International Journal of Cancer Management
Volume 16 · Issue 1 · e133155

OPEN PEER REVIEW

Aspergillus Species and Human Papillomavirus Infections in Epithelial Tumors of Nasal and Paranasal Cavities

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SUBMITTED	REVISED	ACCEPTED	DOI
14 Nov 2022	17 Dec 2022	22 Jan 2023	10.5812/ijcm-133155

About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

2 comments · 23 Nov 2022 – 23 Nov 2022

Referee 1 Reviewer

MINOR REVISION 23 Nov 2022

Hi dear author
Thanks for your valuable article. I think the text needs some corrections:
1-It is better to revise the wording of the text.
2-The wording of the references should be corrected.
3-Line number 109 should be corrected.
4-Reference number 1 should be corrected.

Mojtaba Rashidi Reviewer

MINOR REVISION 23 Nov 2022

1. What is the importance and application of the results of this article?
2. If Aspergillus is involved in pathogenesis, why are only 10 of the 57 samples positive for Aspergillus?
3. The sequences of the primers should be mentioned.
4. The abbreviation FFPE should be spelled out in the patients and methods section.
5. Were only serotypes 18 and 16 of Aspergillus investigated? As you know, other serotypes can also cause a neoplasm.

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear editorial team:

We would like to express our sincere gratitude to the reviewers for the thorough and detailed reading of our manuscript and for the informative comments with important suggestions. We have made every attempt to revise our paper along the lines outlined by the reviewer. We believe the revisions have resulted in a substantial improvement in our manuscript. We have highlighted the changes to the manuscript.

Best regards

Reviewer Comments:

Reviewer 1: Highlighted in purple

Hi dear author

Thanks for your valuable article, I think the text needs some corrections:

1. It is better to revise the text in terms of writing.

Thanks for your kind suggestion. Some changes have been made by an English editor according to your comment and the few grammatical errors are corrected.

2. References should be corrected in terms of writing.

We really appreciate for your kind advice. We tried to match the reference list to journal guidelines.

3. Line number 109 should be corrected

It has been revised.

4. Reference number 1 should be corrected

We would like to thank the reviewer for this very valuable comment. Reference number 1 is a book chapter and has been revised according to the journal guidelines.

Reviewer 2: ***Highlighted in green***

1. What is the importance and application of the results of this article?

We would like to thank the reviewer for this very valuable comment. First, the identification of fungal DNA in tissue samples by PCR improves diagnostic accuracies for fungal infections, and PCR conducted on FFPE tissues provides an alternative to culture-dependent identification methods. The results of the present study support research indicating that PCR amplification accurately diagnoses fungal species in FFPE specimens.

On the other hand, establishing the etiology of invasive fungal infections is important to guide therapeutic options and for epidemiologic purposes.

Moreover, the findings of the present study indicate that despite the important role of high-risk HPV types in head and neck cancers, it seems they do not play a crucial role in the epithelial tumors of nasal and paranasal cavities.

2. If the aspergillus involves in pathogenesis, why only 10 samples among 57 samples are positive for aspergillus?

Thank you very much for your attention. Basically, malignant tumors in the sinuses are very rare and account for approximately 5% of all head and neck malignancies and occur annually in approximately 1 per 100000 individuals worldwide. As the respected reviewer knows, the power of the analysis increases in rare cancers and a 17.54% of detection rate may propose a possible etiologic role for the pathogen in this type of malignancy. On the contrary, SCC may occur first, causing inflammation, resulting in poor ventilation and inappropriate immune mechanisms, resulting in a fungal infection. However, this study was too small for establishing an etiologic role of aspergillus in pathogenesis or development of nasal and paranasal cavities' tumors.

3. The sequences of primers should be mentioned.

We really appreciate for your kind advice. **Table 1, which provides the sequences of primers, is included in the manuscript according to your comment.**

Table 1 The sequence of primers used in this study

Primer Name	Sequences (5’ to 3’)	Product size (bp)
PC03	ACACAACTGTGTTCACTAGC	110
PC04	CAACTTCATCCACGTTCACC	
AFU7S	CGG CCC TTA AAT AGC CCG	405
AFU7AS	GA CCG GGT TTG ACC AAC TTT	
AFU5S	AGG GCC AGC GAG TAC ATC ACC TTG	236
AFU5AS	GG RGT CGT TGC CAA YYCC TGA	
MY09	GCMCAGGGWCATAAYAAYTGG	452
MY11	CGTCCMARRGGAWACTGATC	
GP5+	TTTGTTACTGTGGTAGATACTAC	140–150
GP6+	GAAAAATAAACTGTAAATCATATTC	
16E6F1	CTGCGACGTGAGGTATATGACTTT	405
16E6R1	TTGTCTCTGGTTGCAAATCTAACA	
16E6F2	GGTCGGTGGACCGGTCGATG	129
16E6R1	TTGTCTCTGGTTGCAAATCTAACA	
18E6F1	CACTTCACTGCAAGACATAGA	322
18E6R1	GTTGTGAAATCGTCGTTTTTCA	
18E6F2	ATGCTGCATGCCATAAATGT	139
18E6R2	CACCGCAGGCACCTTATTA	

Degenerate base code: H=A, T, or C; M=A or C; R=A or G; V=G, A, or C; W=A or T; Y=T or C.

4. An abbreviation of FFPE should be completed in the patients and methods section.

Thank you very much for your attention. It has been revised.

5. Only serotypes 18 and 16 of aspergillus had investigated? As you know other serotypes also can be the cause of neoplasm.

In response to the respected reviewer, it should be mentioned that we used MY09/MY11 and GP5+/6+ general primers which detect 23 mucosotropic cancer causing HPV types. However, due to the importance of HPV 16 and 18 types in the etiology of dysplasia and cancer, we additionally rechecked the presence of these viruses by specific primers and PCR assays again.

2 Revision 1

0 comments

No public comments in this round.