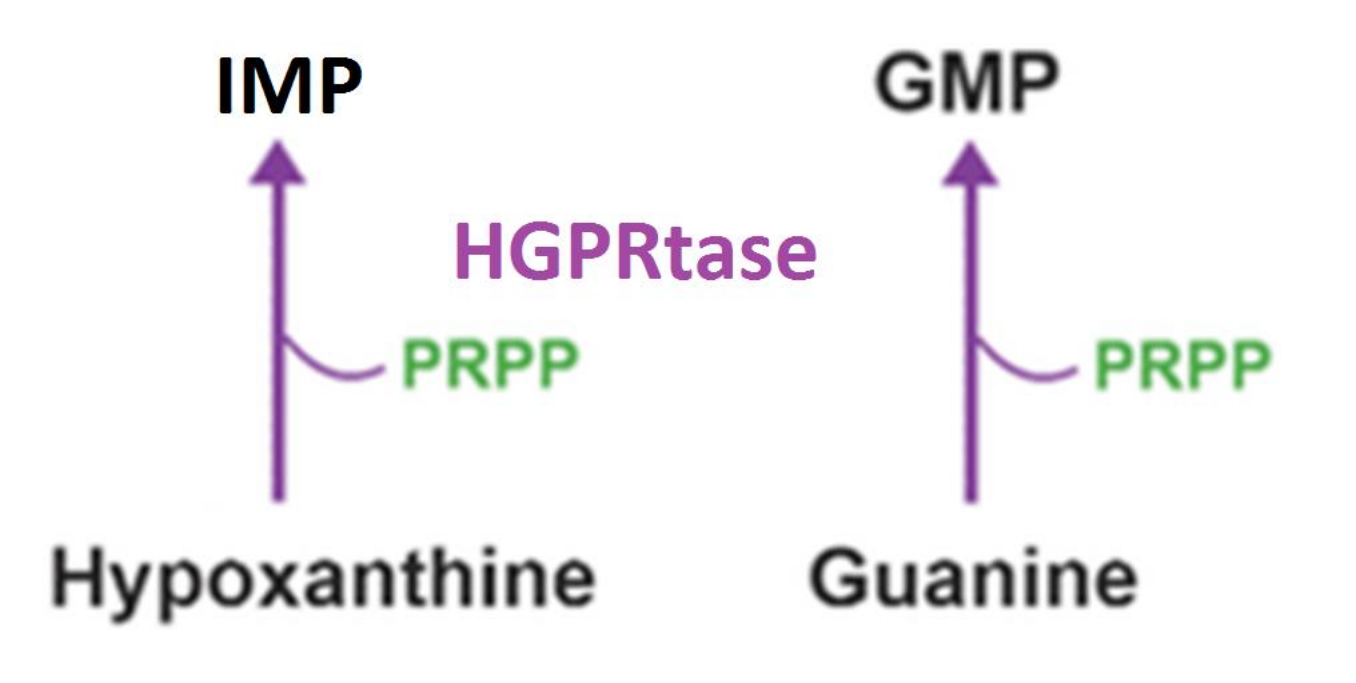
Adenine Phosphoribosyltransferase

PRPP:

Phosphoribosyl Pyrophosphate

HGPRTase:

Hypoxanthine Guanine Phosphoribosyltransferase



Dezazma Pazhuh
Intelligent Science, Real Impact
www.dezazma.com

Deficiency of HGPRtase leads to:
Lesch-Nyhan syndrome

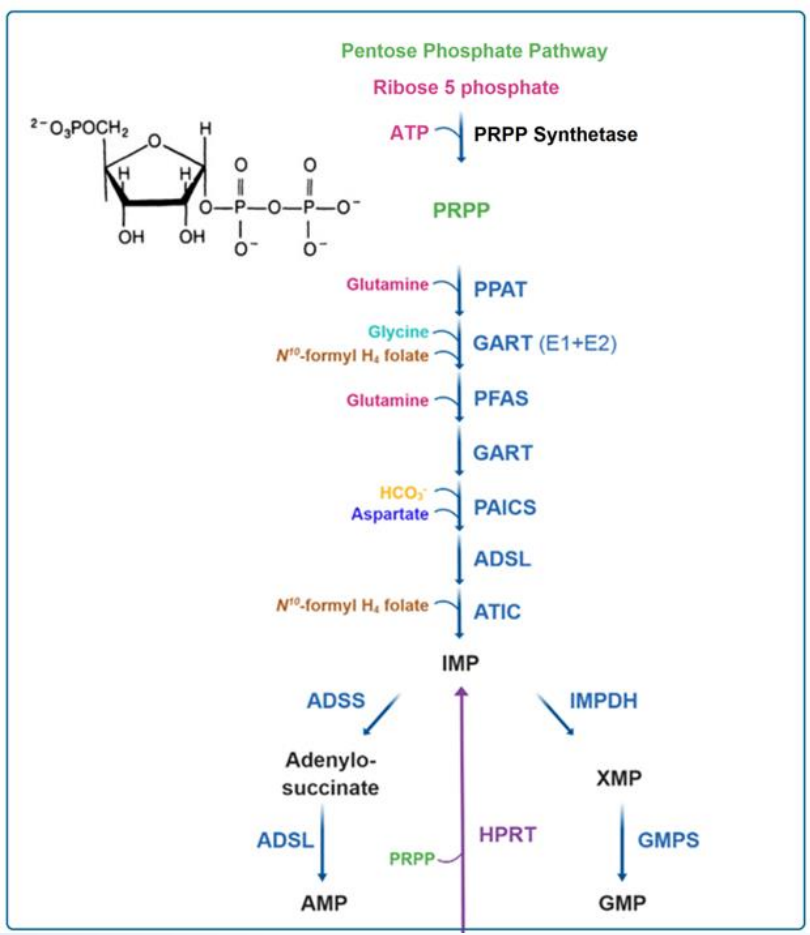
Lesch–Nyhan syndrome:

1. Neurologic dysfunction
2. Cognitive deficits (mental retardation)
3. Behavior abnormalities including self-mutilation
4. Uric acid overproduction (hyperuricemia).

Dezazma Pazhuh
Intelligent Science, Real Impact
www.dezazma.com

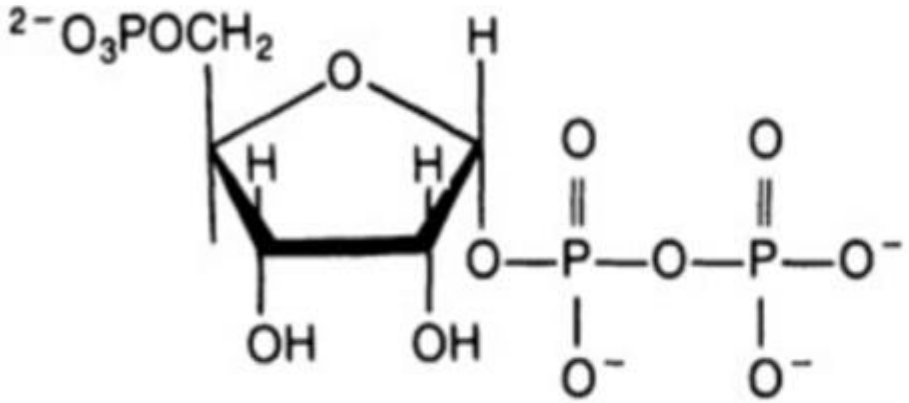
De novo purine synthesis

Dr Hadi Ansarihadipour



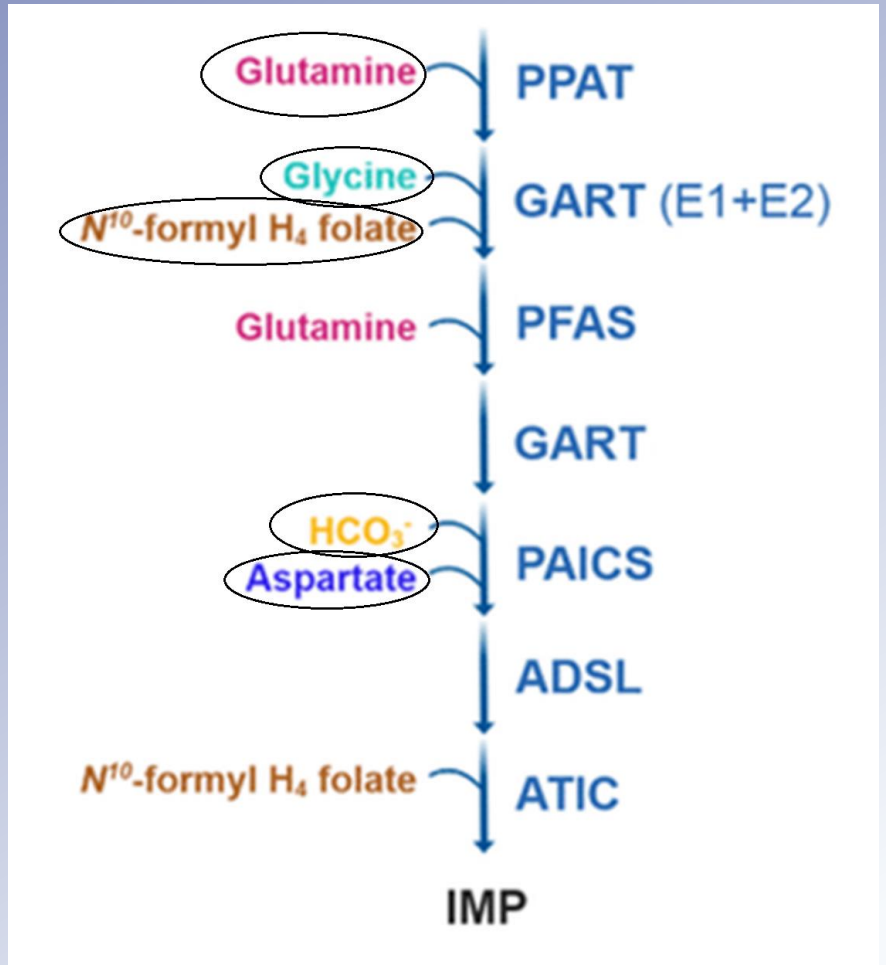
Pentose Phosphate Pathway

Ribose 5 phosphate

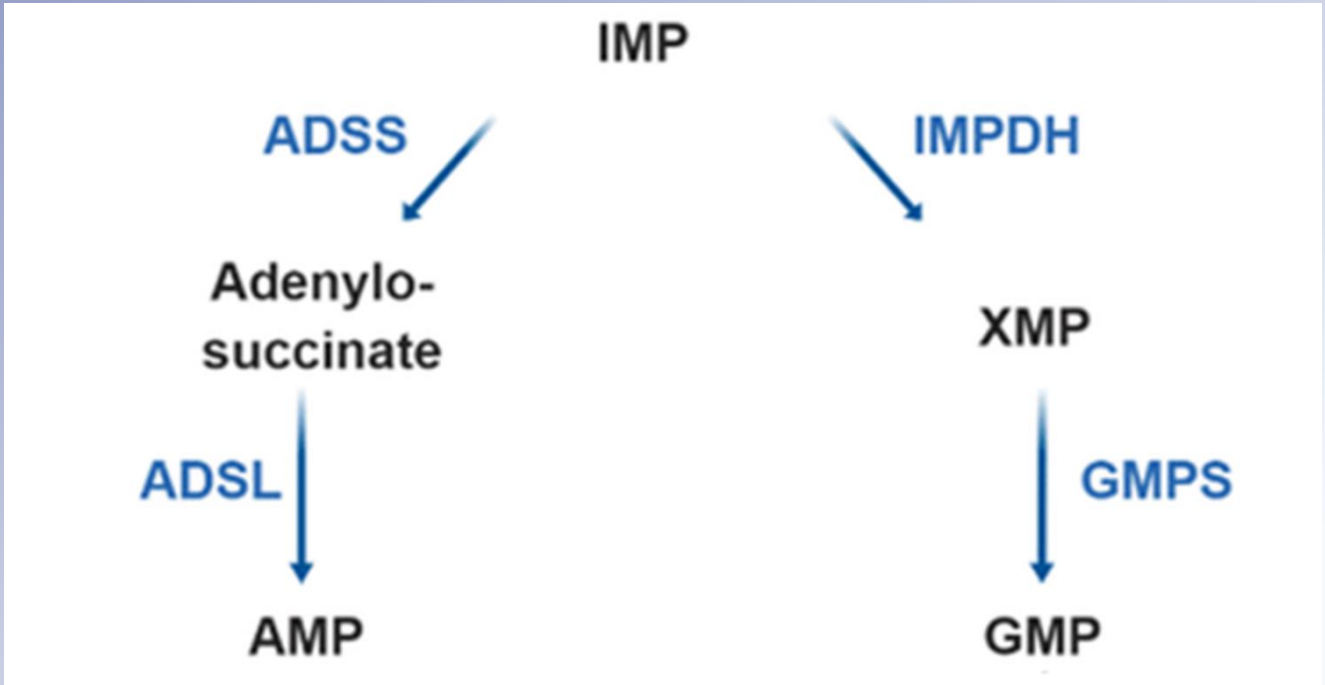


ATP → PRPP Synthetase

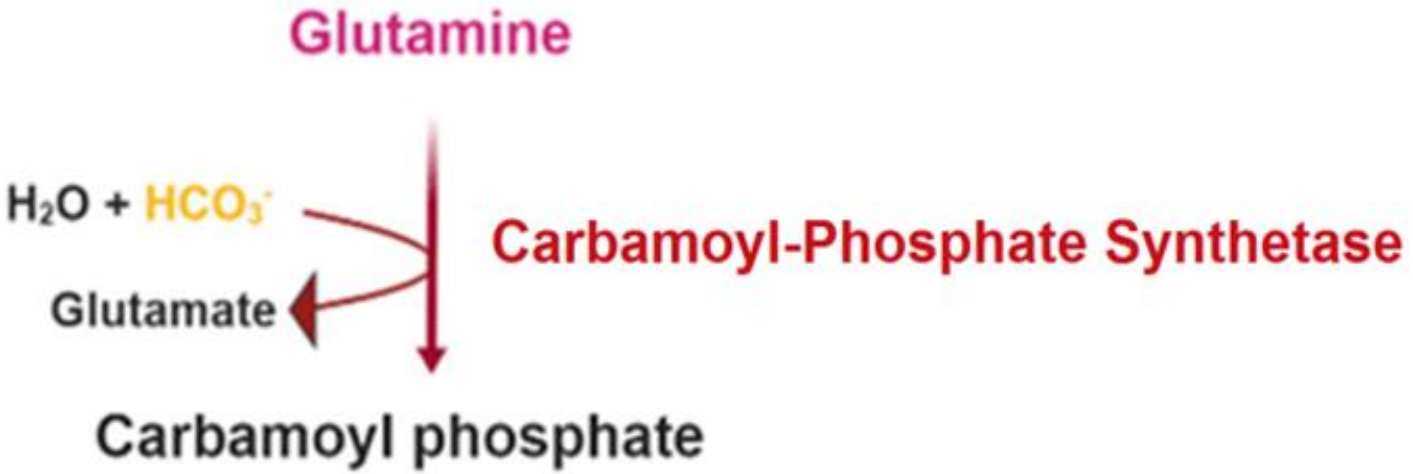
PRPP



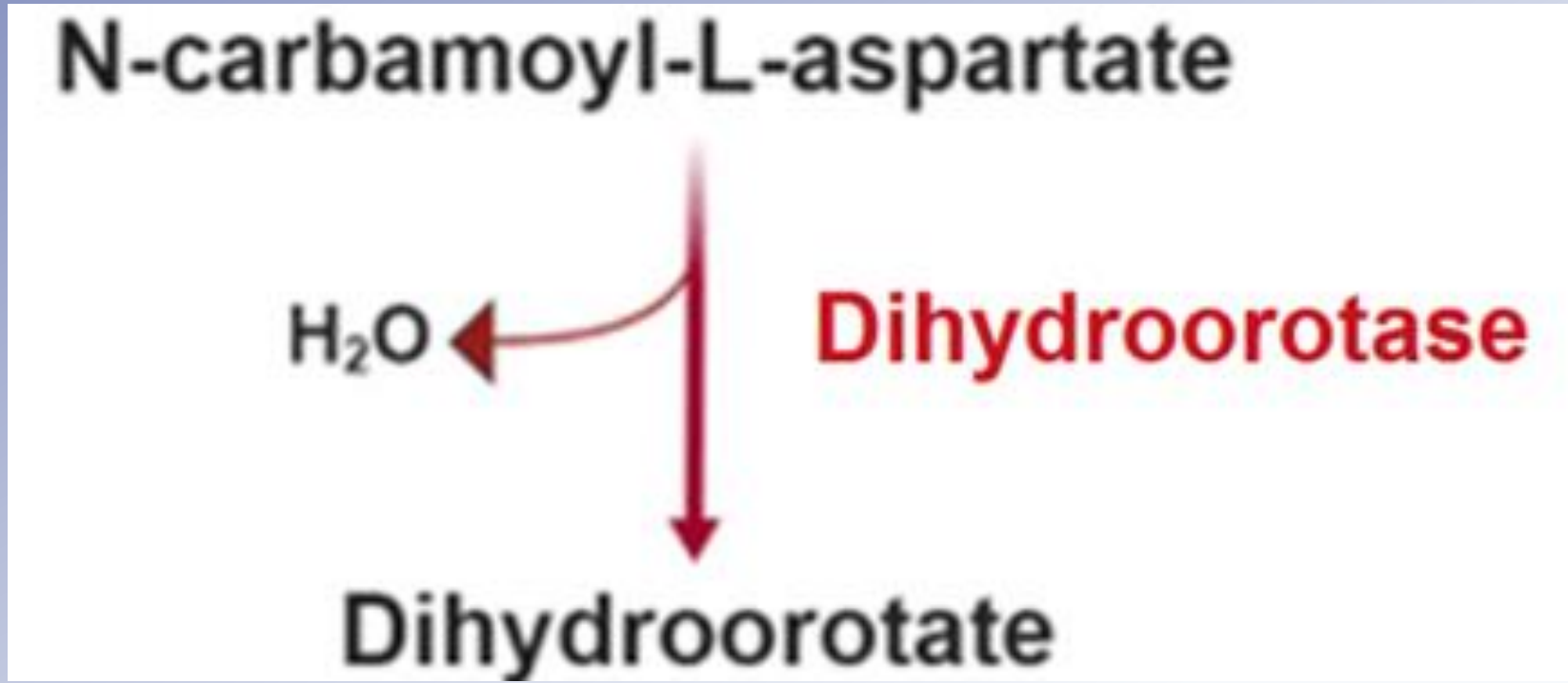
IMP: Inosine Monophosphate

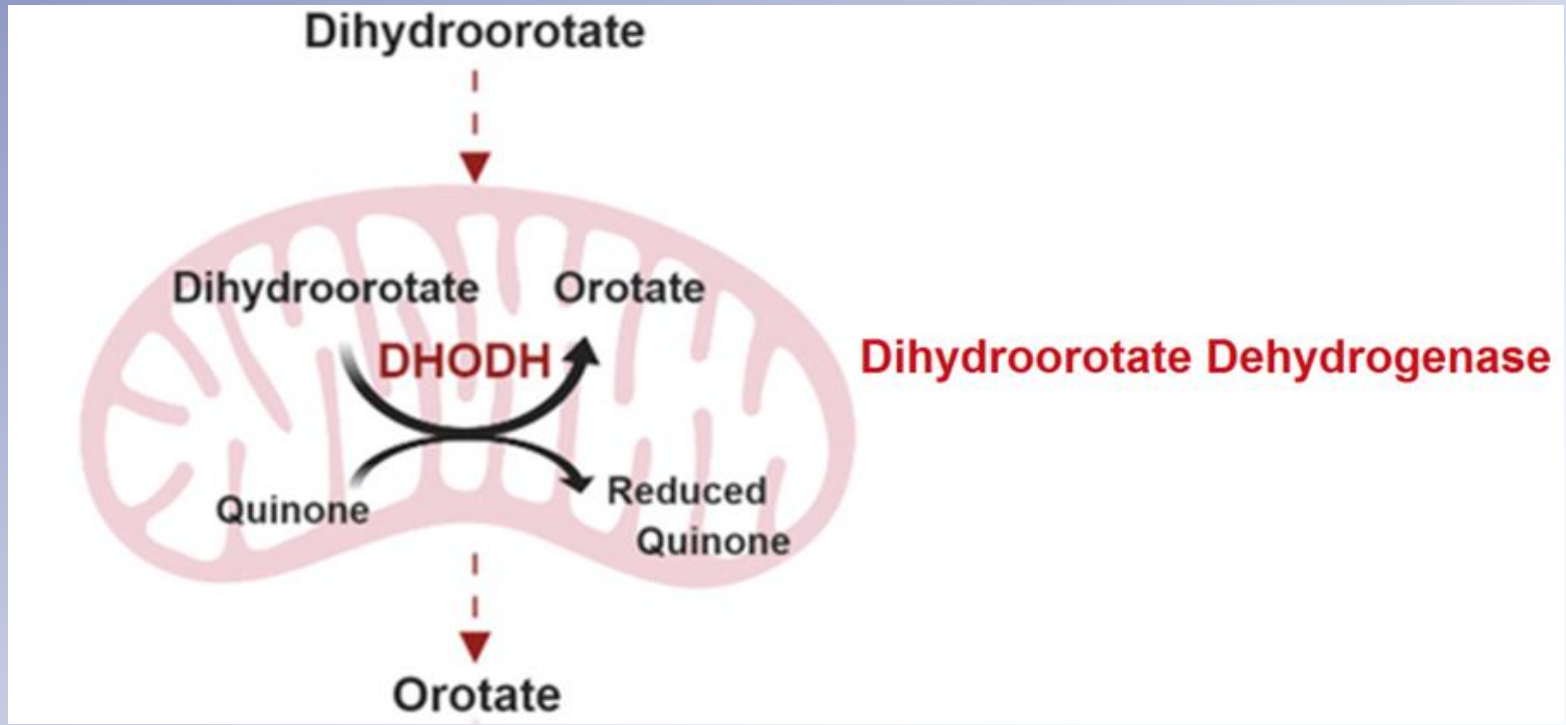


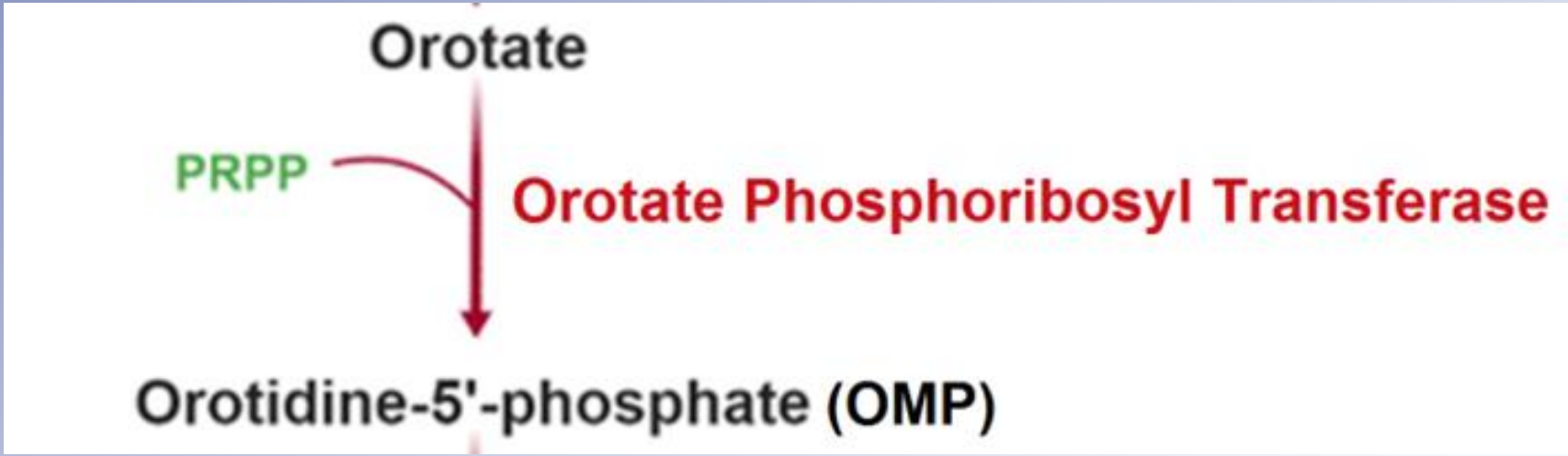
De novo pyrimidine synthesis

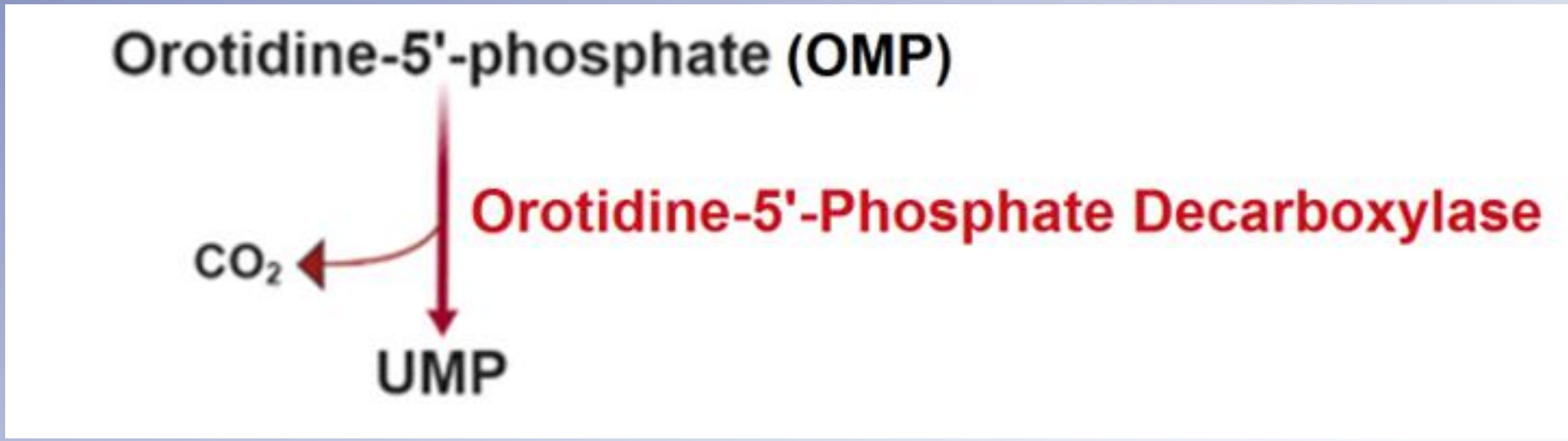


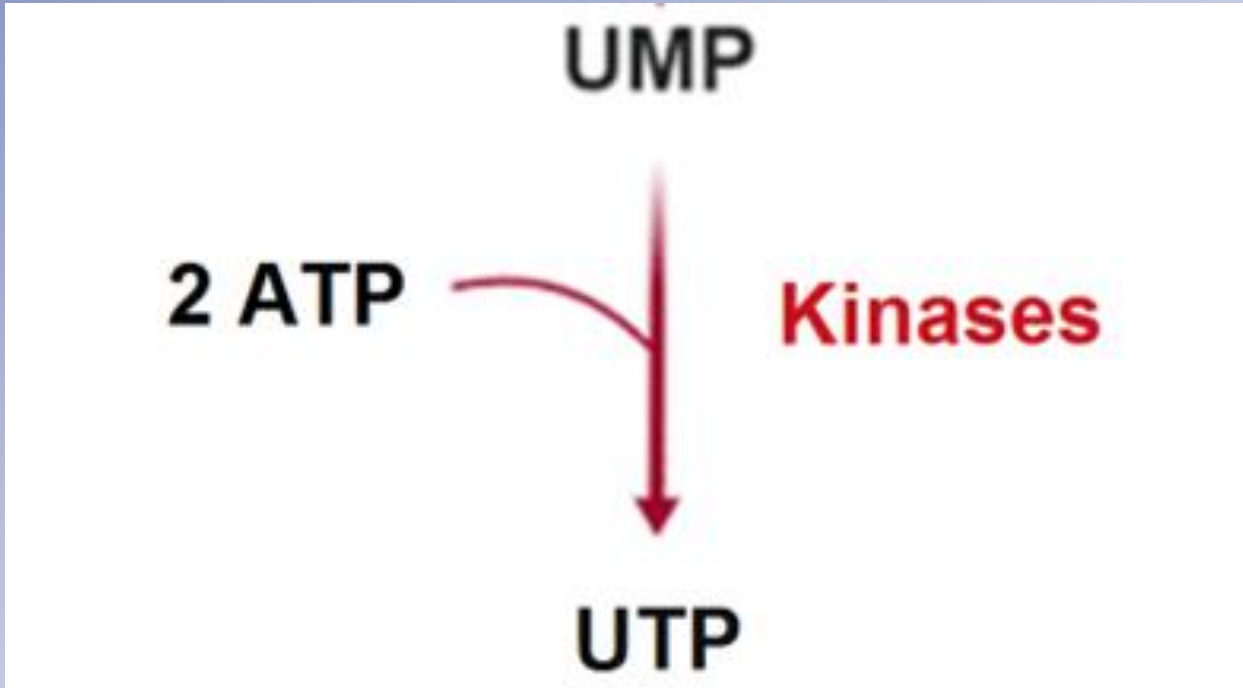

Carbamoyl phosphate
Aspartate
Aspartate Carbamoyl Transferase
N-carbamoyl-L-aspartate

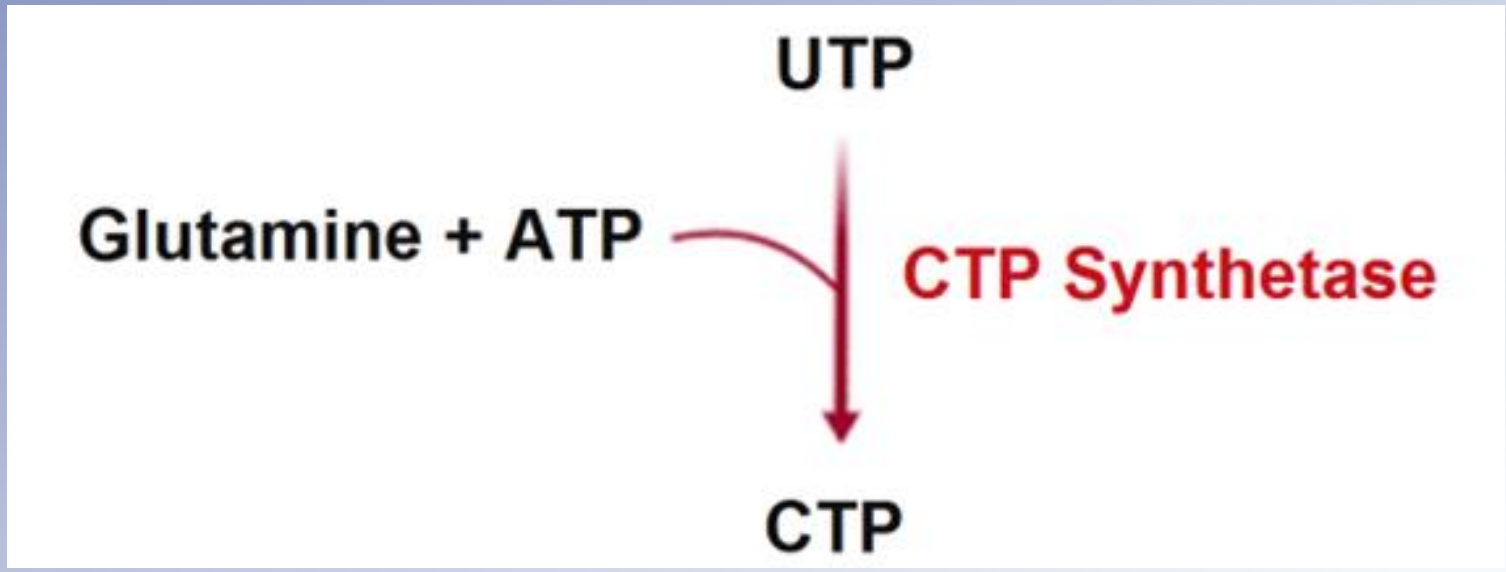

N-carbamoyl-L-aspartate
H_2O
Dihydroorotase
Dihydroorotate


Dihydroorotate
Dihydroorotate
Orotate
DHODH
Quinone
Reduced
Quinone
Orotate
Dihydroorotate Dehydrogenase


Orotate
PRPP
Orotate Phosphoribosyl Transferase
Orotidine-5'-phosphate (OMP)


Orotidine-5'-phosphate (OMP)
Orotidine-5'-Phosphate Decarboxylase
CO_2
UMP


UMP
2 ATP
Kinases
UTP



Dezazma Pazhuh
Intelligent Science, Real Impact
www.dezazma.com

Nucleotide degradation

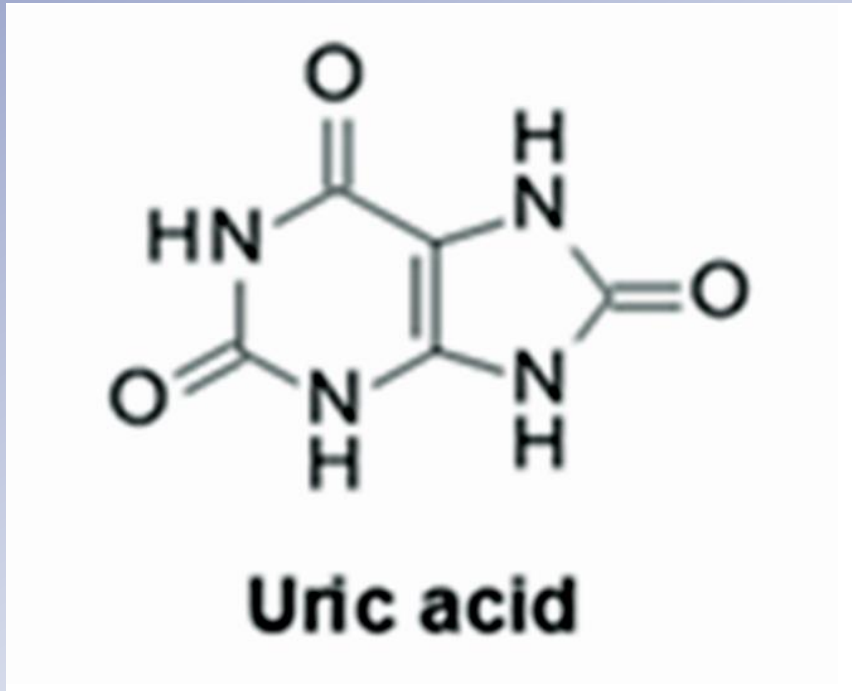
Pyrimidines degradation

In humans:

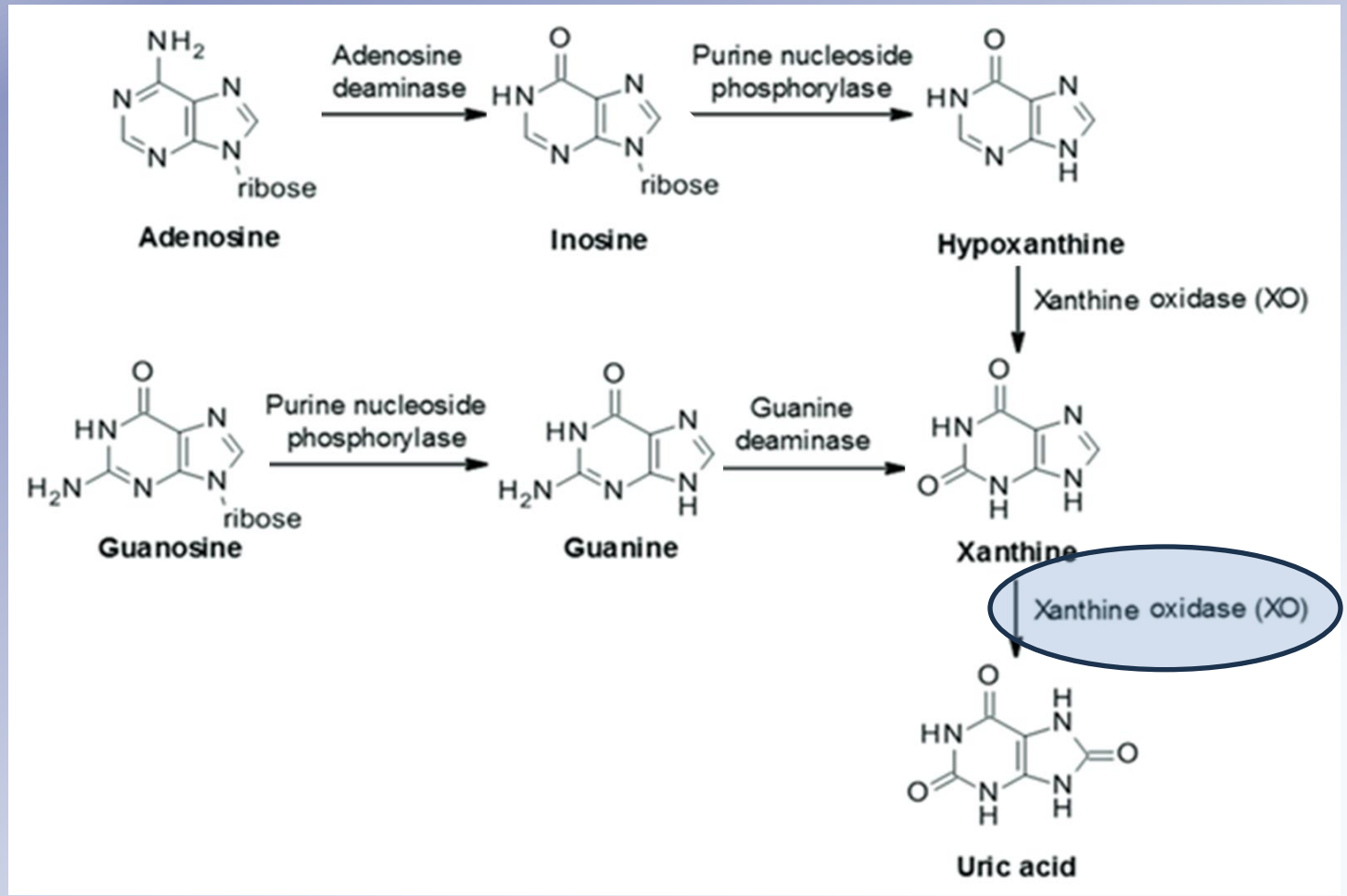
Pyrimidines (C, T, U) are degraded to CO_2 and NH_3

Purines degradation

Purines (A and G) are oxidized to uric acid



Uric acid



Uric acid in plasma

Men: 3–7 mg/dL (200–430 µmol/L)

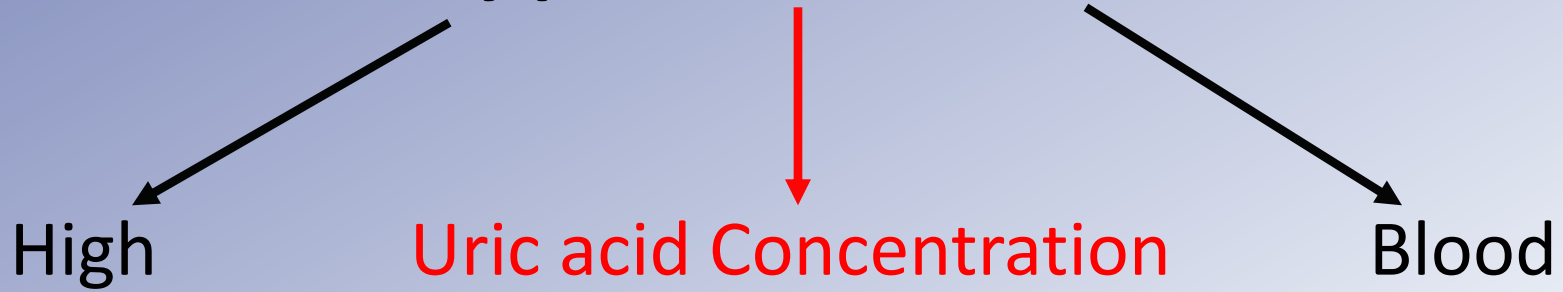
Women: 2–6 mg/dL (140–360 µmol/L).

Hyperuricemia

Plasma uric acid> 6-7 mg/dl

Dezazma Pazhuh
Intelligent Science, Real Impact
www.dezazma.com

Hyperuricemia



Hyperuricemia:

1. Diet: high intake of dietary purines
2. Reduced excretion of uric acid via the kidneys.
3. Fasting or rapid weight loss
4. Certain drugs, such as thiazide diuretics which interfer with renal clearance.

Hyperuricemia

1. Lesch–Nyhan syndrome
2. Cardiovascular diseases
3. Type 2 diabetes mellitus (T2DM)
4. Kidney stones

Gout

Joints

Capillaries

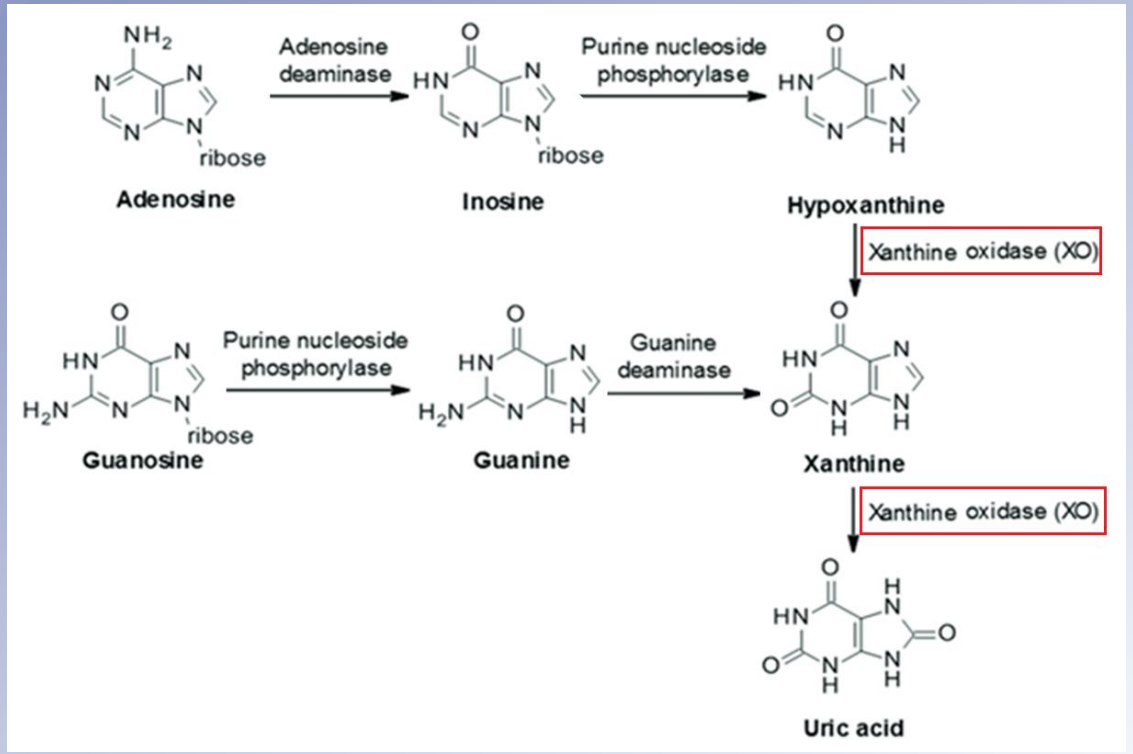
Skin

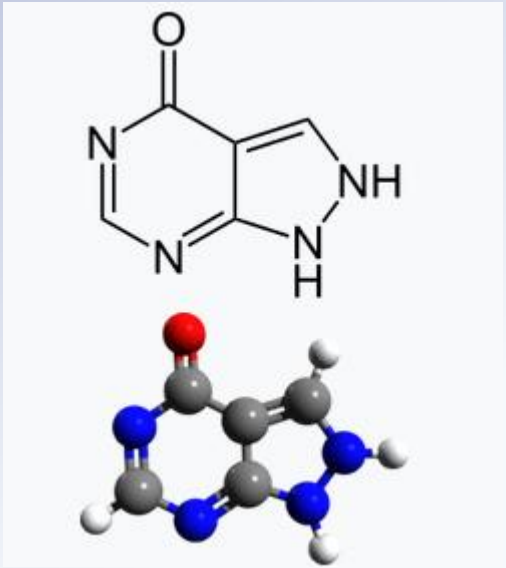
Dezazma Pazhuh
Intelligent Science, Real Impact
www.dezazma.com

Gout

Allopurinol

Xanthine Oxidase Inhibitor





Uric acid crystals in urine

Hypouricemia:

plasma uric acid< 2-4 mg/dl

Dezazma Pazhuh

Intelligent Science, Real Impact

www.dezazma.com