Review of: "Exploring the Autoimmune Hypothesis of Type 1 Diabetes: Investigating the Potential Role of Peritoneal Membrane Defects in the Pancreatic Tail and Revisiting Alternative Theories of Disease Etiology"

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Potential competing interests: No potential competing interests to declare.

Overall, the review is interesting and suggests a possible new mechanism of autoimmune attack for type I diabetes. It makes sense that the loss of mesothelium integrity in the pancreatic tail can lead to the exposure of beta cell-derived antigens to peritoneal leukocytes, leading to the development of an immune reaction. However, there is a lack of information to complete and enrich this review that I suggest to perform:

1. A paragraph on peritoneal leukocytes (macrophages, T and B cells) should be added: The study lacks detailed information on the different types of leukocytes residing within the peritoneal cavity, either floating in the serous liquid or stored inside milky spots of the great omentum and mesenteric adipose tissue. The authors should detail which of the peritoneal cavity leukocytes could be in potential contact with beta cell-derived antigens in the case that the integrity of the peritoneal membrane covering the pancreas tail is damaged, thus allowing the permeability to leukocytes and their migration inside the pancreatic stroma.
2. I also suggest incorporating an additional figure with the design of a peritoneal membrane separating on one side the pancreatic stroma with one Langerhans Islet and on the other side the intraperitoneal space with the different types of leukocytes, and to connect the possible factors (cells and cytokines, etc.) that could access the pancreatic stroma in a part of the peritoneal membrane where the barrier integrity is lost, opening a way to access the pancreatic tail stroma and therefore the exposure to beta cell antigens.
3. The authors could also develop a small paragraph to explain why the infiltration of peritoneal leukocytes inside the pancreatic stroma could be determinant in developing T1DM by comparison to the systemic (blood) access of circulating leukocytes to beta cell antigens. This means to compare two ways of leukocytes accessing the pancreatic stroma, either from blood circulating leukocytes that can access if the vascular integrity is lost, versus a loss of peritoneal membrane integrity, which instead allows the access of peritoneal cavity leukocytes.