**Treating autoimmune diseases by spinal cord stimulation**

**1. Research Hypotheses**

Neuromodulation involves the direct stimulation of nerves by delivering electrical impulses to peripheral nerves or specific brain areas using active implanted medical devices. Neuromodulation addresses a wide range of diseases and symptoms, from headaches and tremors to spinal cord injuries and urinary incontinence. The modern era of neuromodulation began in the early 1960s with deep brain stimulation for chronic pain relief and expanded to include spinal cord stimulation (SCS) by the end of the decade. Since the initial applications of SCS for pain treatment, the development of numerous innovative methods has enabled the creation of safe, minimally invasive, and highly effective SCS-based therapeutic approaches for serious clinical conditions.

Considering that most peripheral nerves originate from the spinal cord, SCS is expected to have broad therapeutic applications in the coming decade. Among these applications, neuromodulation is emerging as a promising approach for immune-mediated inflammatory diseases (IMIDs). Autoimmune diseases, in particular, have demonstrated potential for treatment through neuromodulation of peripheral nerves as demonstrated by a recent success for human rheumatoid arthritis [1] and Colitis [2]. However, the success of this application has been hindered by challenges related to anatomical accessibility, neural organization within nerves, and the movement of neural targets.

Our hypothesis posits that clinically-approved SCS can act as an efficient, minimally invasive, and secure approach for addressing IMIDs.

**2. Project Objectives**

Autoimmune diabetes, also known as Type 1 diabetes (T1D), is one of the most prevalent IMIDs and is a chronic, incurable disease characterized by the loss of insulin-secreting cells. Currently, T1D is managed through daily insulin administration. In a seminal study, we recently demonstrated that electrostimulation of the pancreatic nerve effectively inhibits T1D progression in diabetes-prone mice [3]. However, translating this approach to humans is challenging due to the complex neural anatomy of the pancreatic region, which differs significantly from mice.

Our long term goal is to provide proof of concept that SCS can serve as a novel treatment modality for T1D in mice, which is the most relevant animal model for T1D.

We are confident that our team is well-equipped to tackle this challenge, given our pioneering role in the field. We have already substantiated the proof of concept that peripheral nerve electrostimulation can be highly effective in treating conditions like Crohn's disease [4] and autoimmune diabetes [3].

**3. Internship Objectives**

In pursuit of this objective, the internship will encompass the following goals:

• Objective 1: Establish the connection between the pancreas and the spinal cord through retrograde tracing in non-obese diabetic mice (NOD mice).

• Objective 2: Ascertain the optimal SCS stimulation parameters (location, electrical characteristics, etc.) that elicit evoked potentials within the pancreatic nerve.

• Objective 3: Assess the influence of SCS on the proliferation of pathogenic T cells in NOD mice.

Note: No hazardous materials will be used during this internship. However, the project includes experiments in mice. Depending on the training of the selected student, the mouse manipulation phase (deliberately reduced) will be carried out by the student himself, if he has the appropriate training, or by team staff.

**4. References**

1. Koopman et al. PNAS. 2016;113:8284–9.

2. Bonaz et al. Neurogastroenterol Motil. 2016;28:948–53.

3. Guyot et al. Nat Biotech. 2019;37:1446–51.

4. Brinkman DJ, Simon T, et al. J Neuroinflammation. 2022 ;19(1):155.