

MASTER THESIS PROJECT PROPOSAL

Investigating Cytokine-Mediated Alterations in Hepatic Gluconeogenesis: In Vitro and In Vivo Insights

Project Background

Recent advances highlight the intricate relationship between the immune system and energy distribution across the body, known as immunometabolic regulation. This balance is vital for maintaining energy homeostasis in both healthy and diseased states. The liver, a central hub of energy metabolism, plays a critical role by storing glucose as glycogen, releasing it through glycogenolysis, and synthesizing it de novo via gluconeogenesis. Disruptions in liver metabolism, particularly gluconeogenesis, are implicated in chronic diseases such as type 2 diabetes and acute conditions like sepsis where glucose homeostasis is impaired.

The primary aim of this project is to establish robust in vitro and in vivo (mouse) assays to accurately assess hepatic gluconeogenesis. Once these assays are validated, the second objective is to investigate how pro-inflammatory cytokines influence this pathway, simulating disease conditions. This two-way approach will enable the study of gluconeogenic changes under normal and pathological states, providing a foundation for exploring metabolic dysfunctions driven by cytokines.

This research will establish critical methodologies for assessing gluconeogenesis while providing insight into how cytokines disrupt energy homeostasis. The findings will allow the development of new therapeutic strategies for conditions involving impaired liver metabolism, such as type 2 diabetes and inflammatory diseases.

Tasks of the Master Student

In Vitro Assay Development:

- Establish a reliable in vitro assay to study gluconeogenesis in primary hepatocytes using different non-carbohydrate precursors.
- Test the assay by studying the effects of various pro-inflammatory cytokines on gluconeogenesis.

In Vivo Assay Development:

- Develop an in vivo assay to measure gluconeogenesis in mouse models.
- Test the assay by analysing the influence of pro-inflammatory cytokines on gluconeogenesis in vivo.

Methods to Be Learned and Applied:

- Isolation and cultivation of primary hepatocytes from liver tissue.
- Cell culture techniques for maintaining and studying primary hepatocytes.
- Development of a robust and standardized in vitro testing model.
- Molecular biology methods such as ELISA and qPCR to assess gluconeogenic activity.
- Animal experimentation, including handling mice and conducting in vivo studies (LTK1 training provided).

Profile of the Master Student

We are looking for a motivated, organized student who is eager to learn and grow in the field of immunometabolism. No prior experience is required; all necessary training will be provided. The student should be comfortable performing animal experiments as part of the in vivo component of the project.

Contact

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