August 1, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11838-review.doc).

Title: "Patterns of airway involvement in Inflammatory Bowel Diseases"
Author: Ilias Papanikolaou, Konstantinos Kagouridis, Spyros A Papiris
Name of Journal: *World Journal of Gastrointestinal Pathophysiology*

ESPS Manuscript NO: 11838

The manuscript has been improved according to the suggestions of reviewers:

1. Reviewers 02940086 and 00043396 have made no comments/suggestions.
2. We have incorporated all the grammar corrections of reviewer 00004485.
3. Regarding point 2 raised by reviewer 00004485 we agree that there is no definite pathogenetic theory that explains pulmonary involvement in IBD. This is discussed in great detail in the "Pathogenesis" section of our manuscript where we present the most recent data and theories and further explain how the pulmonary – intestinal cross talk functions. Therefore attributing some of the pulmonary changes to an altered immune system and others to a pure coexistence as the reviewer suggests is not justified not only by the available literature but also by the epidemiological studies.
4. Regarding point 3 raised by reviewer 00004485 we clearly state that "PFT and DLCO abnormalities in asymptomatic IBD are frequent" and that "It is currently unknown however whether DLCO could serve as a disease activity marker". Available data, and especially more recent data, present a much greater prevalence and incidence of pulmonary manifestations in IBD that are in discordance with older studies. As already discussed in our paper many of these manifestations are asymptomatic or present in times that the intenstinal manifestations are in

remission which explain why they are underdiagnosed by the clinicians. As a matter of fact this is why we think our review is useful especially for gastroenterologists.

5. Regarding point A1 raised by reviewer 02953764 we do not agree that Casella's classification in Journal of Crohn's and Colitis is the only or the best classification system for pulmonary involvement in IBD. We prefer to keep the anatomical classification which is more relevant and help introduce the reader in the core of our review which is "Patterns of airway involvement in IBD".
6. Regarding point A2 raised by reviewer 02953764 we think that the paragraph describing PFTs answers directly to the reviewer's remark. Should the reviewer prefers a more detailed explanation of PFTs for the non-specialist we are more than willing to provide it.
7. Regarding point A3 raised by reviewer 02953764 upper airways cannot comprise a category with small airways by definition. If we unify the paragraphs of upper and large airways as "large airways" as the reviewer suggests then the presentation of airway involvement will get really complicated starting from lesions in the pharynx and ending in bronchiectasis all in one category. Moreover our large airways category which is the anatomic site most commonly involved in IBD should be presented as a separate category for educational as well as classification purposes.
8. Regarding point A4 raised by reviewer 02953764 there is no evidence that corticosteroids have a role in managing bronchiectasis and we have added reference 47 from BTS guidelines that renounce the use of steroids for bronchiectasis except in the case they coexist with asthma. [Pasteur MC, Bilton D, Hill AT; British Thoracic Society Bronchiectasis non-CF Guideline Group. British Thoracic Society guideline for non-CF bronchiectasis. *Thorax*. 2010 ;65 Suppl 1:i1-58.]
9. Regarding pointsB1 to B18 raised by reviewer 02953764 we have complied with all requirements for language polishing as discussed in point 2 of this letter.

Moreover we have complied with all the requirements as asked to do so in the edited version of our

article from the Journal;s editorial office. All changes/corrections are highlighted.

Thank you again for publishing our manuscript in the *World Journal of Gastrointestinal Pathophysiology*.

Sincerely yours,

Spyros A Papiris MD, PhD,
Professor of Medicine,
2nd Pulmonary Medicine Department, "Attikon" University Hospital,
Rimini 1 Street, 12462 Haidari, Greece,
Athens Medical School, National and Kapodistrian University of Athens,, Greece,
e-mail: papiris@otenet.gr, tel: +302105832361, fax: +302105326414