



**GASTROINTESTINAL RESEARCH
DEPARTMENT OF PHYSIOLOGY & PHARMACOLOGY
PONCE SCHOOL OF MEDICINE & HEALTH SCIENCES
PONCE, PR 00732-7004**

September 24, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 13132-review.docx).

Title: Immunohistochemical Expression of SP-NK-1R-EGFR Pathway and VDR in Colonic Inflammation and Neoplasia

Author: Raymond A. Isidro, Myrella L. Cruz, Angel A. Isidro, Axel Baez, Axel Arroyo, William A. González-Marqués, Carmen González-Keelan, Esther A. Torres, and Caroline B. Appleyard

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 13132

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

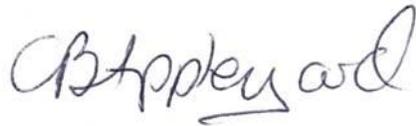
1. Title has been shortened to 12 words.
2. Revision has been made according to the suggestions of the reviewers:
 - a. To address comments from reviewer 00068278, "healthy controls" has been changed to "normal controls."
 - b. To address comment from reviewer 02908309, we added the total number of patients and the number of patients in each of the five groups to the "Patients and Tissue Samples" section of the materials and methods section on page 7.
 - c. There are no comments to address for reviewer 00068404, whom we thank for an enthusiastic review.
 - d. With regards to comments from reviewer 00069055, we agree with this reviewer and other reviewers that the sample size per group is small. Therefore, we have included this in the "Peer review" section of the highlighted Comments, using the following sentence from reviewer 00068278: "Although the number of the samples is small the findings are beneficial." Also, we would like to point out that the Discussion section includes a section that addresses the small sample size and that the only other study to look at VDR expression in dysplasia and cancer (Wada et al., 2009) used 7 and 6 patients, respectively, similar to our 6 patients for colitis-associated cancer and our 5 patients each for sporadic dysplasia and cancer. Regarding the comments on creativity and similarity of results with previous reports, we respectfully disagree: first, previous studies have not addressed expression of the four proteins under study in Hispanic

patients nor have they compared expression between colitis-associated and sporadic neoplasia; second, in the study by Wada et al., (2009), while VDR was reduced in ulcerative colitis and colitis-associated dysplasia and cancer when compared to normal, VDR levels in dysplasia were higher than those in cancer, thus differing from our findings.

3. Figure legends and references were corrected.
4. First pages of references without PMID or DOI are provided.
5. "Peer review" section of COMMENTS was added.

Thank you again for considering our manuscript for publication in the *World Journal of Gastroenterology*.

Sincerely,

A handwritten signature in black ink, appearing to read 'C B Appleyard', written in a cursive style.

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