Medical University of Graz

# Effect of glucagon-like peptide-1 receptor (GLP-1R) agonist liraglutide on T cell glucose metabolism

## Summary

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| Supervisor: | Prof. Dr. Philipp Eller |
| Availability: | This position is available. |
| Offered by: | Medical University of Graz |
| Application deadline: | Applications are accepted between February 10, 2020 00:00 and March 30, 2020 23:59 (Europe/Zurich) |

## Description

Background: GLP-1 is an incretin hormone, which is produced in the terminal ileum and is released with food intake in order to mediate glucose uptake and storage. GLP-1R agonists are currently used for treatment of type 2 diabetes. Recent large randomized controlled trials provided compelling evidence that GLP-1R agonists have cardio- and nephroprotective effects (1). One potential explanation is the fact that GLP-1R agonists inhibit proliferation of T cells by changing their glucose metabolism. Thus, GLP-1R agonists might have inherent immunosuppressive effects. They seem to inhibit glycolysis, which is critically needed for T cell to proliferate quickly (2). We now plan to elaborate this crucial finding in detail.

Hypothesis and Objectives: We hypothesize that GLP-1R agonists inhibit glycolysis of T cells and thereby block their clonal proliferation. We plan to follow this observation in detail by using human Jurkat T cells. (i) Jurkat T cells will be stimulated and analysed for their GLP-1R expression. (ii) They will be analysed for their metabolic status in the presence and absence of the GLP-1R agonist liraglutide by using various evaluations including lactate and glucose uptake measurements. (iii) Förster resonance energy transfer (FRET)-based probes will be used in collaboration with Roland Malli in Jurkat T cells to visualize intracellular ATP dynamics as well as acidification due to anaerobic glycolysis using a pH-sensor FRET probe (3). (iv) In a next step, we will try to visualize the dynamics of glucose metabolism also in primary T cells isolated from mice and humans.

Methodology: The PhD student will learn to perform multiple techniques including cell culture experiments with Jurkat T cells, transfection with FRET-probes, real-time PCR, Western blot, FACS, and confocal microscopy. Finally, he/she will need to isolate T cells from mice and humans.

References:

1. Marso SP, et al. *N Engl J Med*. 2016; 375: 311–322.
2. Moschovaki-Filippidou F, et al. *Am J Pathol*. 2020; 190(2):400-411.
3. Depaoli MR, et al. *Cell Rep.* 2018; 25:501–512.

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