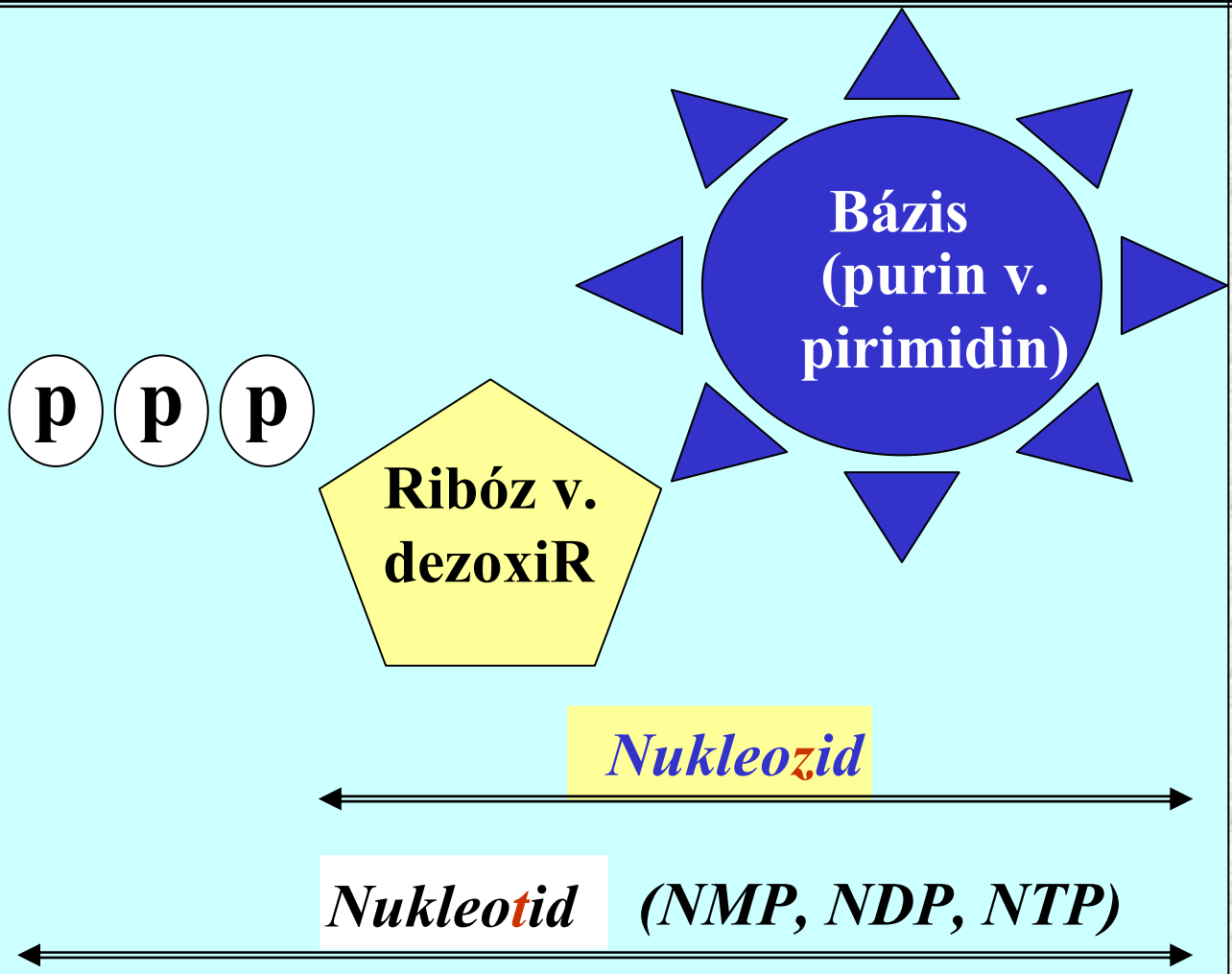
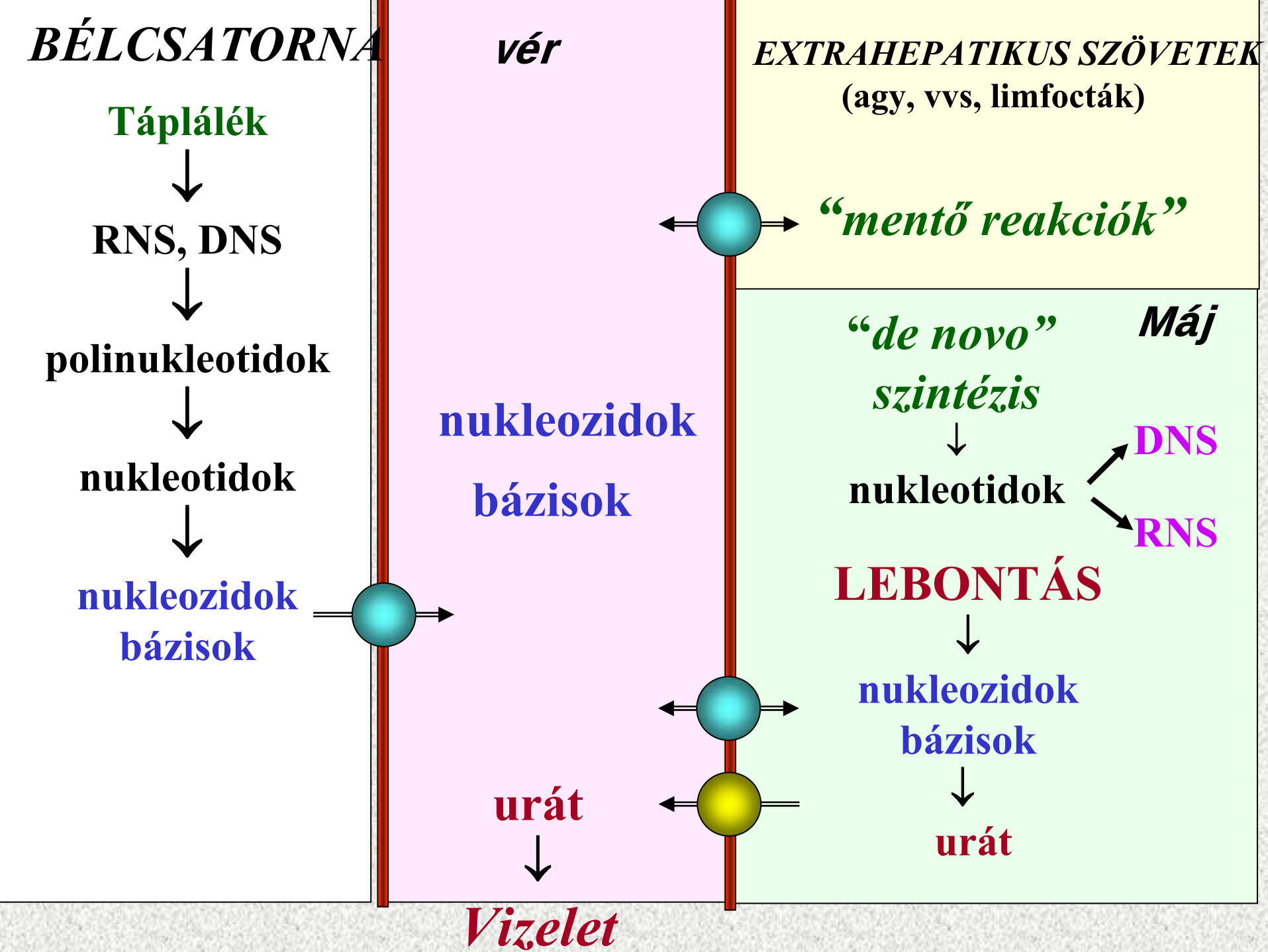
Dr. Sasvári Mária

Nukleotid anyagcsere
Purin nukleotidok

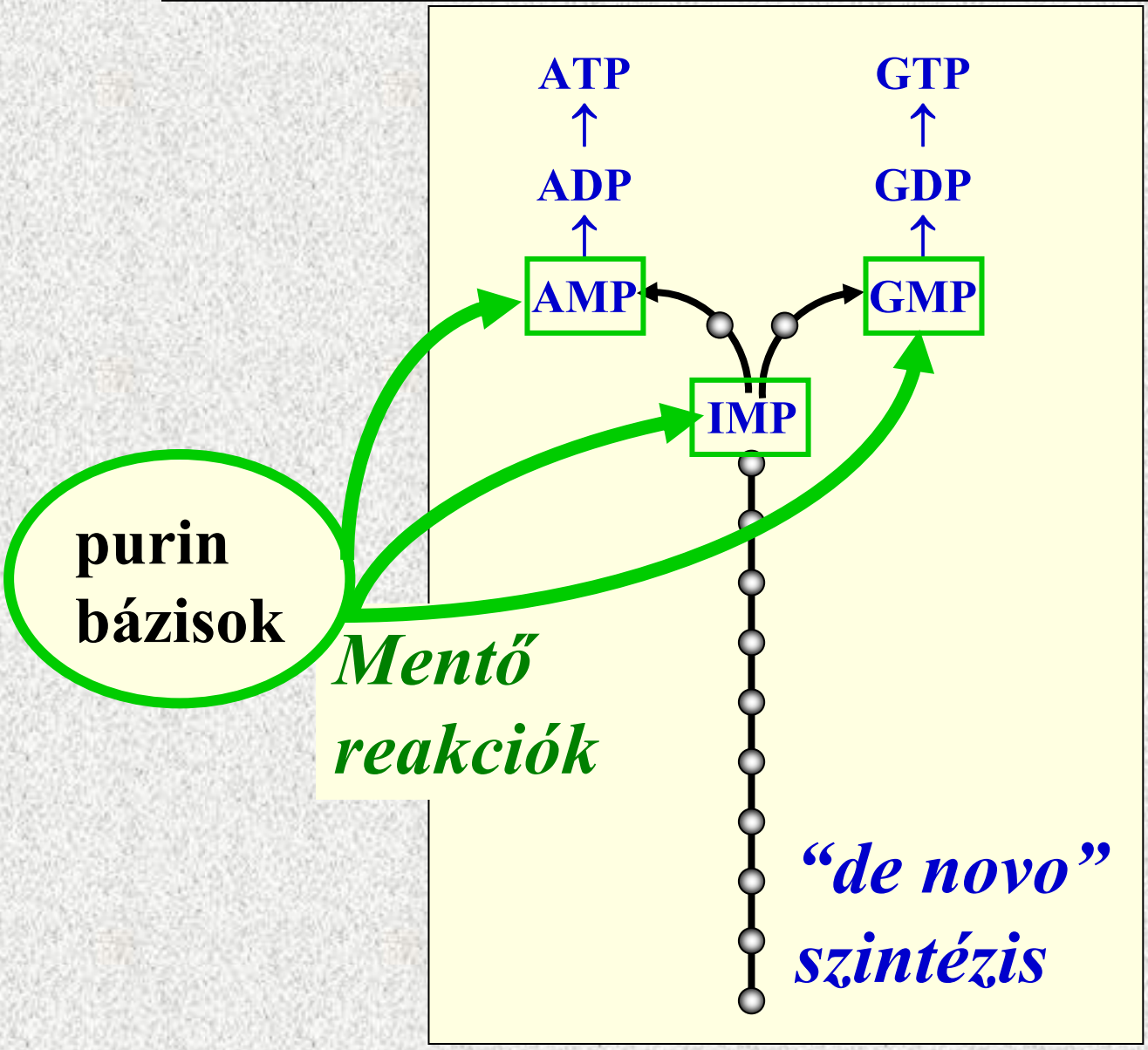
A nukleotidok szerkezete

Nukleozid és bázisanalógok (ismétlés)

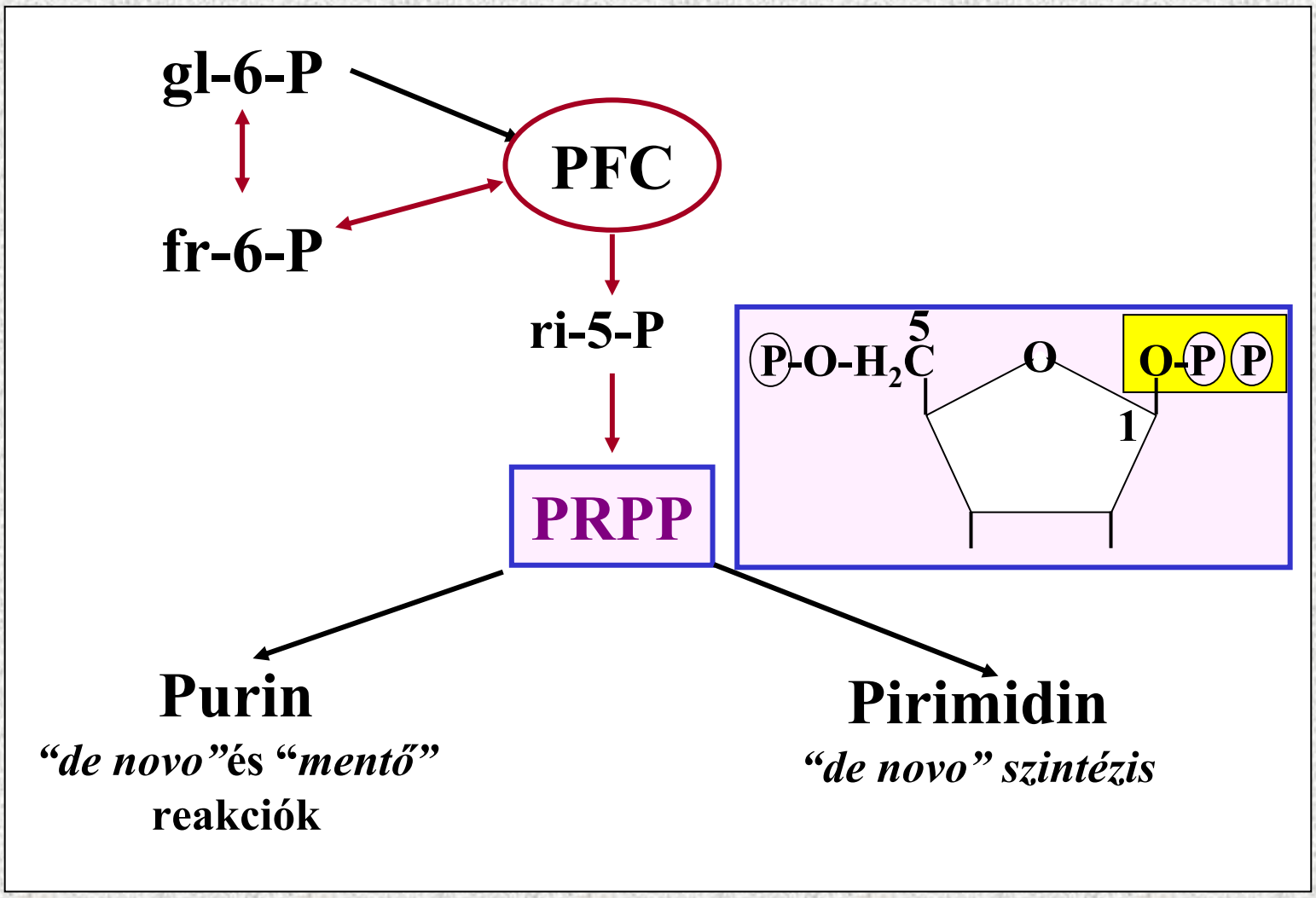



BÉLCSATORNA
vér
EXTRAHEPATIKUS SZÖVETEK
(agy, vvs, limfocták)
Táplálék
RNS, DNS
polinukleotidok
nukleotidok
nukleozidok
bázisok
"mentő reakciók"
Máj
"de novo"
szintézis
nukleotidok
DNS
RNS
LEBONTÁS
nukleozidok
bázisok
urát
nukleozidok
bázisok
urát
Vizelet

Purin nukleotid szintézis



A ribóz-foszfát eredete



PRPP= foszforibozil pirofoszfát

A purin váz eredete

C donor

N^{10}formil H_4F

N^{10}formil H_4F

CO_2

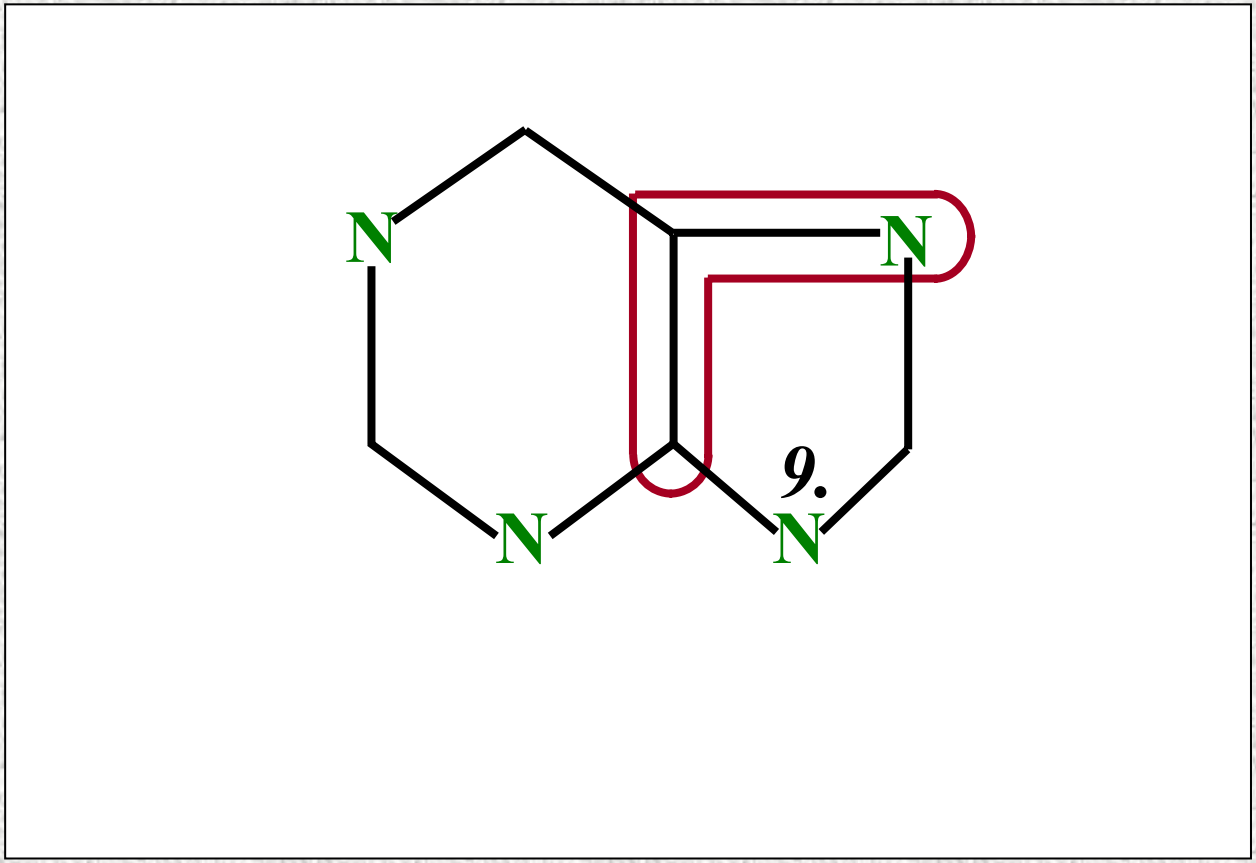
N donor

Gln

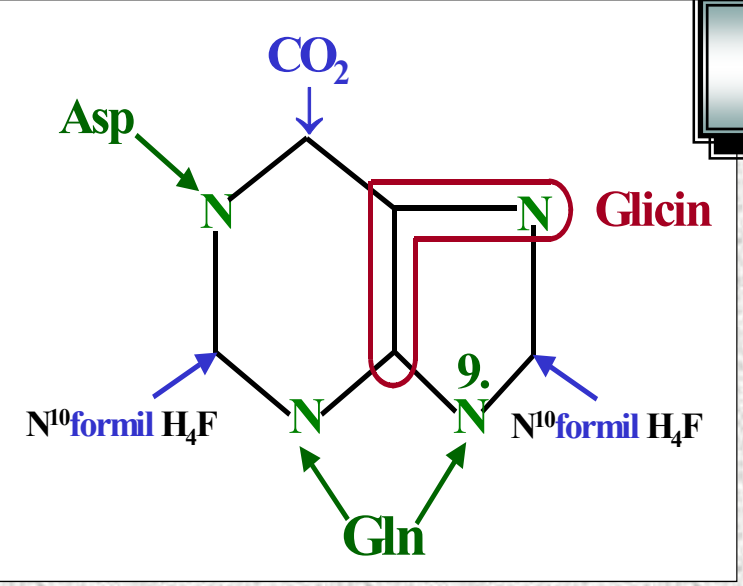
Gln

Asp

Glicin



“de novo” purin szintézis



PRPP

1. Gln → Glu

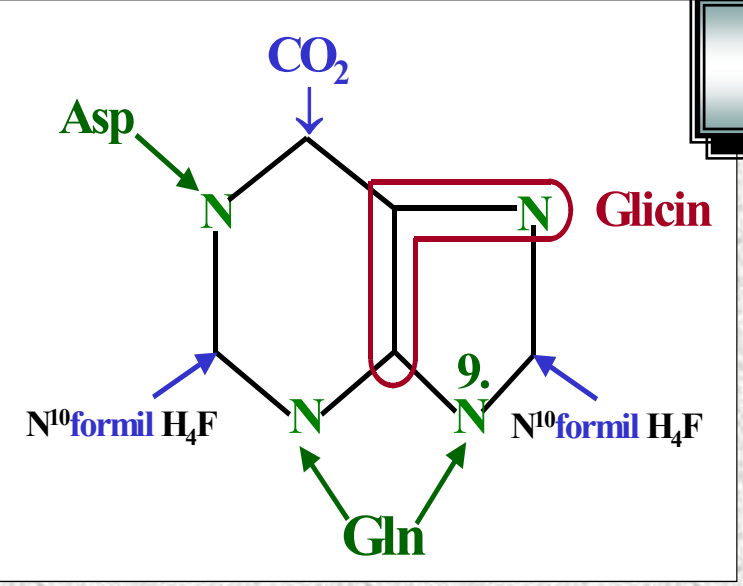
9. NH_3^+ — ri-5-P

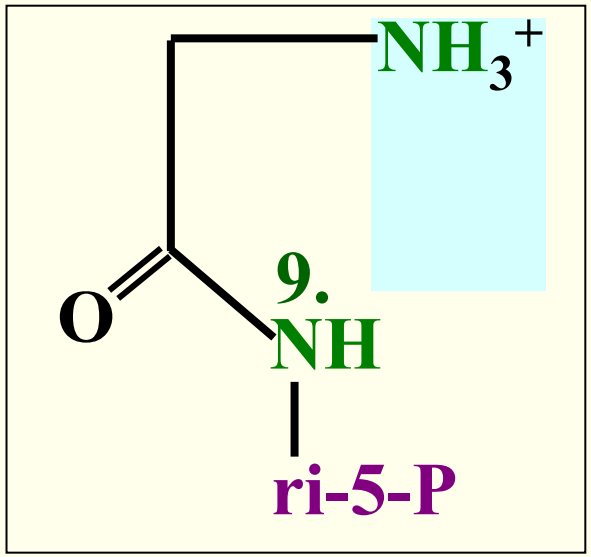
PRA

(P-ribozilamin)

2. Glicin, ATP → $ADP + P_i$

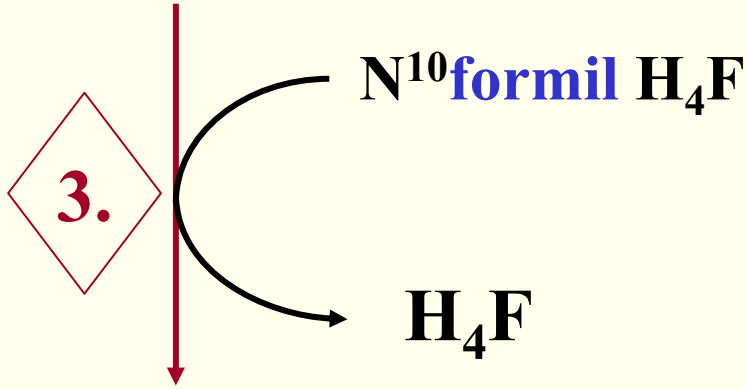
“de novo” purin szintézis



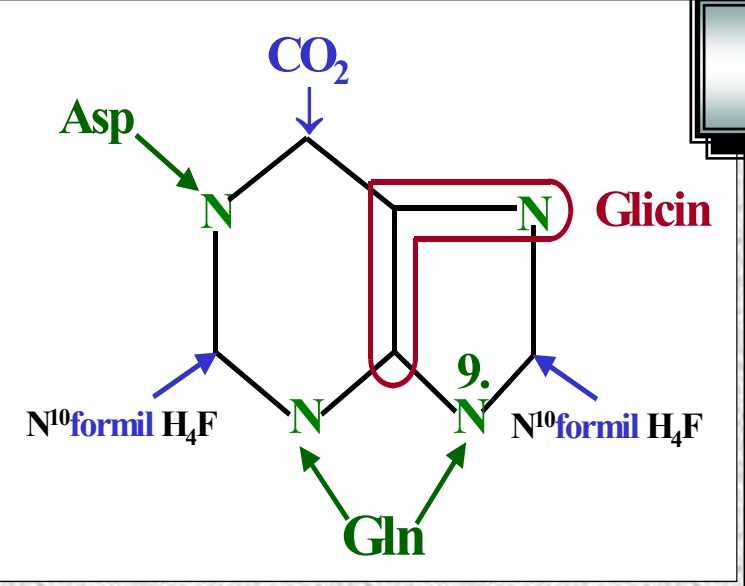


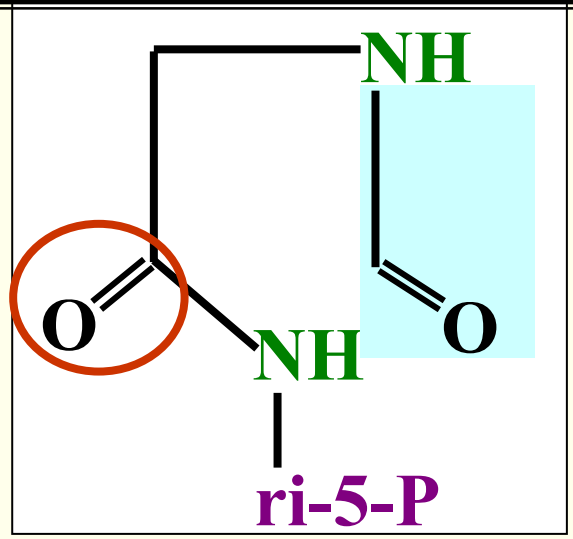
GAR

(Glicin-amid-ribozil-5P)

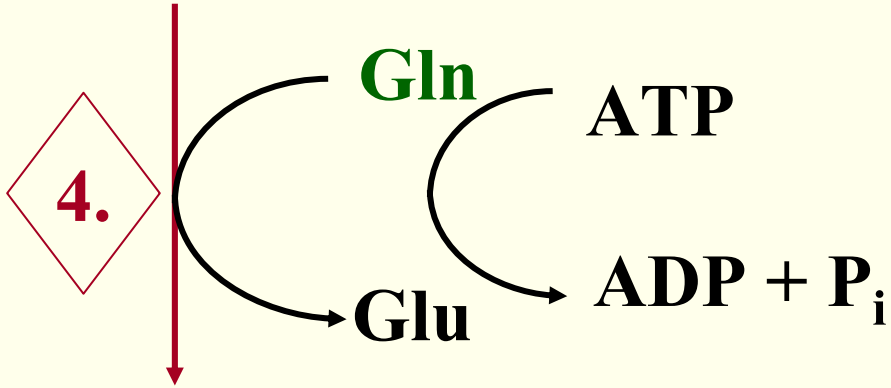


“de novo” purin szintézis

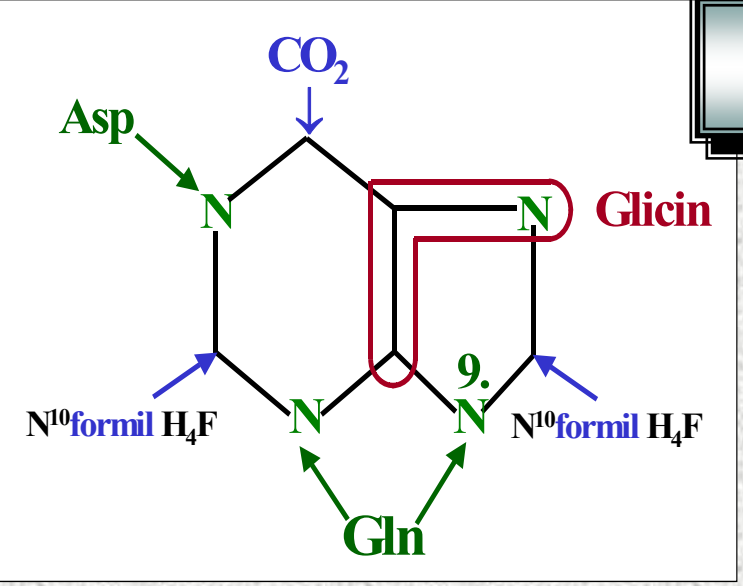


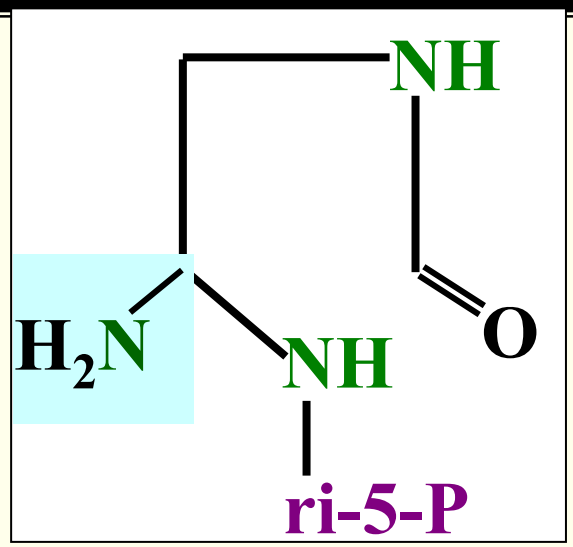


FGAR
(formil-GAR)



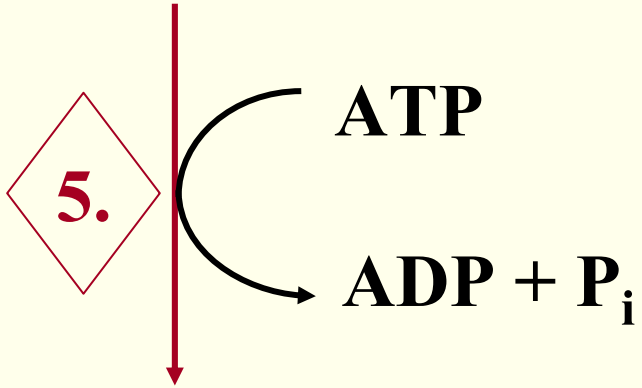
“de novo” purin szintézis



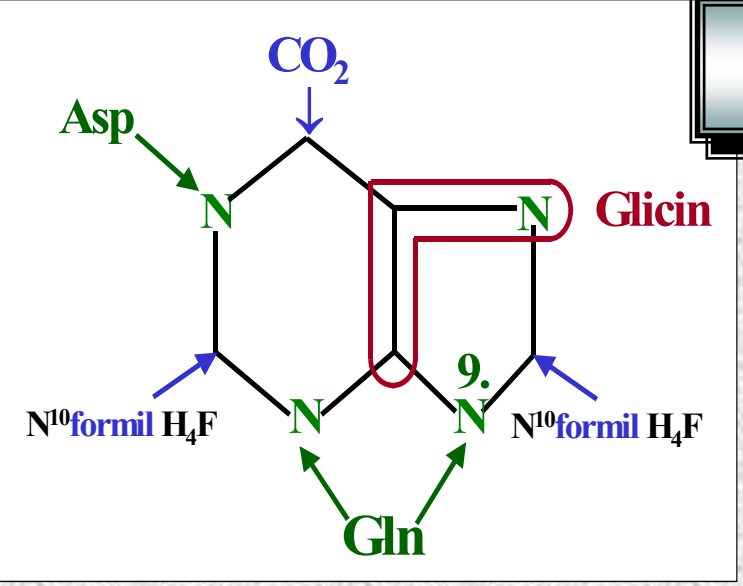


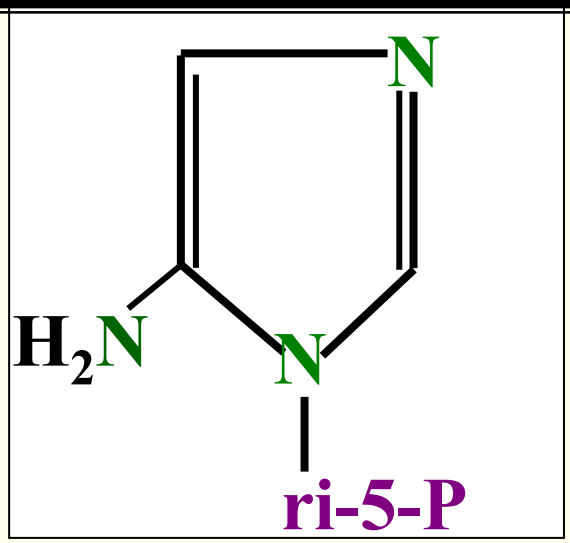
FGAM

(formil-Glicin-Amidin-Ri-5-P)



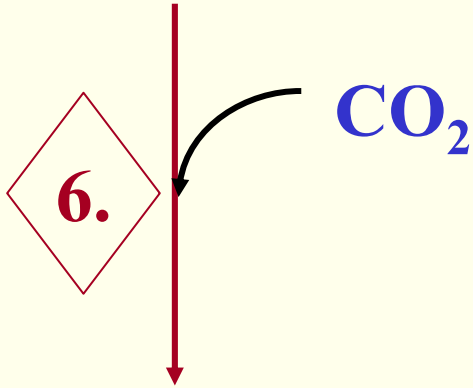
“de novo” purin szintézis



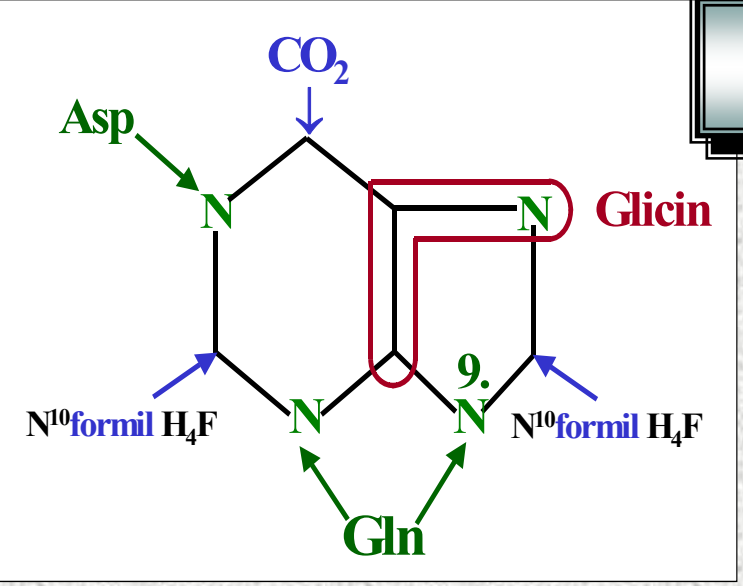


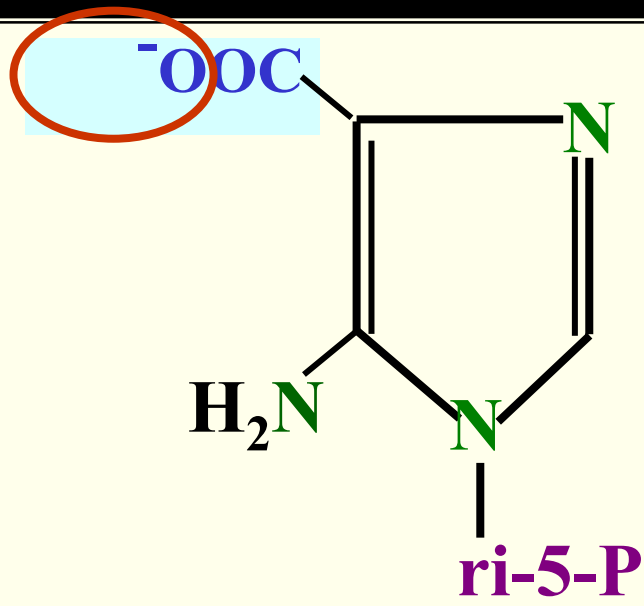
AIR

(Amino-Imidazol-Ri-5-P)



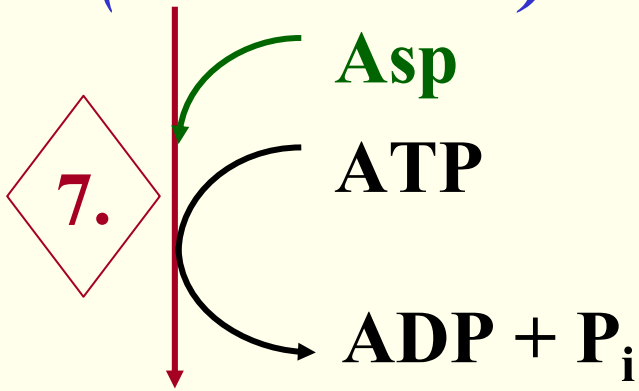
“de novo” purin szintézis



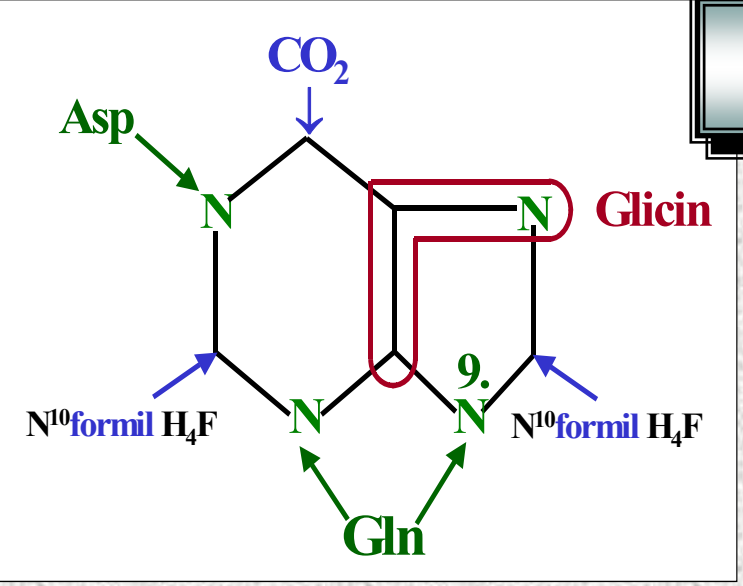


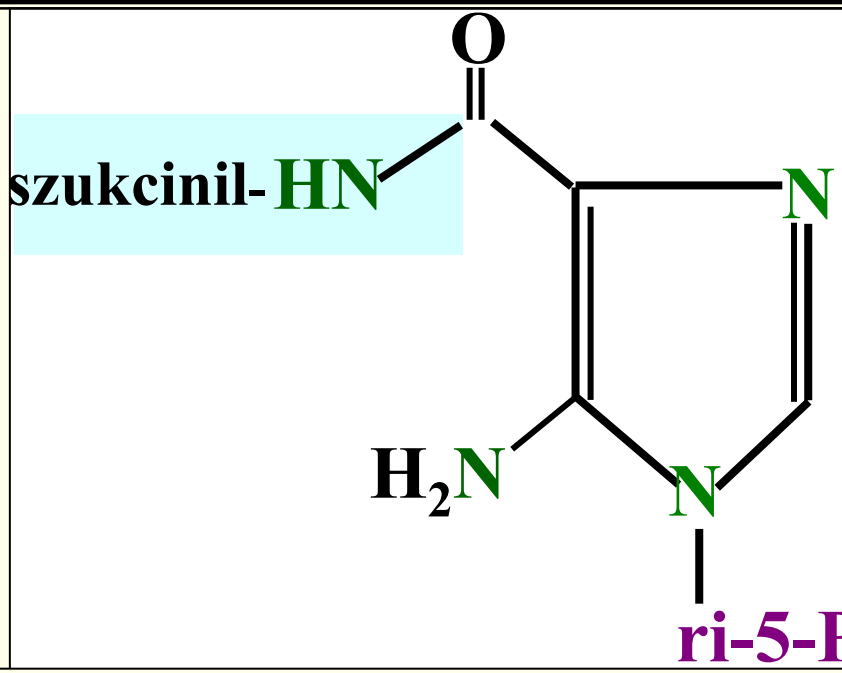
CAIR

(Carboxi-AIR)



“de novo” purin szintézis





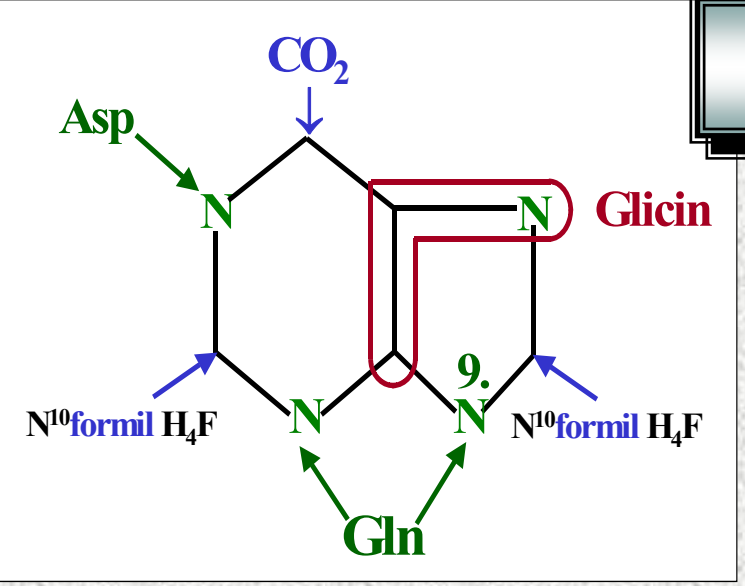
SAICAR

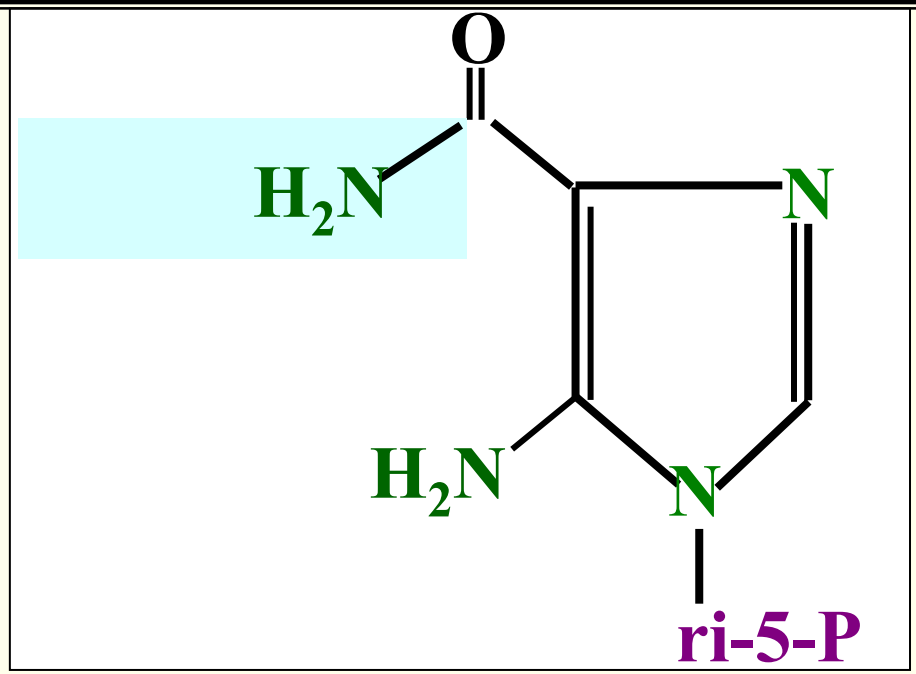
(Szukcinil-amino-imidazol-karboxamid-ri-5P)

8. **Adeniloszukcináz (ASA)**

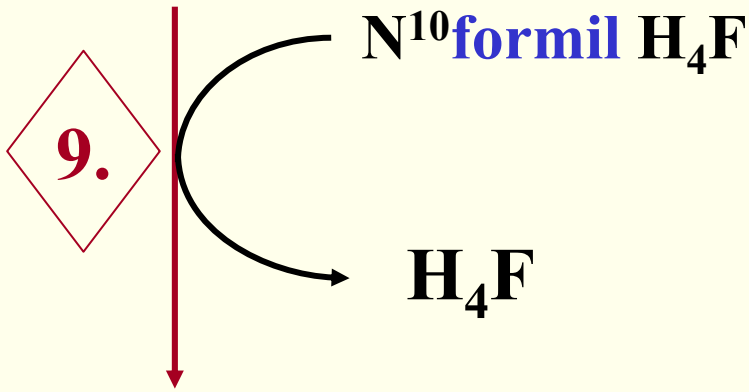
fumarát

“de novo” purin szintézis

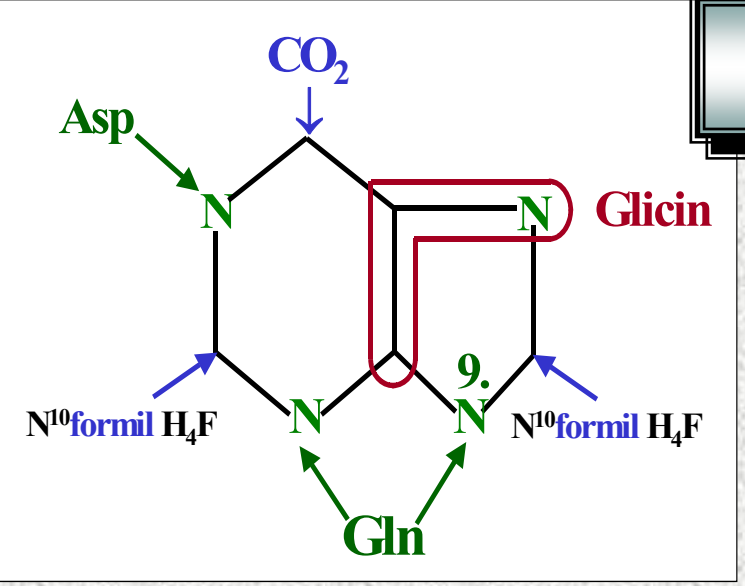


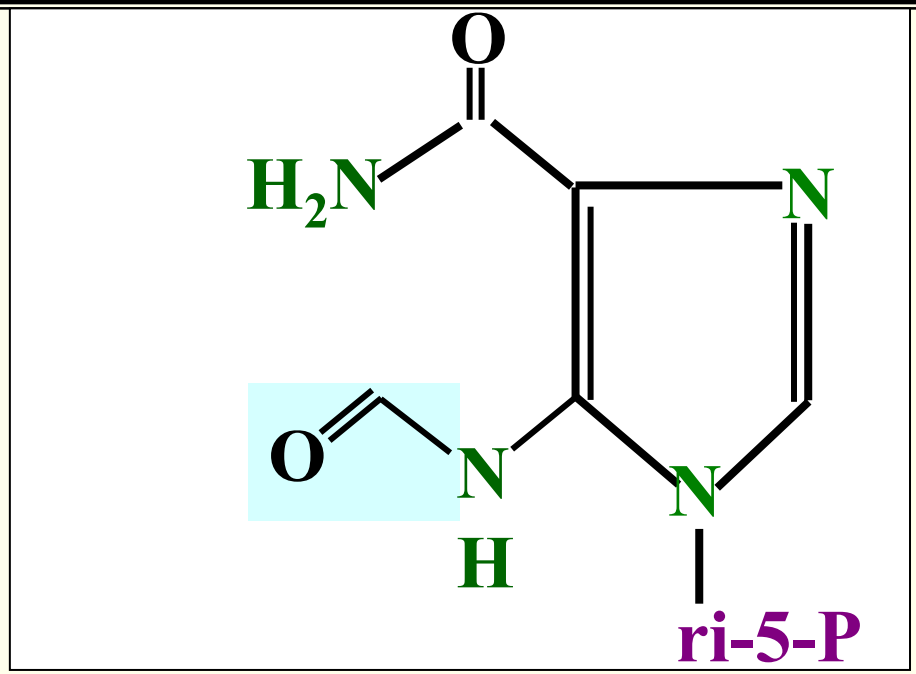


AICAR

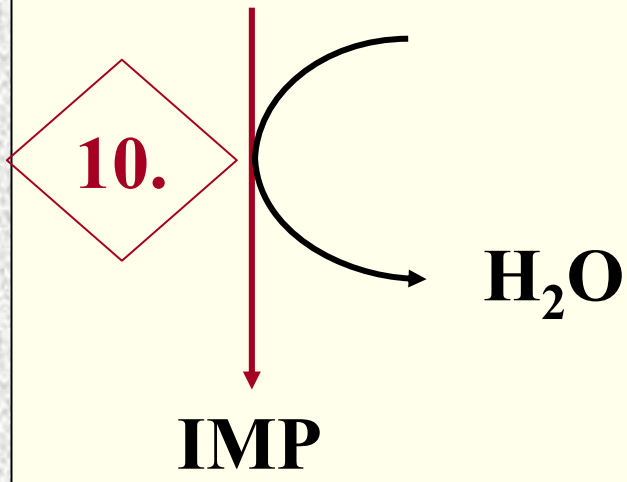


“de novo” purin szintézis

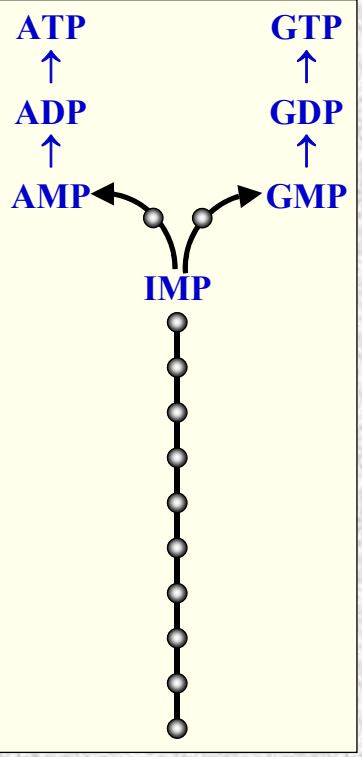




FAICAR



“de novo” purin szintézis és a purin nukleotid ciklus



AMP
(6-amino)

AMP DA

GMP
(2-amino-6-oxo)

ASA

fumarát

ADP+P_i+ Glu

ATP

Gln

Adenilo-szukcinát

Xantozin-MP
(2,6,-dioxo)

GDP+P_i

NADH + H^+

GTP

IMPDH

NAD^+

Asp

H_2O

IMP(6-oxo)

AMP= adenilát
DA=dezaminász
DH=dehidrogezáz

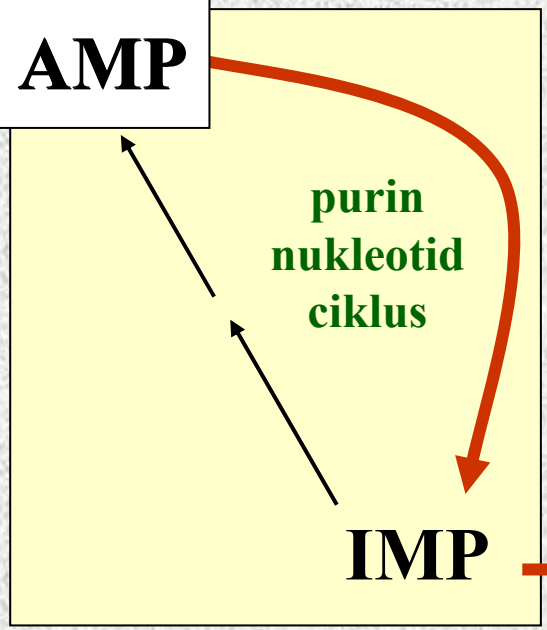
A purin nukleotid ciklus

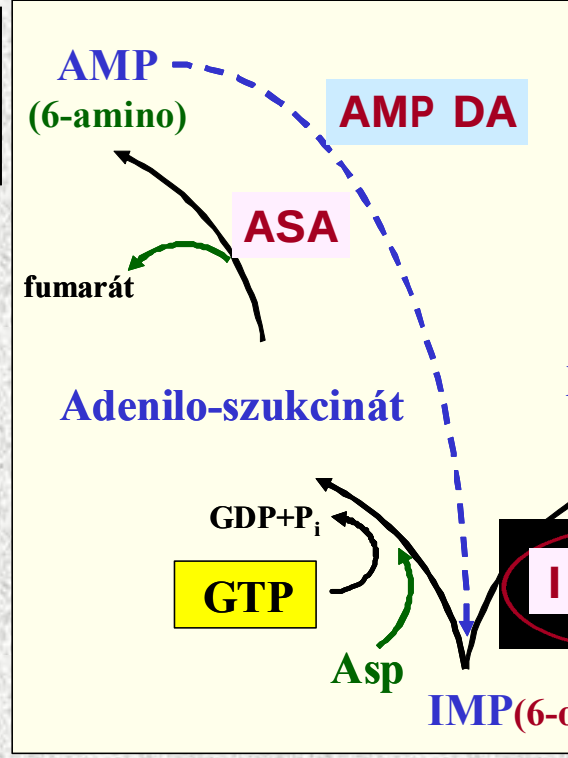
2 ADP

AMP kináz

alacsony energiaszint

ATP + AMP



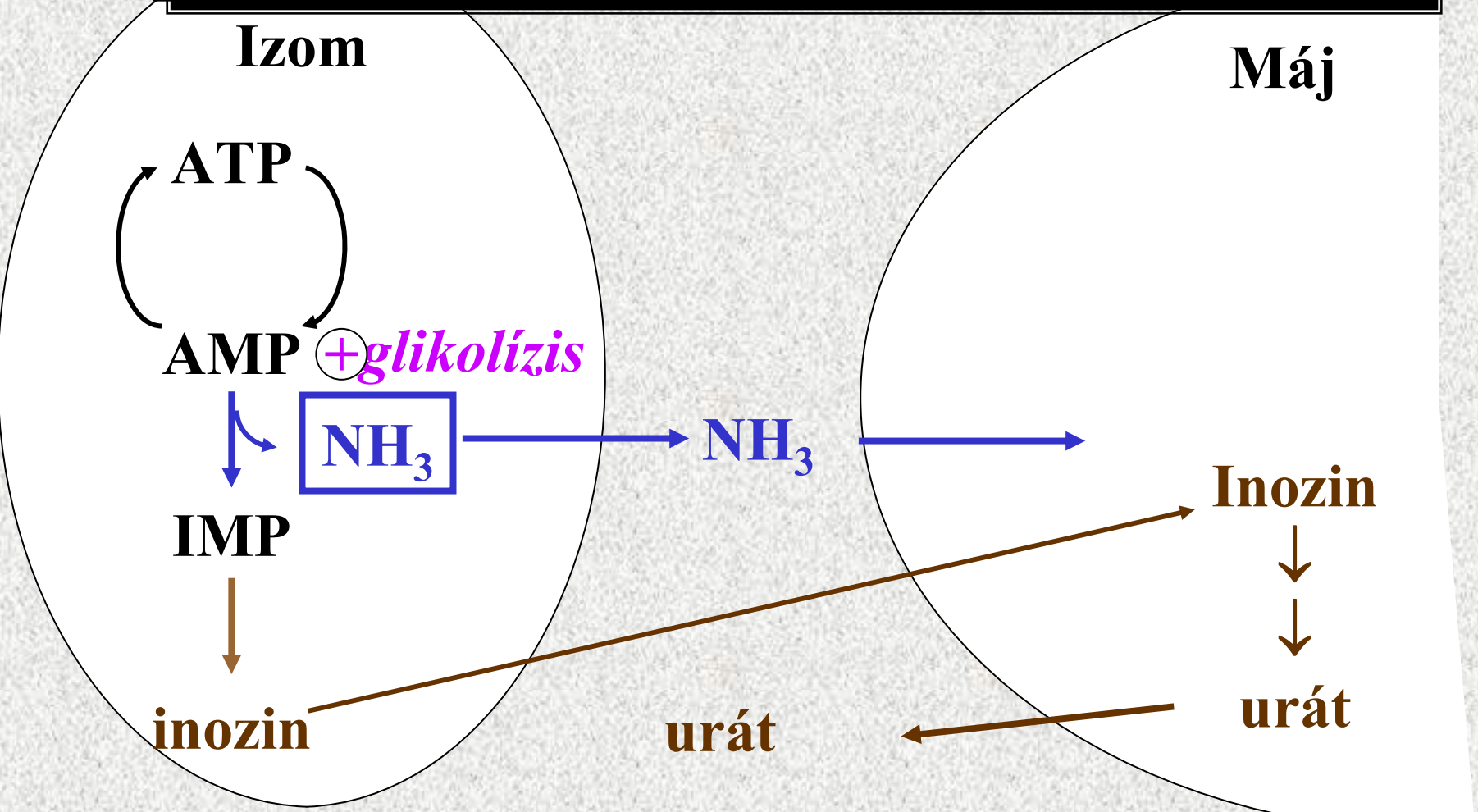


→ → urát (vizelet)

[AMP]↑ → → húgysav (urát) túltermelés

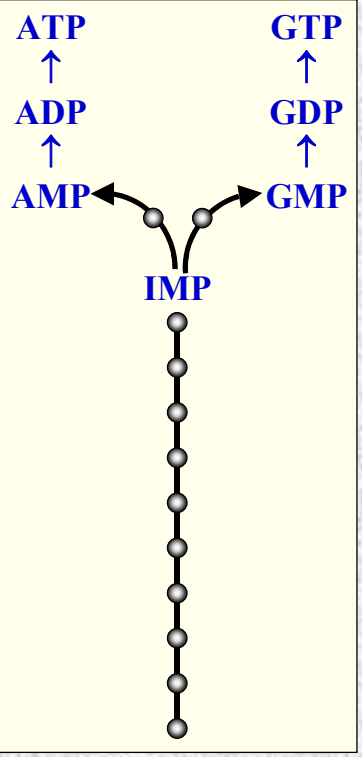
Pl. fruktóz intolerancia

Izom: magas AMP deamináz szint



Erős munkavégzés: NH_3 ↑, urát ↑

Izom AMP DA def.: **izomgörcs, NH_3, urát NEM nő**



GMP

purin monofoszfát kináz

ATP

ADP

GDP

purin difoszfát kináz

ATP

ADP

GTP

AMP

adenilát kináz

ATP

ADP

ADP

Szubsztrát szintű/oxidatív foszforiláció

$+ P_i \rightarrow$ ATP

Purin mentő reakciók

PRT (foszforibozil transzferáz)

bázis → NUKLEOTID

APRT

adenin → AMP

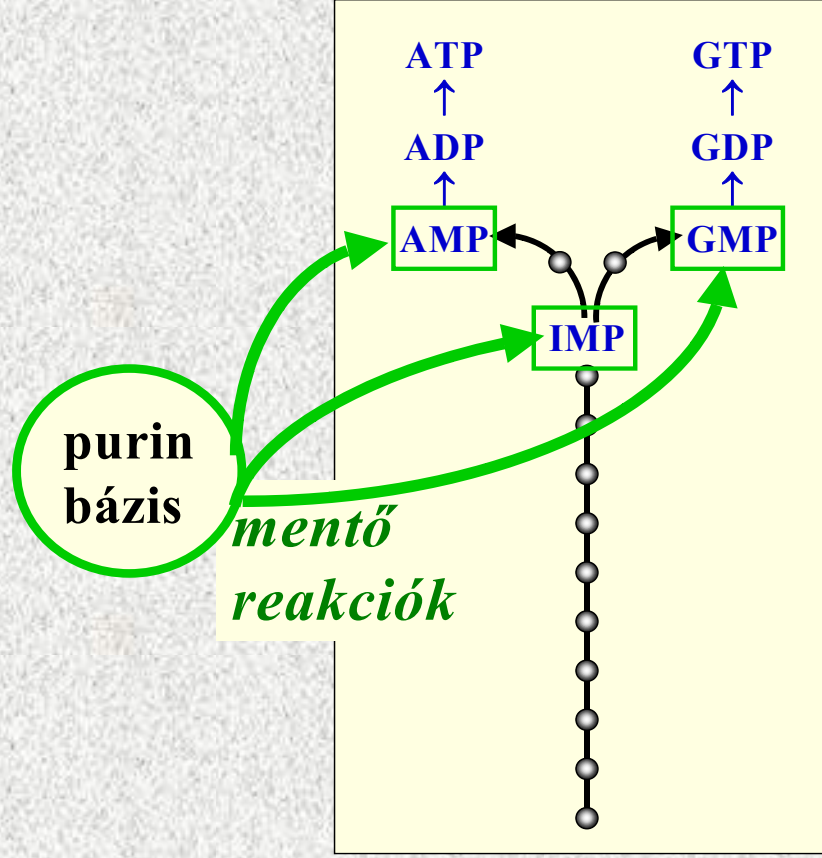
PRPP → PPi

HPRT

hipoxantin → IMP

guanin → GMP

PRPP → PPi



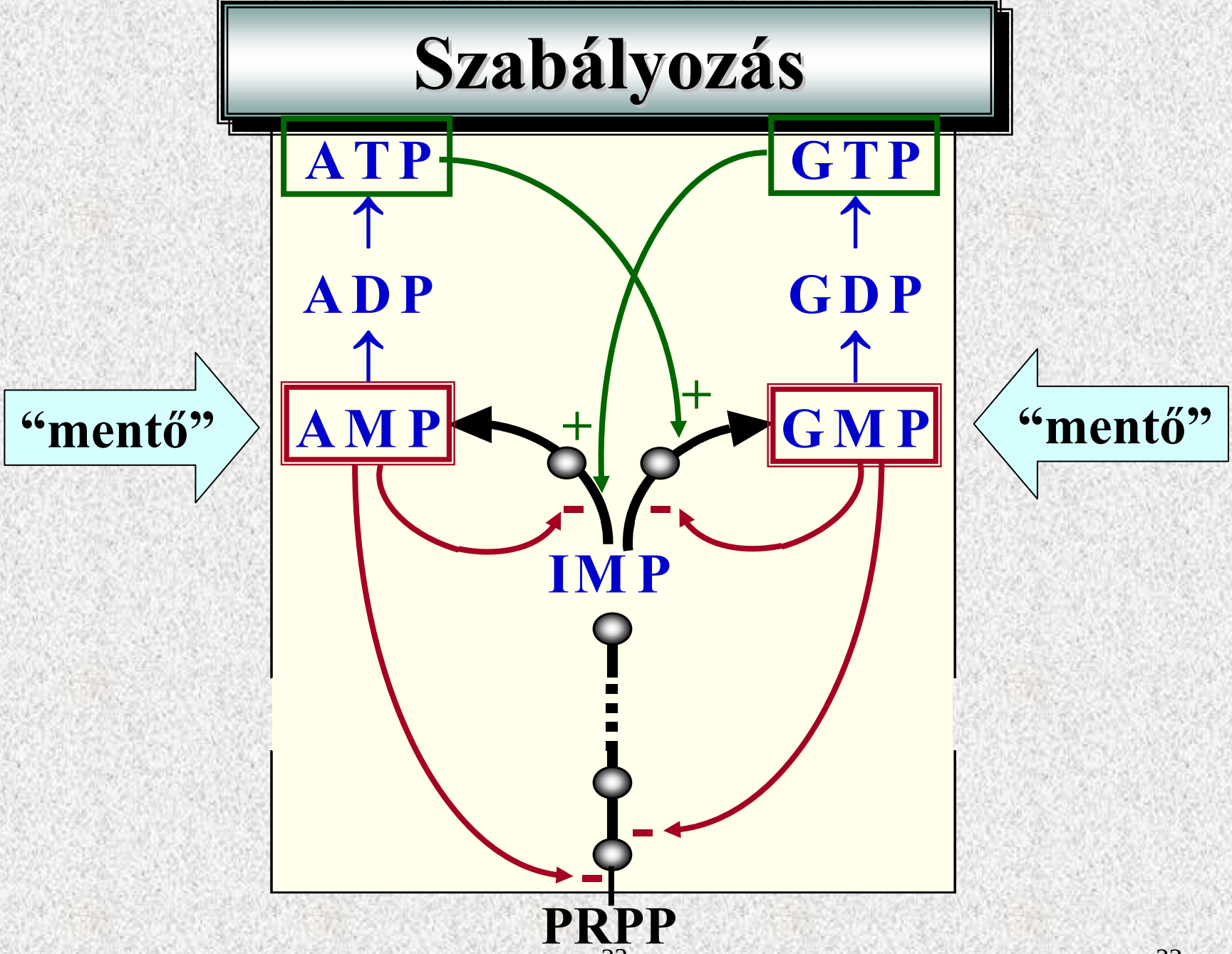
A Lesh-Nyhan szindróma

HPRT hiány:

A bazális ganglionok GTP szintje alacsony lesz

X-kromoszómához kapcsolt
mentális retardáció
öncsonkítás
hyperuricemia

Szabályozás



A purin “ de novo” és “mentő” reakcióutak aránya különböző szövetekben

	“de novo” út intenzitása (amido-PRT aktivitás)	“mentő” út intenzitása (HPRT aktivitás)
MÁJ	*magas*	*alacsony*
VVS bazális ganglionok	*alacsony*	*magas*

A “de novo” út gátlószerei: **Ribavirin (IMP DEH)**
Acivicin (Gln analóg)

Vírusfertőzés, tumorok, vvs paraziták ellen

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