

OFFER FOR MASTER THESIS

`Diacylglycerol lipases α/β triggers inflammatory pathways in the human term placenta`

Background

Diacylglycerol lipase α/β (DAGL α/β) belong to the serine hydrolase superfamily and hydrolyse arachidonic acid (AA) esterified diacylglycerols (DAGs) to generate 2-arachidonoylglycerol (2-AG). 2-AG is one of the main endocannabinoids and the most abundant ligand for cannabinoid receptors. Both, 2-AG and AA, serve as substrates for downstream prostaglandin synthesis that mediate inflammatory responses. It has been shown that pharmacological inhibition and genetic disruption of DAGL α/β suppress induction of 2-AG and prostaglandin expressions induced by lipopolysaccharide (LPS). Moreover, that effect is accompanied by decreased TNF α and IL1 β secretion (1–3). The endocannabinoid system (ECS) is involved in several reproductive events and its deregulation has been associated with pregnancy complications such as compromised placentation (4) and miscarriage (5). Thus, we are interested in lipid signaling pathways and their contribution in placental physiology and disease.

Aims

The proposed project focuses on placental DAGL α/β and its activity in inflammation. How the enzymes and substrates act upon the release of cytokines is still unknown. We are keen to investigate how DAGL α/β inhibition affects secretion of cytokines and respective signaling pathways in placental explants and primary cells.

Methods

Preparation of placental explants with subsequent cultivation in hypoxia workbench and isolation of primary trophoblast cells for LPS treatments and DAGL inhibitor studies. The generated samples will be analysed by various molecularbiological techniques such as qPCR, Immunoblot and ELISA.

Call is open now until 06/21, duration of thesis approximately 6-8 months.

Requirements

- Bachelor degree in life sciences or comparable
- Interested in medical basic research and dedicated to hands-on lab work
- Being proactive and motivated

What we offer

- Working on a hot topic of placental research and processing of human samples
- Opportunity to broaden technical laboratory skills
- Supervision and guidance during experiments, data analysis and thesis writing
- Part of a highly motivated team and an international lab-environment
- Publication of data

Further information or to submit an application, please contact:

Wadsack Christian, PhD

Medical University of Graz

Department of Obstetrics and Gynecology

P: +43-316-385-81074; Email: christian.wadsack@medunigraz.at

Literature Cited

1. Hsu K-L, Tsuboi K, Adibekian A, Pugh H, Masuda K, Cravatt BF. DAGL β inhibition perturbs a lipid network involved in macrophage inflammatory responses. *Nat Chem Biol* 2012; 8(12):999–1007.
2. Ogasawara D, Deng H, Viader A, Baggelaar MP, Breman A, den Dulk H et al. Rapid and profound rewiring of brain lipid signaling networks by acute diacylglycerol lipase inhibition. *Proc Natl Acad Sci U S A* 2016; 113(1):26–33.
3. Shin M, Buckner A, Prince J, Bullock TNJ, Hsu K-L. Diacylglycerol Lipase- β Is Required for TNF- α Response but Not CD8+ T Cell Priming Capacity of Dendritic Cells. *Cell Chem Biol* 2019; 26(7):1036-1041.e3.
4. Costa MA, Fonseca BM, Keating E, Teixeira NA, Correia-da-Silva G. 2-arachidonoylglycerol effects in cytotrophoblasts: metabolic enzymes expression and apoptosis in BeWo cells. *Reproduction* 2014; 147(3):301–11.
5. Maccarrone M, Valensise H, Bari M, Lazzarin N, Romanini C, Finazzi-Agrò A. Relation between decreased anandamide hydrolase concentrations in human lymphocytes and miscarriage. *The Lancet* 2000; 355(9212):1326–9.