

Robert Zimmermann (ORCID: 0000-0002-7354-870X): Role of monoglyceride lipases in the metabolism of polyunsaturated fatty acids

Research interest and scientific background: Polyunsaturated fatty acids (PUFAs) and PUFA-derived metabolites are well established modulators of inflammation and therefore modulation of their biosynthesis and degradation are promising approaches to anti-inflammatory drug treatment. PUFAs can be mobilized by phospholipase A2 (PLA2) enzymes. This process liberates free arachidonic acid (AA) and other PUFAs for metabolization by cyclooxygenase (COX) and lipoxygenase (LOX), leading to synthesis of pro- or anti-inflammatory lipids. Importantly, recent evidence suggests that in specific cell-types, such as astrocytes, PUFAs are provided by monoglyceride lipase (MGL) rather than by PLA2 enzymes. The present project focuses on two enzymes, MGL and α/β hydrolase domain-containing 6 (ABHD6), both of which possess monoglyceride (MG) hydrolase activity and have been associated with a number of diseases including cancer, neurodegenerative, and metabolic disorders. We hypothesize that MG hydrolases play critical roles in specific tissues/cell types by degrading signaling lipids (such as the endocannabinoid 2-arachidonoyl glycerol) and providing ω -3- and ω -6-PUFA for conversion via COX and LOX pathways. The central objective of this project is to generate a comprehensive profile of changes in ω -3/ ω -6-PUFAs and PUFA derived metabolites in tissues and serum of mice lacking MGL or ABHD6 under basal and inflammatory conditions.

Approach and methods: The student will utilize MGL/ABHD6 - deficient mouse models as *in vivo* model to investigate PUFA metabolism. Special expertise is available for gene cloning, protein expression, enzyme characterization, cell and tissue culture techniques, lipid analysis using mass spectrometry, and for the generation and characterization of mutant mice.

Affiliation: The experimental work will be done at the Institute of Molecular Biosciences (IMB) at the University of Graz. This project is directly connected to the doc.fund Molecular Metabolism.

References:

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