

Answering to the Reviewer and Editor comments

We thank the reviewer and Editor for their valuable suggestions. We tried our best to answer them. Please note, all the corrections/ modifications suggested by the reviewer and Science Editor are mentioned in color in the text manuscript.

Reviewer #1:

The authors have analysed the mutational status at the hotspot regions of H-Ras, K-Ras and N-Ras genes by PCR-RFLP and DNA sequencing method using tumor tissues of 87 cases of urothelial carcinoma of bladder (UCB). Although their focus and aim of the study are interesting, the quality of submitted manuscript is insufficient for publication. This manuscript requires extensive editing including English usage. Introduction section is too long and redundant. It should be shortened and clarify the aim of study.

Manuscript is revised thoroughly for any grammatical/ typological errors. Introduction section is shortened. Changes are marked in color.

The section of materials and methods is also too long. As their methods of investigation, both of PCR-RFLP and DNA sequencing, are well known, details of its methods could be omitted.

As suggested, PCR-RFLP and DNA sequencing methods are shortened in materials and methods section.

Their results include clinicopathological summary and point mutation detection in Ras, K-Ras and N-Ras genes but results of analysis for correlation of clinicopathological factors and point mutation were not performed.

We collected all the relevant clinicohistopathological information of the studied patients and described in the sections: materials and methods, results and table 4. All the 87 samples showed negative results (absence of point mutation in Ras isoforms by PCR-RFLP as well as by DNA sequencing), hence we could not perform statistical correlations/ associations between patients' variables and mutation results. Had there been point mutation detected in the given exons of Ras genes by any of the methods, we would have statistically examined the results with the clinical variables.

Science Editor #2

Scientific quality: The manuscript is an observational study of mutational analysis of hot spot regions of K-Ras, H-Ras and N-Ras genes in patients with urothelial carcinoma of bladder. The topic is in the scope of WJCC. (1) Classification: C. (2) Summary of the peer-review report: The article is interesting. However, the section of materials and methods is also too long. As their methods of investigation, both of PCR-RFLP and DNA sequencing, are well known, details of its methods could be omitted.

As suggested, PCR-RFLP and DNA sequencing methods are shortened in materials and method section.

Their results include clinicopathological summary and point mutation detection in Ras, K-Ras and N-Ras genes but results of analysis for correlation of clinicopathological factors and point mutation were not performed.

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(3) Format: 4 tables and 3 figures. 29 references were cited, including 1 reference published in the last three years. No self-citation.

Reference no. 9 is a self-cited reference. Total references cited are 31. Two more studies published in 2019 and 2020 (ref 14 and 31) are added in the manuscript.

2 Language evaluation: C. Language editing certificate was not properly provided, please upload language certificate by language editing company.

This is to bring to your kind attention that for one of my earlier manuscripts published in World J Clinical Oncology [Maurya N, Singh R, Goel A, Singhai A, Singh UP, Agrawal V, Garg Minal. Clinicohistopathological implications of PhosphoSerine9 glycogen synthase kinase-3 β / β -catenin in Urinary bladder cancer patients. World J Clinical Oncology. 2019 Apr 24;10(4):166-182. ISSN No. 2218-4333], we obtained "language editing certificate" by one of the English Professor "Prof Nishi Pandey" after

extensive review. Prof Nishi Pandey is a serving professor of eminence in Department of English and Modern European Languages, University of Lucknow, Lucknow, U.P., INDIA for more than 35 years.

We obtained the permission to submit the certificate by English Professor working in reputed Govt. University from Prof Fang-Fang Ji, Science Editor, Editorial Office via email dated 24th January 2019 for the above mentioned manuscript.

Besides, language editing company charges for editing and issuing the certificate. Our institute does not provide financial support towards the cost of the certificate. Hence it is difficult for us to obtain the required certificate from the company. We request you to permit us to submit the certificate from the English Professor of repute.

3 Academic norms and rules: The authors signed the conflict-of-interest disclosure form and copyright license agreement. The written informed consent was waived. The biostatistics review certificate was provided. The STROBE statement should be provided with page number, please.

The STROBE statement (with page numbers) is uploaded.

The grant application form was not uploaded.

Grant application document has been uploaded.

No academic misconduct was found in the CrossCheck investigation and the Bing search. 4 Supplementary comments: (1) Invited manuscript. (2) Supported by Department of Science and Technology, Govt. of India SR/SO/HS-0113/2010. (3) Corresponding author has published 6 articles in BPG. 5 Issues raised: (1) Please write the “article highlights” section at the end of the main text. (2) The title should be no more than 12 words. (3) Please upload the grant application form or funding agency copy of any approval document. 6 Re-Review: Required. 7 Recommendation: Conditional acceptance.

Article highlights are added at the end of main text. The title of the manuscript is shortened to 12 words. It is now titled as “Mutational analysis of Ras hotspots in urothelial carcinoma of bladder patients”.

Grant application document is uploaded. Manuscript is revised thoroughly and incorporated the corrections/ modifications as suggested. Changes are marked in color.

It may be further noted that we could not get DOI for the references no. 1, 8, 15, 16, 25 and 30.