



SDI Review Form 1.6

Journal Name:	Journal of Cancer and Tumor International
Manuscript Number:	Ms_JCTI_19336
Title of the Manuscript:	Differential expression of Claudin-1, Claudin-3, and Claudin-4 in bladder lesions
Type of the Article	Original Research Article

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	<p>The manuscript described the differential expression of Claudin-1, Claudin-3 and Claudin-4 in invasive and noninvasive urothelial lesions. Generally, this is an observational study which may has the potential interest to clinicians and pathologists. There are some weaknesses in the current version which requires revisions:</p> <ol style="list-style-type: none"> 1. The authors should use a figure or table summarizing the final staining score of Claudin-1, Claudin-3 and Claudin-4 in different groups (IUCC, PUNLMP, CIS, CG), which will make readers easily understand. 2. Can the authors explain why Claudin-1 and Claudin-3 have high expression in both normal urothelium and invasive lesions? 3. The authors should at least discuss the differential functions/role of Claudin-1, Claudin-3 and Claudin-4 in bladder cancer development, since they have differential expression. 4. Why they did not detect Claudin-2, does it not express in urothelial lesions? 	<p>Thank you for your valuable comments.</p> <ol style="list-style-type: none"> 1. We added new charts to show staining scores of Claudin-1, Claudin -3 and Claudin-4. 2. Claudins are transmembrane proteins and found in normal epithelium. They expressions are upregulated in some cancers but the mechanism was not clearly understood yet. As you said this is an observational study, we reported our results. 3. About Claudin -4, we summarize our opinion in last part of discussion. Claudins are recently found transmembrane proteins and their functions and roles in cancer development are still under investigation. There are several studies about Claudins in molecular level. Further discussion in this study will be very detailed and out of our specialty. 4. In reported studies (such as Szekeley et



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		al, 2011; Soini Y, 2005) we saw that Claudin-2 has similar staining pattern with Claudin-1 but staining with Claudin-2 didn't give significant results. Therefore, we thought Claudin-1 is more meaningful and excluded Claudin-2.
<u>Minor</u> REVISION comments		
<u>Optional/General</u> comments		