Reviewer 1 report:
Scientific Quality: Grade C (Good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Accept (General priority)
Specific Comments to Authors: TNFR2 is more affected than TNFR1 in myenteric ganglia in the duodenum of type 1 diabetic rats. The topic is interesting and has instruction for clinical practice.

Answer to Reviewer 1:
Thank you very much for your report and your support regarding the acceptance of our manuscript.

Reviewer 2 report:
Scientific Quality: Grade D (Fair)
Language Quality: Grade B (Minor language polishing)
Conclusion: Major revision
Specific Comments to Authors: 1.the β cell secretary function and insulin resistance should be detected and discussion. 2.Oxidative stress should be detected and discussion. 3.Intestinal flora should be detected and discussion.

Answer to Reviewer 2:
Thank you very much for your report and suggestions. According to your comments, we prepared our revised manuscript.
1. We have been using this experimentally induced type 1 diabetic rat model for many years in our research. Among others, the histology of pancreatic islets reveals ß-cell destruction and weak insulin-immunoreactivity in the islets of diabetic rats (Wirth et al 2021). In the present study, the immediate insulin treatment was not preventive, but rather it had confusing effect on TNFR expression. In our previous studies, we have also experienced that the effectiveness of insulin replacement was not preventive regarding different parameters and gut segments (Bódi et al 2012, Bódi et al 2021). We agreed with your comment about the importance of insulin sensitivity or insulin resistance, therefore we cited more studies to highlight it in the discussion part of the revised manuscript.
2. Thank you for your remark. Impact of oxidative stress in diabetes-related histological and molecular alterations is really unavoidable. Therefore, we have already investigated the diabetic oxidative status as well as the endogenous antioxidant defense system in different gut segments of the same rat model (Jancsó et al 2015, Chandrakumar et al 2017). We established a gut region-dependent accumulation of reactive oxygen species and segment-specific activation of heme oxygenase system. These papers were cited at the beginning of the introduction, but we did not detail them to avoid the overrepresentation of our previous studies. However, according to your comment, we highlighted them in the revised manuscript.
3. Thank you for your comment. Alterations of intestinal microbial composition are critical in development and progression of several diseases, like diabetes, inflammatory bowel disease or even neurodegenerative diseases. Feeling the importance of that, we have recently studied this topic and displayed regionally distinct alterations in the gut microbiota regarding the luminal content and also the mucosa-associated microbiota in type 1 diabetic rats (Wirth et al 2014, 2021). We did not want to take the focus away from original goal of the study, however, based on your

comment, we also mentioned them for better emphasizing our previous comprehensive investigations.