

ESPS PEER-REVIEW REPORT

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ESPS manuscript NO: 31321

Title: B2 adrenergic receptors and morphological changes of the enteric nervous system in colorectal adenocarcinoma

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| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---|--|--|--|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade D: Rejected | <input type="checkbox"/> Plagiarism | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E: Poor | | <input type="checkbox"/> No | <input type="checkbox"/> Major revision |
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COMMENTS TO AUTHORS

In the current submission Ciurea RN et al investigated the neuro-neoplastic interrelationship in colon cancer. Authors assessed the expression pattern of beta-2 adrenergic (B2A) receptor and morphological changes of the enteric nervous system in 48 primary colorectal cancer and 9 control non-colon cancer specimens. Using multispectral unmixing microscopy they observed differential expression and localization pattern of B2A receptor in different cell types in normal colon mucosae and colon adenocarcinoma specimen. In particular, they have reported the nuclear membrane staining of B2A receptor in colon cancer cells. Authors found that increased B2A receptor expression directly correlated with increased tumor grading, while relative area of Auerbach and Meissner plexuses negatively correlated with tumor grading. Furthermore, authors observed that B2A receptor area and IOD were significantly associated with clinicopathological features in colorectal cancer including tumor size, tumor invasion and lymph node metastasis. Based on these findings authors concluded that B2A receptors could serve as a prognostic factor in colorectal cancer. Comments: 1. Authors have not cited their previously published work on B2A receptors "Neuro-neoplastic



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interrelationships in colorectal level – immunohistochemical aspect in three cases and review of the literature”. Did they include the same 3 patients into this larger cohort? Discuss how are the two studies similar/dissimilar? 2. In the group of 16 patients with undifferentiated colon cancer was the perinuclear expression of B2A receptor uniformly distributed in all cells? What percentage of cells were positive for peri-nuclear localization? 3. In figure 4, D/E/F axis labeling of IOD is missing. 4. Although B2A receptors have been mentioned in detail in the discussion section, the introduction section should have a brief description of B2A receptors- why is this the focus of the research and what is its relevance? 5. It would be interesting to perform similar clinical outcome studies as a follow up in this patient cohort to assess the association between tumor recurrence and B2A receptor levels. 6. Some minor grammatical errors
