Dear Editor and Reviewers,

Thankyou for considering our manuscript, Manuscript NO: 36037, entitled **"Abundance of *Enterobacteriaceae* in the colon mucosa in diverticular disease"** for publication in World Journal of Gastrointestinal Pathophysiology. We have tried to answer the questions raised by the reviewers, and we think that the revision has improved the manuscript. All changes are marked in yellow. Please reconsider this manuscript for publication.

This is an interesting and well-written research on possible colonic microbiota differences between healthy subjects and patients with diverticulosis/SUDD. Follow some major comments: 1) The study clearly needs to be compared with the previous paper published on Gut by Barbara et al from which the results differ significantly. In that paper a reduced percentage of Enterobacteriaceae and Akkermansia was detected in SUDD, while increased level of Bacteroides was seen in SUDD patients. Authors should comment more in depth differences between their and Barbara's work (some discussion is indeed present in the current version), including: different techniques used in the experiments, expected differences if they had tested faeces + mucosal biopsies and why other types of microbes such as Akkermansia and bacteroides were not analyzed

Reply: We have now more thoroughly compared our study with the study of Barbara et al. (Ref No 17). The present study enrolled mainly symptomatic patients examined by colonoscopy to exclude organic diseases or patients with heredity for colon cancer. Barbara *et al.* used asymptomatic or symptomatic patients enrolled to colonoscopy in a screening program to exclude malignancy or as follow-up after polyp resections. Thus, the control group in Barbara *et al.* consisted of a smaller cohort (n = 14) of asymptomatic subjects, compared to our 35 controls, where a majority had symptoms. Also, in Barbara et al., a lower percentage of DD was symptomatic, with gender and age differences between groups, which was not found in our study. The microbiota composition differed between mucosal biopsies and feces in Barbara *et al.* We decided not to analyse fecal microbiota in our study, since there is greater differences between fecal and mucosal microbiota than between individual subjects (Tang et al. 2015, ref No 29), and it is considered more reliable to measure microbiota composition in mucosa than feces. The general composition estimated by microbial diversity may be more important to health than the levels of individual bacterial strains (Ref No 9, 10, 14), why we chose to estimate diversity indices instead of several types of microbes, page 13, last section and page 14, first section.

2) Authors should discuss about methodological limitations, in particular the small sample size and the lack of strict matching between cases and controls (age, sex, habits), since controls and cases were just 'consecutive' patients referred for colonoscopy

Reply: Since the patients were enrolled consecutively, there was no matching between cases and controls of e.g., age, gender or lifestyle habits. In a larger study, some of the demographic parameters and lifestyle habits could have shown statistically significant influence on the gut microbiota. We chose to initially perform this as a pilot trial with a limited amount of patients, as the methodology is very expensive. When it now has been shown that there are differences

in DD according to the gut microbiota, it is important to continue with further studies and more extensive analyses, page 16, line 6-12.

Bodil Ohlsson, professor