



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Clinical Cases*

**Manuscript NO:** 86561

**Title:** Multinucleated giant cells of bladder mucosa are modified telocytes: Diagnostic and immunohistochemistry algorithm and relation to PD- Y expression score

**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 03850246

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Doctor, Professor

**Reviewer's Country/Territory:** Italy

**Author's Country/Territory:** Bulgaria

**Manuscript submission date:** 2023-06-25

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2023-06-25 15:57

**Reviewer performed review:** 2023-06-25 16:04

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



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<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

Conclusion is that the giant stromal cells in non-tumor and tumor bladder can be used as a characteristic and relatively constant histological marker for chronic bladder damage. Likewise, according to the morphological and IHC of the mono and multinucle-ated giant cells in the bladder, they are most likely represent telocytes capable of adapting their morphology to the pathology of the organ. The manuscript is clear and presented in a well structured manner. The study is well designed. Materials and methods are described in detail. Results are reported clearly and appropriate. Tables and figures properly show the data. The discussion is adequate with current citations. The conclusions are consistent with the evidence.



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**Peer-review model:** Single blind

**Reviewer’s code:** 05487696

**Position:** Peer Reviewer

**Academic degree:** MD, MSc

**Professional title:** Consultant Physician-Scientist, Doctor, Lecturer

**Reviewer’s Country/Territory:** Egypt

**Author’s Country/Territory:** Bulgaria

**Manuscript submission date:** 2023-06-25

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-07-11 13:33

**Reviewer performed review:** 2023-07-11 14:28

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

-Abstract: “ more often in high-graded”. Do you mean high-grades? -Introduction: “Prof. Popescu and his collaborators from Bucharest in 2005 discovered a brand-new entity of interstitial cells in various organs, and they named them telocytes [3,4]” You cite here two references and ignored Popescu studies which are numerous and related to this telocyte. Kindly refer to some of these articles. -“ Discovered 16 years ago” Better to write since .. -“Urothelial carcinoma (UC) of the bladder is a multifactorial disease characterized by an aggressive course, frequent recurrences, and high mortality worldwide. The morphology of bladder carcinoma is well known. Still, its stroma is insufficiently studied. Moreover, some of its components, such as mononuclear giant cells and MGCs, are almost unknown” Kindly refer to at least one source here, such as : Wijesinghe HD, Malalasekera A. Giant Cell Urothelial Carcinoma of Bladder. Case Rep Urol. 2021 Jul 15;2021:8021947. doi: 10.1155/2021/8021947. -In methods you should mention the process of diagnosis, if you re-examined H& E slides or noand if yes, you should mention how did y consider the agreement, I realized that you included “76cases with invasive low-grade (LG) and high-grade (HG) UC, but the low grade invasive



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tumors incidence is low (mostly <5%) so it is recommended to re-examine slides to assure the grading -In table1: kindly revise the typing of markers (eg, cd should be CD) -Why you mention only ANOVA test in your methods section, however you used other tests ? - In results grammar and typo errors are seen 9eg, in well-differentiated UC (G1) - in 6/37 of cases (16.2%). Also presenting these results in table is advised. - Figure 1 can replaced or included in a table - In histological and IHC figures, you write "Figure x. IHC examination of UC of the bladder", You should replace by something like Figure 4x. CD31 IHC staining of a case of UC; ... (to avoid confusion and to clear the type of marker under corresponding inage. -Figure 5& 6: revise the power of magnification - Figure 7 is not seen as a proper differential diagnosis of MGCs, can you explain? - In discussion; a good review for giant cells in different organs presented, - "The role of p16 extends beyond cell "aging" and tumor pathology. Induction of p16 during these highly proliferative processes is thought to be crucial for maintaining proper tissue homeostasis" Her you should cite related and recent sources referring to the role of p16 in bladder cancer and sources for aging such as: LaPak KM, Burd CE. The molecular balancing act of p16(INK4a) in cancer and aging. Mol Cancer Res. 2014 Feb;12(2):167-83. doi: 10.1158/1541-7786.MCR-13-0350. & Hasan A, Mohammed Y, Basiony M, Hanbazazh M, Samman A, Abdelaleem MF, et al. Clinico-Pathological Features and Immunohistochemical Comparison of p16, p53, and Ki-67 Expression in Muscle-Invasive and Non-Muscle-Invasive Conventional Urothelial Bladder Carcinoma. Clinics and Practice. 2023; 13(4):806-819. <https://doi.org/10.3390/clinpract13040073>



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**Peer-review model:** Single blind

**Reviewer's code:** 05429012

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Doctor, Research Scientist

**Reviewer's Country/Territory:** Jordan

**Author's Country/Territory:** Bulgaria

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**Reviewer chosen by:** Geng-Long Liu

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**Review time:** 7 Days and 7 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

First of all, I would like to congratulate the authors for conducting this interesting study. However, some points have to be addressed: 1- In the methodology section: it will be a good addition if immunohistochemistry protocols were sufficiently described. Although authors mentioned they were adhered to the manufacturer's instructions, variations are always expected. The expression of antibodies was not adequately described from one side, and only expressed as positive or negative, it will be excellent if the authors can put it as a percentage, which will give different findings. 2- In results: Table 1: Antibodies were written using capital letters and small letters, please adhere to capital letters. Figure 2: please add standard deviations into columns for more professional presentation. Other figures: arrows are not always clear. 3. Conclusion: Conclusion is longer than usual. please make it shorter and up to the study aims.