LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

Vorlesung Co-Enzyme

Prof. Thomas Carell
Dr. Stefanie Kellner

Termine

Heute: Dr. Stefanie Kellner

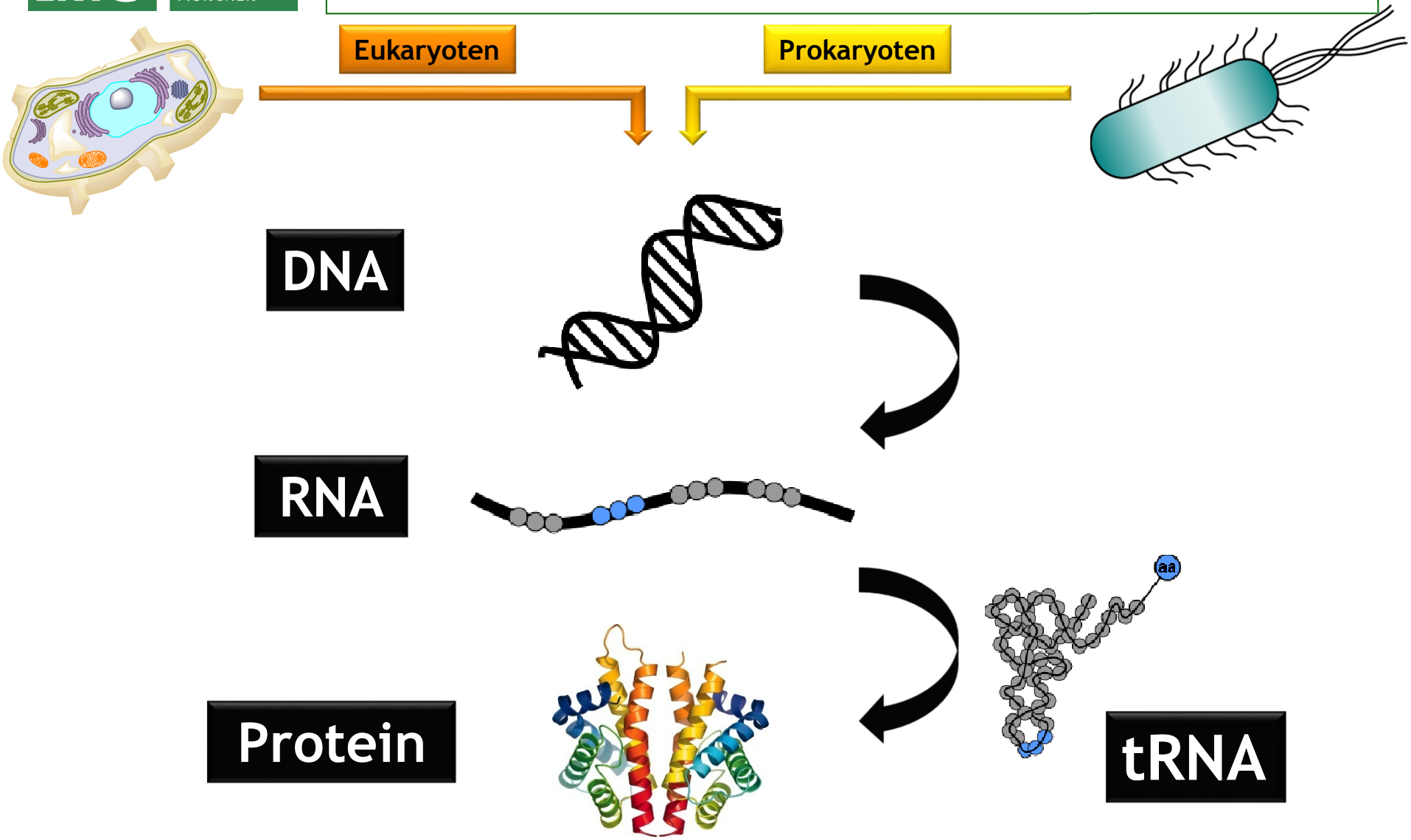
4. Mai, 11. Mai und 18. Mai müssen verlegt werden

Alternativtermine: 26. Mai, 2 Juni und 16. Juni

Absprache mit Prof. Carell am 1. Juni

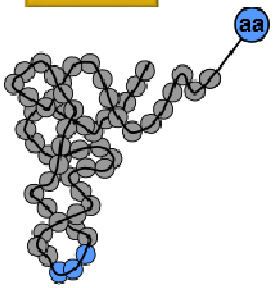
Nächster Termin: 1. Juni mit Prof. Carell

Das zentrale Dogma

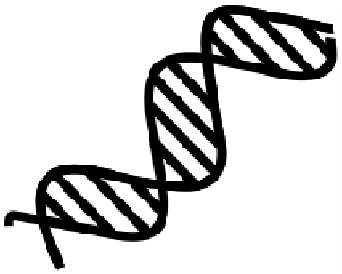


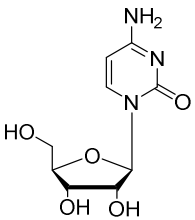
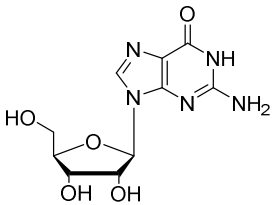
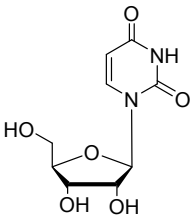
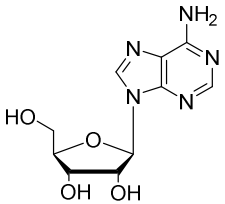
Die Grundbausteine von Nukleinsäuren

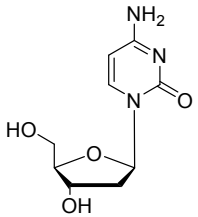
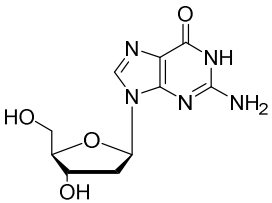
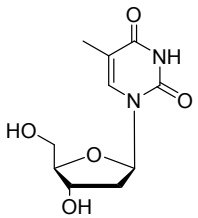
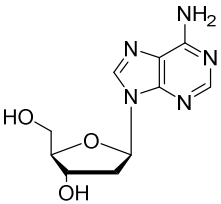
RNA



DNA



Cytidine 	**Guanosine** 
Uridine 	**Adenosine** 

2'deoxycytidine 	**2'deoxyguanosine** 
2'deoxythymidine 	**2'deoxyadenosine** 

Metabolismus von Nukleinsäuren

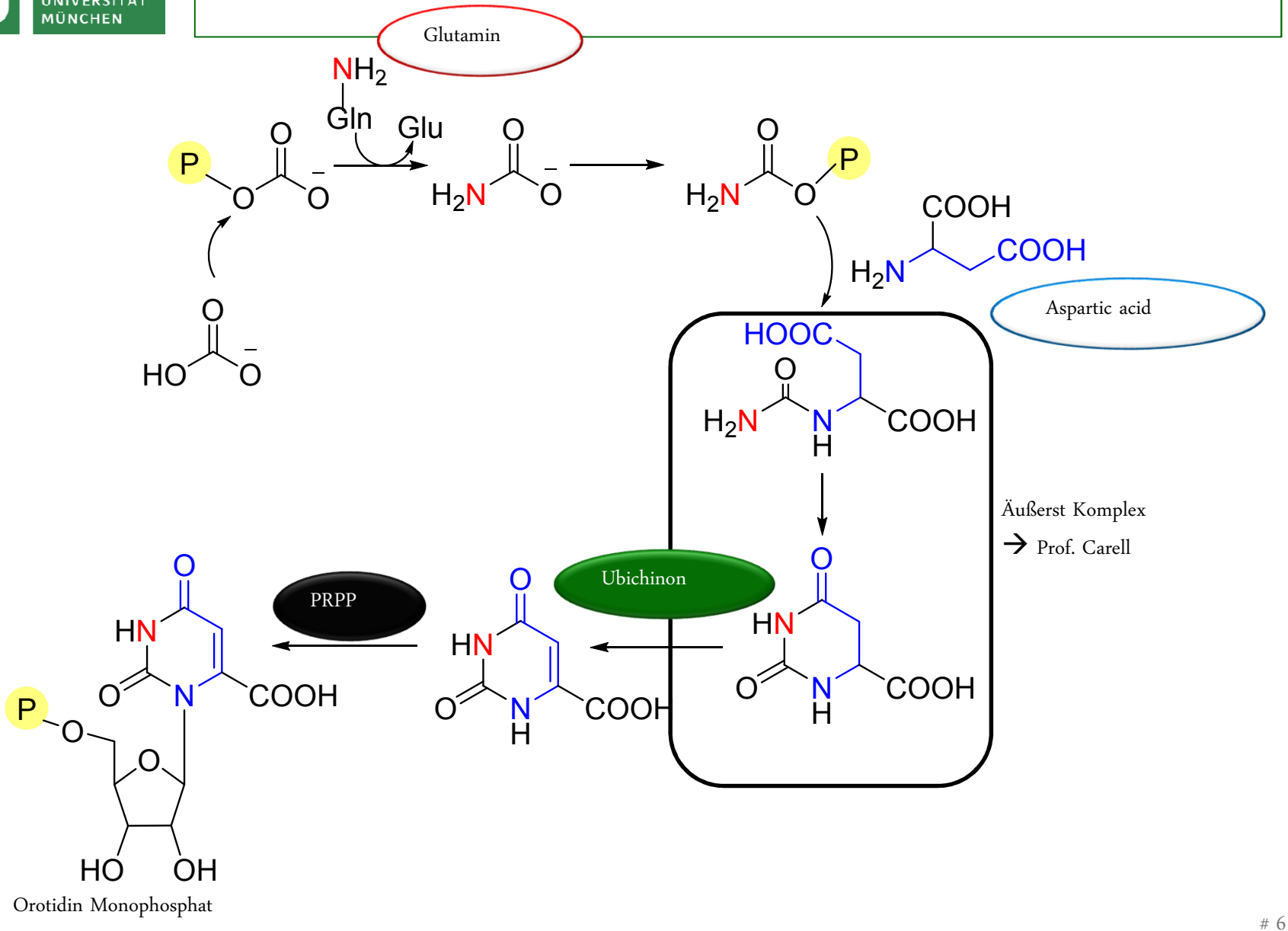
Metabolismus besteht aus:

- Anabolismus: Aufbau von Stoffen
- Katabolismus: Abbau von Stoffen

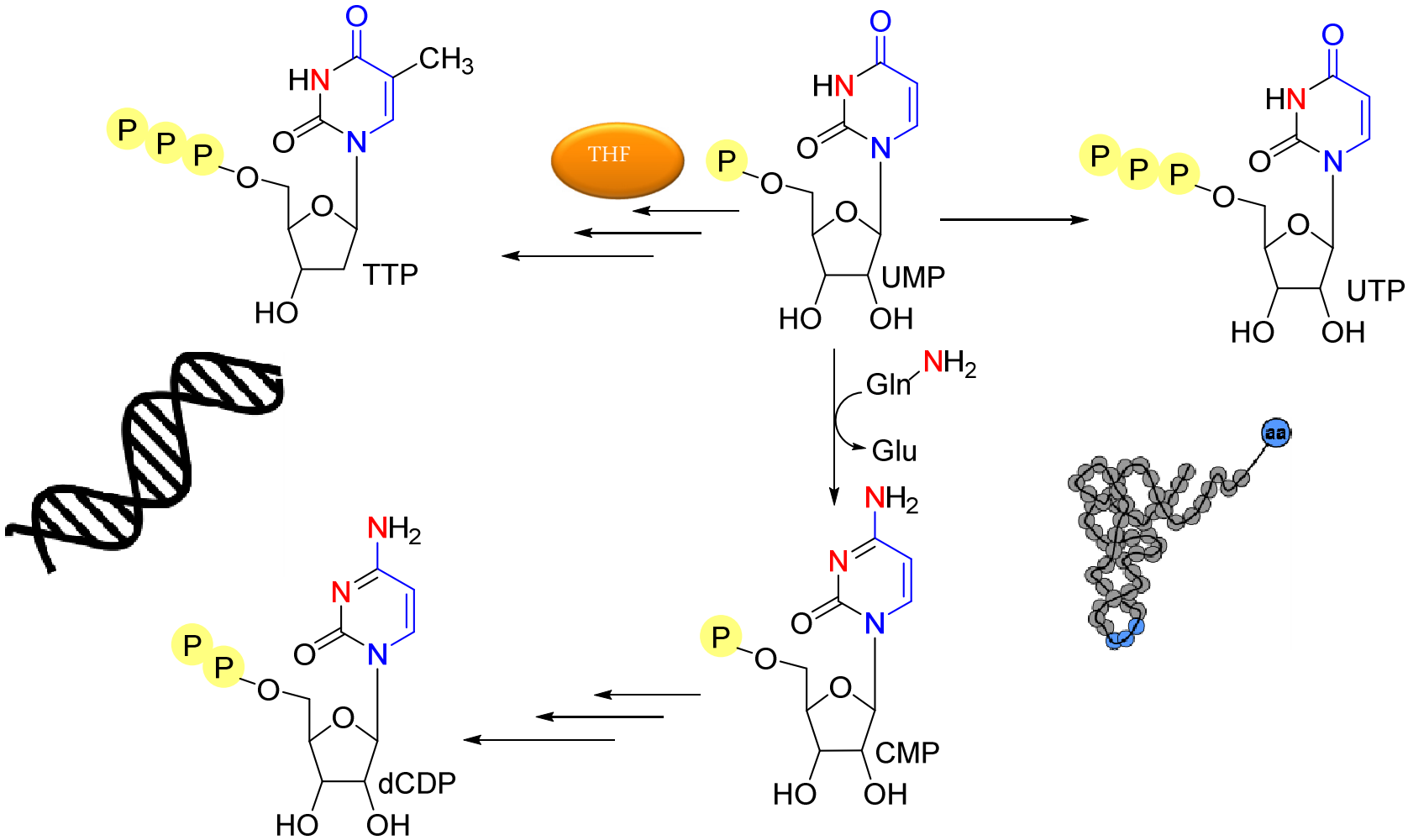
Zum Auf- und Abbau von Nukleinsäuren aus einfachen Grundbausteinen werden Co-enzyme gebraucht:

- NAD (von Niacin = Nicotinamid-Derivate)
- FAD (Flavine = Vitamin B12)
- Ubichinon (Coenzym Q = Vitamin Q)
- THF (Tetrahydrofolsäure-Derivate = Folsäure)

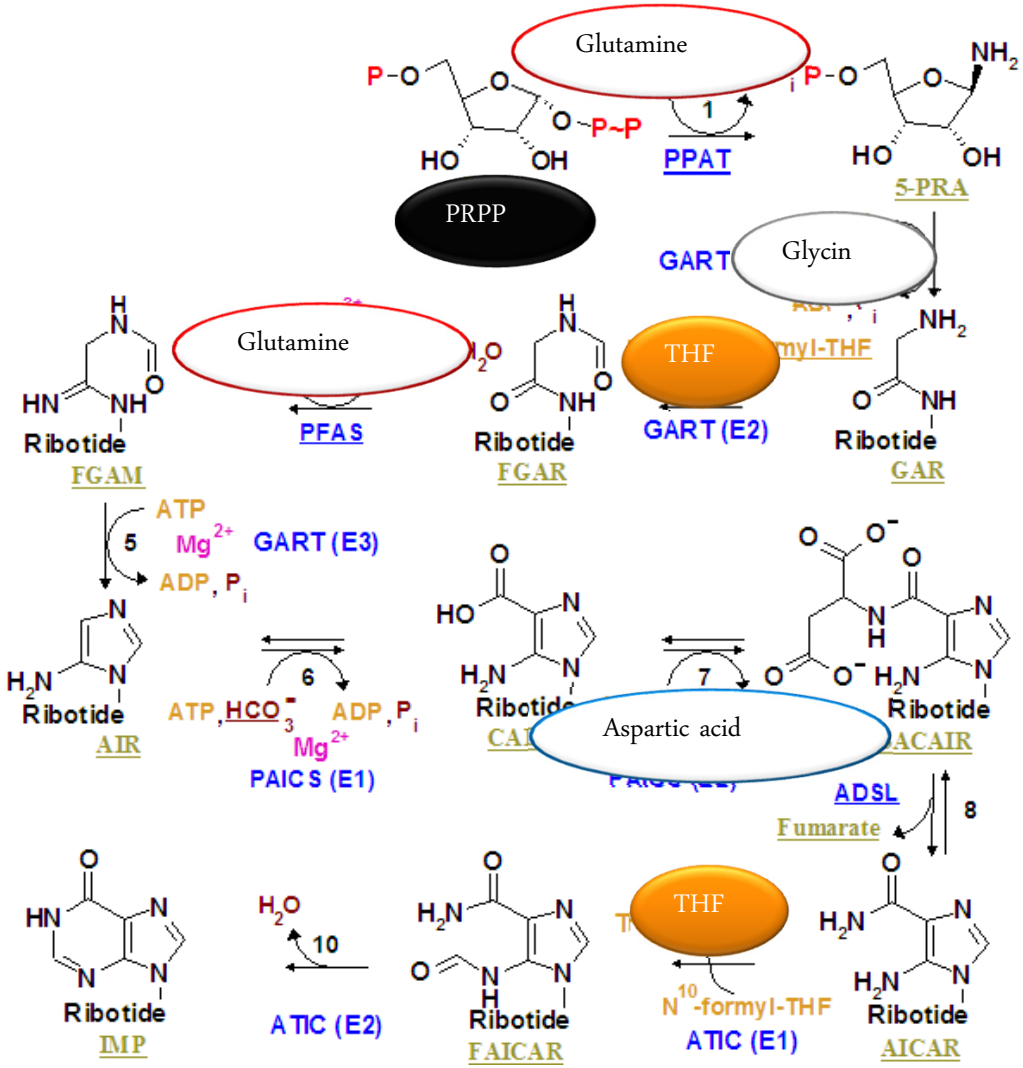
Pyrimidin Biosynthese



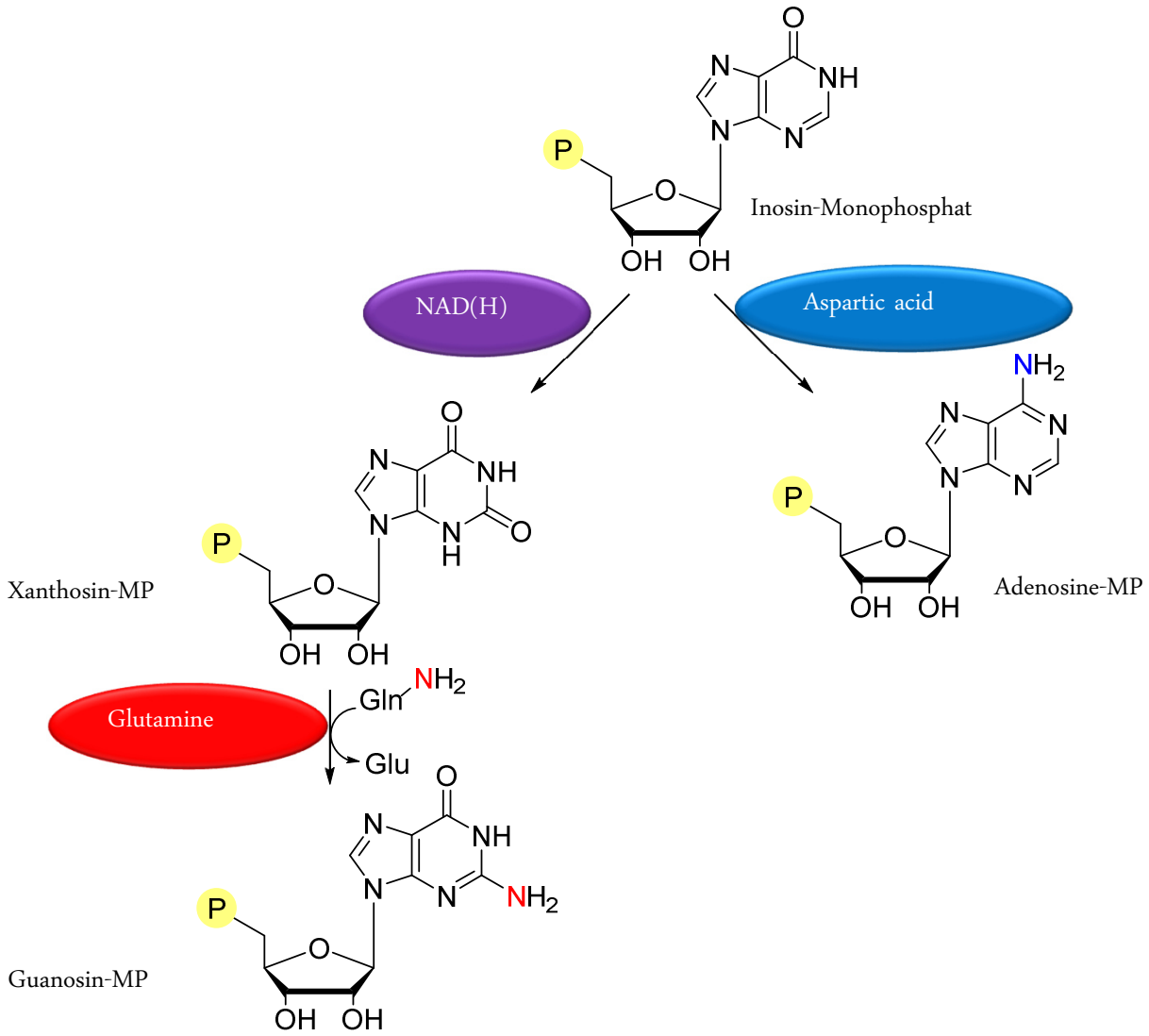
Pyrimidin Biosynthese



Purin Biosynthese

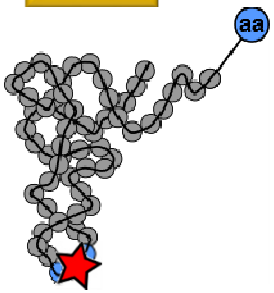


Purin Biosynthese

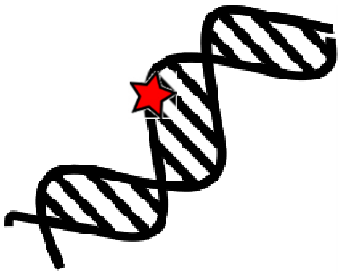


Die Grundbausteine von Nukleinsäuren

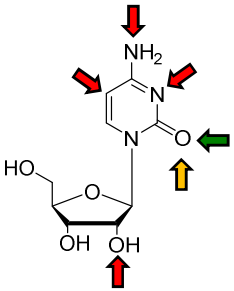
RNA



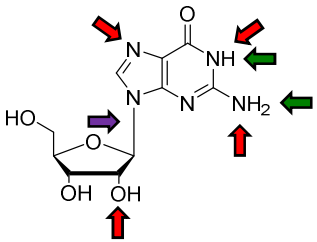
DNA



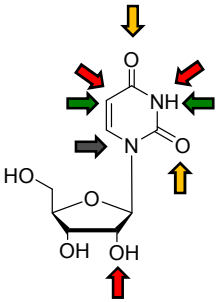
Cytidine



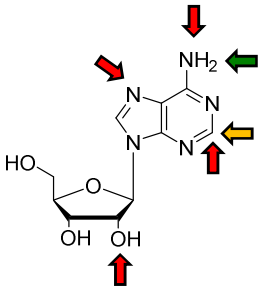
Guanosine



Uridine

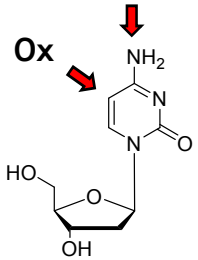


Adenosine

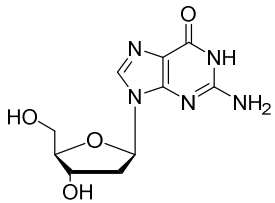


- Methylierung
- Isomerisierung
- Thiolierung
- Gruppenaddition
- Transglyko-silierung

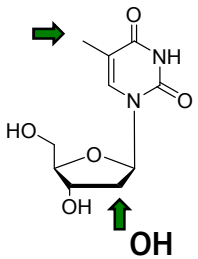
2'deoxycytidine



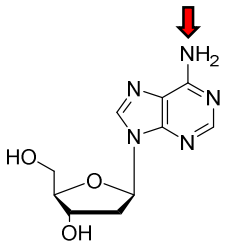
2'deoxyguanosine



2'deoxythymidine



2'deoxyadenosine



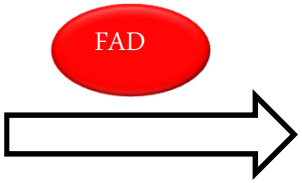
Katabolismus

Pyrimidine:

Cytidin → Uridin

Uridine → Uracil + β-Ribose-1-Phosphat

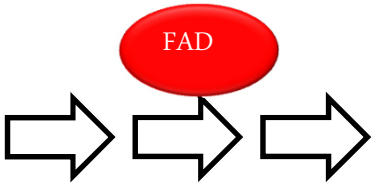
Uridin
Thymidin



Dihydrouridin
5,6-Tetrahydrouridin

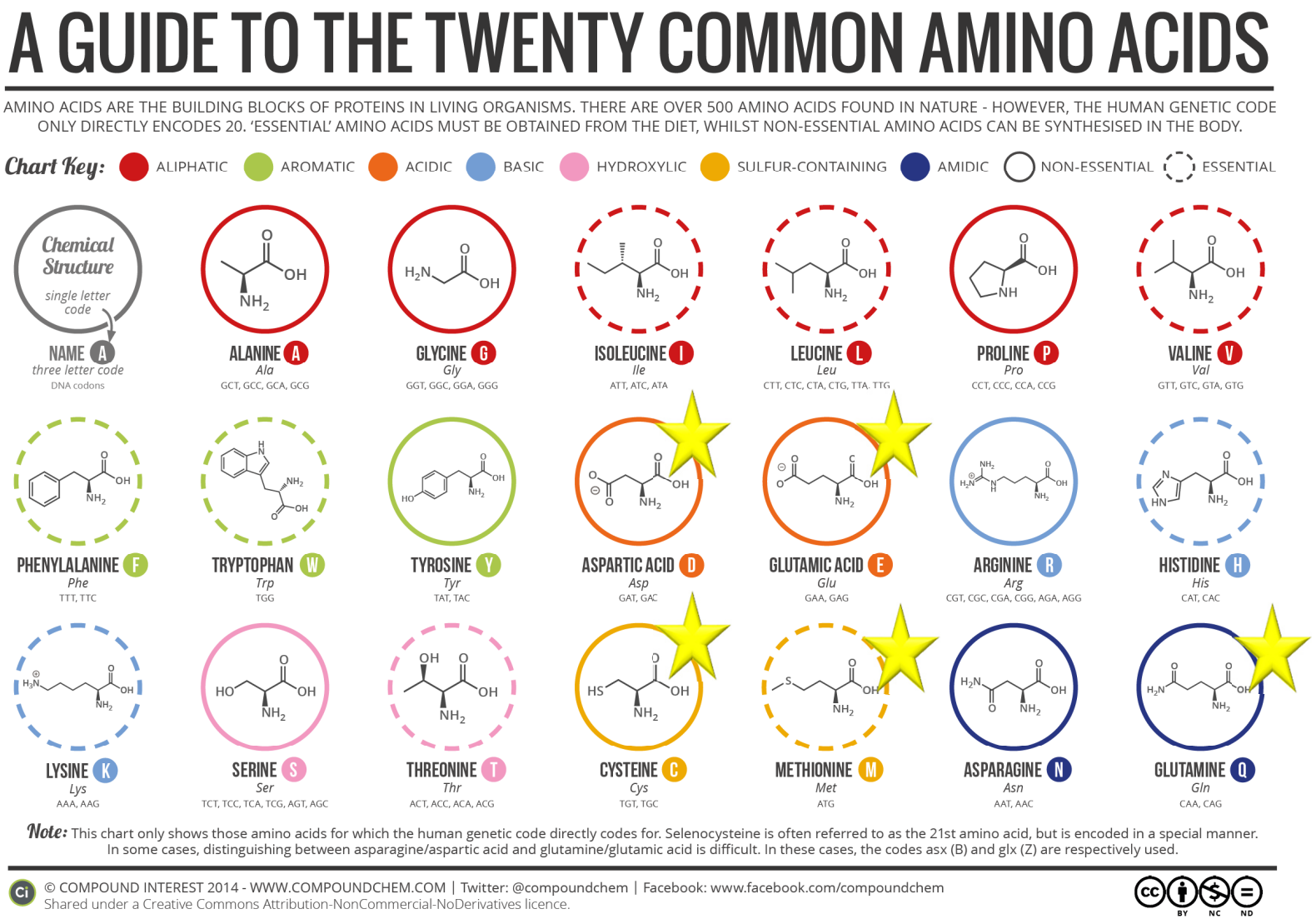
Adenosine → Inosine → Xanthin

Guanosine → Guanin → Xanthin



Harnsäure

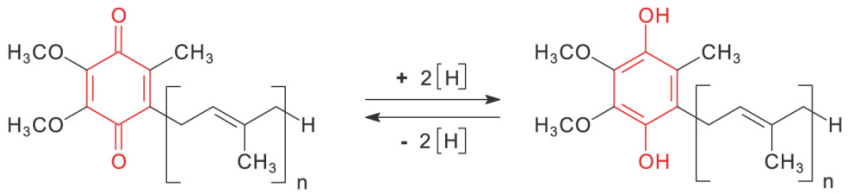
Aminosäuren



Überblick der beteiligten Coenzyme

Ubichinon

Redoxreaktionen

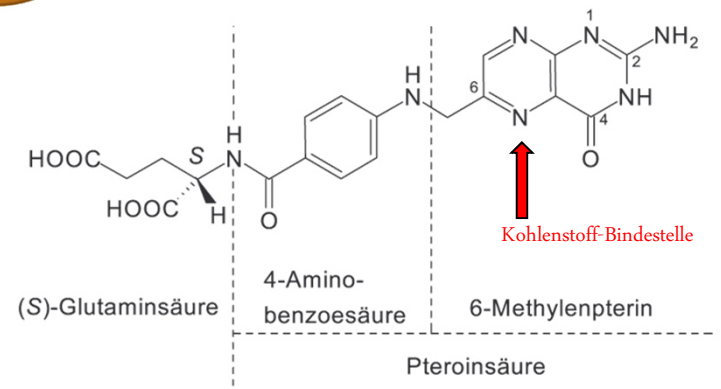


Ubichinon (n = 5 bis 10)

Ubihydrochinon (Ubichinol)

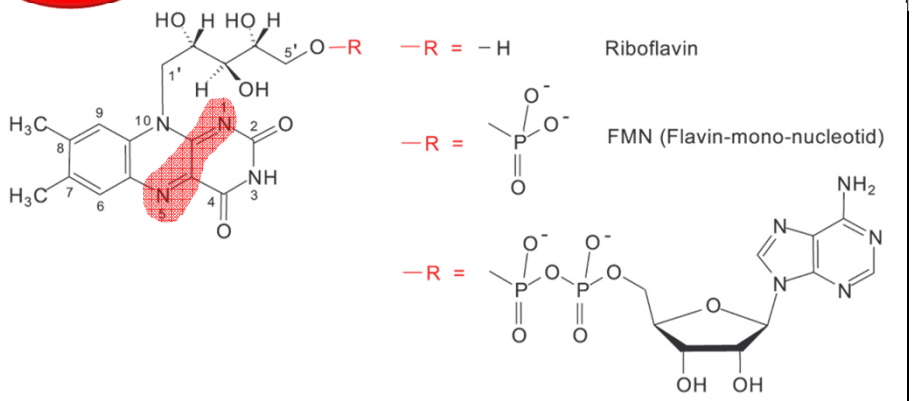
THF

C-Überträger



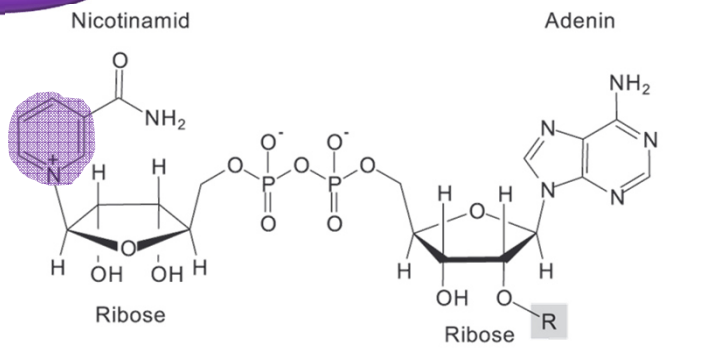
FAD

Redoxreaktionen



NAD(H)

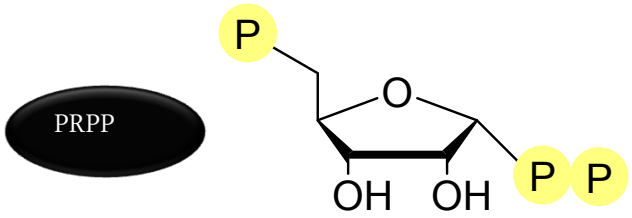
Redoxreaktionen



R = H NAD^+ (Nicotinamid-Adenin-Dinucleotid)

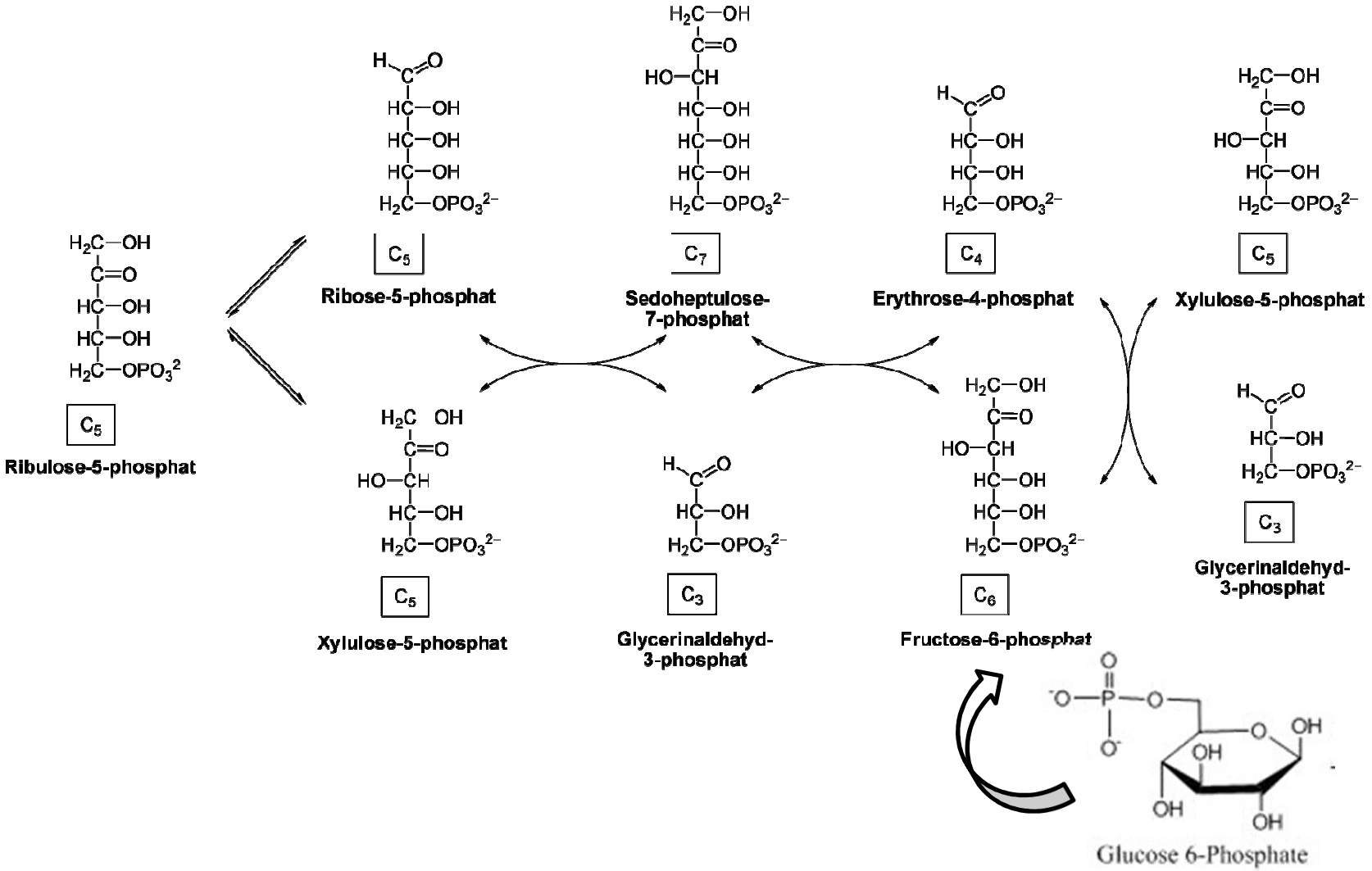
R = PO_3^{2-} $NADP^+$ (Nicotinamid-Adenin-Dinucleotid-Phosphat)

PRPP – der wichtigste Grundbaustein



Alternative

Transaldolasen und Transketolase: Umwandlung von Triosen, Tetrosen, Hexosen und Heptosen



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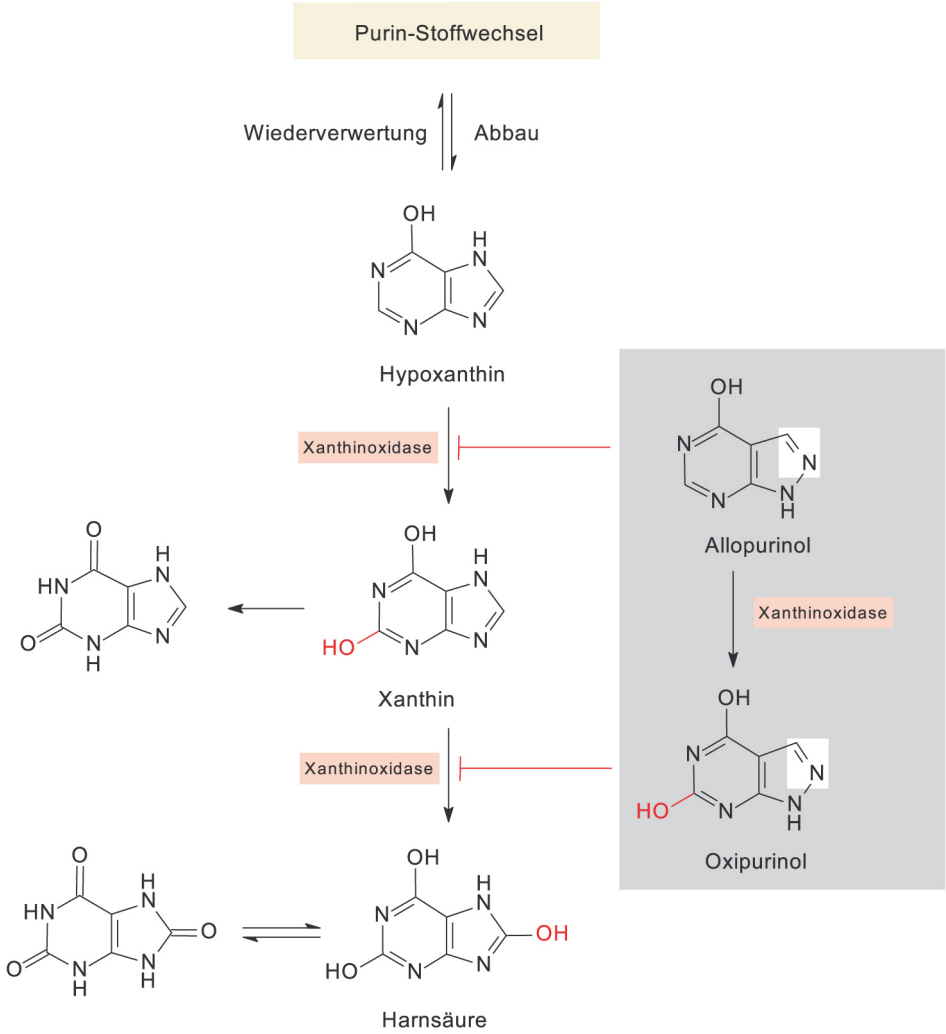
Arzneistoffe die in Nukleosid Metabolismus eingreifen

Krankheiten mit gestörtem Katabolismus

	Gicht
Auslöser	Harnsäure fällt in Gelenken aus und löst Entzündung aus
Therapie	Hemmung der Harnsäure Bildung
Wirkstoffklasse	Xanthinoxidase Inhibitor
Wirkstoffe	- Allopurinol



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Krankheiten mit gestörtem Anabolismus

	Entzündung z.B. Rheumatoide Arthritis	Neoplasien z.B. Krebs	Infektionen z.B. Viren
Auslöser	Autoimmunreaktion Erhöhte Zellproliferation von Lymphozyten	Erhöhte Zellproliferation von entarteten Gewebezellen	Synthese von viralen Nukleinsäuren
Therapie	Hemmung der Zellproliferation = Hemmung der DNA Synthese	Hemmung der Zellproliferation = Hemmung der DNA Synthese	Hemmung der viralen Replikation = Hemmung der viralen RNA und DNA Synthese
Wirkstoffklasse	Immunmodulatoren	Antimetabolite	Nukleosid-Analoga
Wirkstoffe	- Leflunomid - Methotrexat - Azathioprin	- 5-Fluoruracil - Mercaptopurin - Pentostatin	- Aciclovir - Zidovudin - Cidofovir