Stay in the University of Maribor, Slovenia

The stay had a duration of 1 month, from September 30, 2023 to October 30, 2023. This stay was performed in the research group of Dr. Andraz Stozer and in the research group of Dr. Sbastjan Bevc, both in the University of Maribor, Slovenia.

Importance of the stay for the DOKI project

This stay in Slovenia is a part of the DOKI project (Diabetes, Kidney and Obesity). The pathogenesis of obesity and Type 2 Diabetes Mellitus (T2DM) is complex and multifactorial. Patients with T2DM present higher risk to develop severe complications and organ damage specially in the kidneys, heart, circulatory system and brain. One of the most common of these complications is the develop of chronic kidney disease with changes in glomerular hemodynamics, oxidative stress, inflammation, interstitial fibrosis and tubular atrophy. Thus, understand the pathogenesis of T2DM is crucial to prevent and treat the disease. To do this is necessary the use of animal models of obesity, metabolic syndrome and diabetes. Current animal models are mostly genotypic and monogenic and none of them reflect accurately the complex pathophysiology of T2DM. Furthermore, none of them develop the damage in kidney, heart, circulatory system and brain related to diabetes. Thus, the main objective of this stay was the development and the study of a model of T2DM accelerated by Tacrolimus with organ damage, specifically in the kidney.

Abstract of the experiment

Induction of acute diabetes in Sprague Dawley rats to study changes in Ca^{2+} channels (electrophysiology) and insulin vesicles (electronic microscopy). Animals were fed 30 days with HFD for the induction of obesity and metabolic syndrome. After this time, Tacrolimus (1 mg/kg/day) was injected intraperitoneally (IP) during 15 days to induce hyperglycemia. At the end of the experiment, animals were sacrificed and changes in Ca^{2+} channels (by calcium imaging), changes in electrophysiology (by patch clamp) and insulin vesicles (by electronic

Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or European Research Executive Agency (REA). Neither the European Union nor the granting authority can be held responsible for them.

microscopy) were determined.

- **Strain:** Sprague Dawley
- **Number:** 8 males (2 per cage)
- **FN Rats:** 17/08/2023
- **Start HFD:** 29/08/2023 (cages nº 4 and nº 5) and 05/09/2023 (cages nº 2 and nº 3) (1 week laterto perform the experiments sequentially)
- **Duration of HFD:** 1 month to induction of obesity and metabolic syndrome
- **Tacrolimus injection**: 1 mg/kg during 15 days to induce hyperglycemia
- **Sacrifices** with CO2 (+ cervical dislocation) and slices of pancreas for the determination of changes in Ca^{2+} channels dynamics and electrophysiology by patch clamp.
- Tissues were collected and conserved in PFA, Nitrogen and Formalin (cassettes). Blood was collected. Glucose was measured before sacrifice.