Author's response to reviews

Title: Colonic epithelial ion transport is not affected in patients with diverticulosis

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Author's response to reviews: see over
RE: MS #BMC_4976387501295664_article

We would like to thank the reviewers for their helpful comments and editors for giving us the opportunity to improve the quality of the MS. In particular, reviewer 2 provided interesting and challenging comments. We have revised the MS according to comments.

Reviewer 1:

Major comments:

1) Are the biopsies per se taken immediately adjacent to or IN a diverticulus OR in areas with no diverticuli but in a patient that has diverticuli elsewhere:

_The biopsies were taken in normally appearing mucosa, but not in the diverticula. All diverticulosis-Patients had diverticuli in the left part of the colon. We clarify this by changing the last sentence in paragraph 1, page 4._

2) There needs to be commentary concerning the degree of inflammation (if any) associated with the diverticuli. Both require careful clarification in the paper. I would even revise the title with regard to this clarification.

_We acknowledge the comment and clarify the degree (NO) of inflammation, page 9, 3 lines from the bottom._

3) Comment on the title......

_As we have now made clarifications as to the degree of inflammation in the revised MS (see page 9), we believe the title is appropriate._

4) Concerns on the reported conductances obtained on these biopsies........

_We acknowledge and comply with this comment by adding additional arguments and explanations in discussion section (see page 12)._ 

5) Statistics............

_We acknowledge this comment. As mentioned in acknowledgments a statistician - associate professor Annette Kjær Ersbøll, has advised all data-analysis. We found no outlier values that could be dropped using the interquartile rule._
Minor comments

We have complied with all. In particular:

A) I would recommend providing a vertical point of ALL observed conductances for control and diverticular biopsies. Given the very wide range of values, readers would benefit by seeing this distribution. I would likewise report mean as well as median.

We have revised the MS by adding mean and standard error of the mean (SEM) to table 1, 2 and 3 and adding vertical point plot of the conductances and short circuit currents for controls and diverticulosis biopsies.

The editor can choose to use this figure at his discretion

B) Grammar:
   a. Page 3, line 1: difficult treatable TO difficult to treat
   b. Page 3, line 6: diet poor on TO diet poor in
   c. Page 3, 3 lines from bottom: hypotheses TO hypotheses
   d. Page 4, 3 lines from bottom: The sentence, "Media at the serosal...." does not make good sense.
   e. Page 12, 5 lines from bottom: built-up TO build-up
   f. Page 14, line 1: information in TO information is

C) On page 8, why would changes in SCC lead to changes in G? ........

We acknowledge this comment. However the observed has also been demonstrated in other leaky epithelia. Theoretically this would be expected as long as the paracellular resistance is lower than infinity according to the formula for parallel-connected resistances: (1/R_{epithelium} + 1/R_{paracellular}=1/R_{total}). The shunt-resistance is not equal to zero in our tissue. It is not that leaky.

D) On page 10, paragraph 2; the authors make a good case for why biopsies are healthier physiologically than surgical tissue. I would add that biopsies are more readily available for a wider array of diseases, INCLUDING healthy controls (not available surgically).

We comply with this comment and have changed page 10, paragraph 2.

E) There is very little published about electrophysiology of diverticular disease colon. For this reason you should seriously include Mullin et al. ........

We acknowledge this comment. We include and discuss this reference in the revised MS adding text and related reference in discussion section (see page 11).

Reviewer 2:

Major comments - none.

Minor comments

1) There are many repeated items in the References .......

We acknowledge this comment and have changed the reference list.

2) Page 5, lines 1 and 2 from below is “…transport capacity. For amiloride it was
Added…” should be: “…transport capacity with exception for amiloride added…”

We acknowledge this comment and comply by changing the paragraph (see page 5).

3) Pages 8, line 4 and others from above: “t1/2” not defined in Method, and in List of abbreviations.

We acknowledge this comment and comply by adding the sentence "t½ = half time" to the list of abbreviations.

Yours sincerely

Philip S. Osbak (first author) – on behalf of all authors