

## Research Interests

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### Biosynthesis and metabolic roles of tetrahydrobiopterin

5,6,7,8-Tetrahydrobiopterin ( $H_4$ biopterin) is a compound related to the vitamins folic acid and riboflavin which are all characterised by the common pteridine heterocycle. In contrast to folic acid and riboflavin, however, mammals (including humans) synthesise  $H_4$ biopterin from guanosine triphosphate (GTP).  $H_4$ -biopterin is a cofactor for hydroxylating aromatic amino acids – and is hence of crucial importance for neurotransmitter formation –, for nitric oxide (NO) formation from L-arginine – a key molecule for neurotransmission, blood pressure regulation and immune function –, and for alkylglycerol monooxygenase (glyceryl ether monooxygenase) - a little studied enzyme with (until 2010) unknown sequence (Fig. 1).

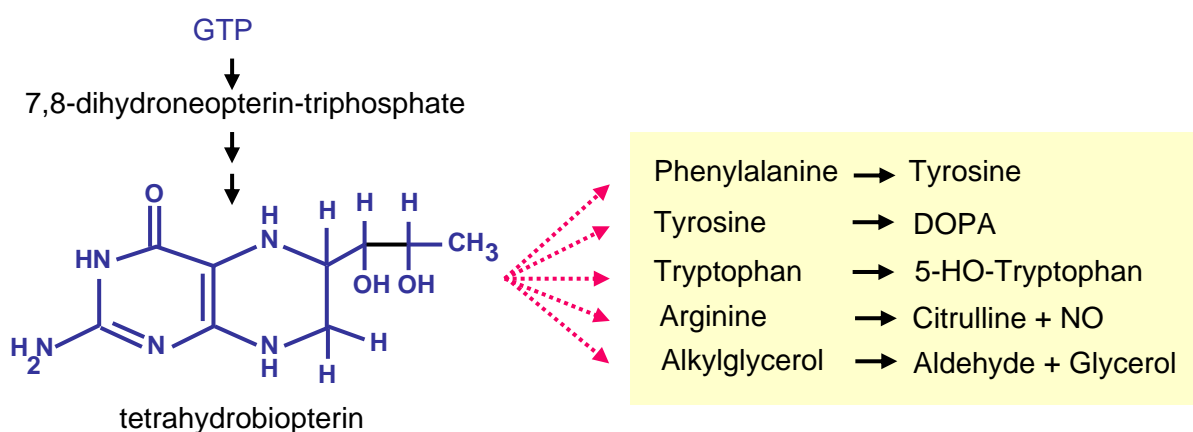


Figure 1: Biosynthesis and known cofactor roles of tetrahydrobiopterin

In previous work we studied the regulation of tetrahydrobiopterin biosynthesis by cytokines, pharmacological effects of tetrahydrobiopterin derivatives, and the role of tetrahydrobiopterin in the nitric oxide synthase reaction.

### Current focus

A main goal of the group is currently to study alkylglycerol (glyceryl ether) monooxygenase. We have developed a novel assay for this enzyme which is 5 orders of magnitude more sensitive than previously used absorbance-based assays (1). We have developed means to monitor the fate of the product of the reaction, toxic fatty aldehydes (2). We managed to assign a sequence to alkylglycerol monooxygenase by expressing candidate genes in CHO cells (3) and characterized its biochemical properties by site-directed mutagenesis (4). We now investigate physiological roles of this enzyme.

In cooperation with the Center of Operative Medicine, Department of Visceral, Transplant and Thoracic Surgery, Innsbruck Medical University, we explore potential and mechanism of action of tetrahydrobiopterin derivatives to attenuate the ischemia-reperfusion injury harming transplanted organs (5).

## References

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