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Responses to Reviewer's Comments

Reviewer #1 (code: 00503125)

Comments to Authors: *Regulatory T cells, a special subset of CD4⁺ T cells, have an important role in preventing autoimmune processes. The role of regulatory T cells in bladder autoimmunity has not been established. The goal of this study was to investigate the role of regulatory T cells in bladder autoimmunity. Through the use of transgenic models, it was demonstrated in this study that CD4⁺ regulatory T cells play an important role in the control of bladder autoimmune inflammation which may be important in patients with interstitial cystitis/bladder pain syndrome.*

Response: We thank the reviewer for his/her effort and favorable comments.

Reviewer #2 (code: 00055095)

Comments to Authors: *Review of the ms "Regulatory T cells suppress autoreactive CD4⁺ T cell response to bladder epithelial antigen" by Wujiang Liu et al. This manuscript reports an elegant study performed to determine the role of regulatory T cells in CD4⁺ T cell-mediated bladder autoimmune inflammation. The manuscript is structured in an understandable manner and the results are clear, but I have some concern regarding the presentation of experimental design. The authors used a complex transgenic cystitis model to identify mechanistic details of bladder inflammation, so it would be highly important to present the protocol as it will serve basis for further studies. "A picture is worth a thousand words" – so I would strongly suggest to include a new figure (replace figure 1) on the overview of the experiments (see example attached). Otherwise there are no major criticisms, the basic science relevance of such investigations would merit publication.*

Response: We thank the reviewer for his/her effort and favorable comments and appreciate his/her inclusion of a sample figure. As suggested by the reviewer, we have replaced the original figure 1 with a new figure. In addition, the figure 1 legend has been updated accordingly.

Reviewer #3 (code: 00503062)

Comments to Authors: *The manuscript by Liu and Luo described the role of regulatory T cells in IC/BPS model mice. The experiments are well designed and the results were clearly presented. Authors have developed elegant autoimmune cystitis with URO-OVA transgenic mice and showed the effects of regulatory T cells on suppression of antigen-specific effector CD4⁺ T cells in their system. It is also interesting to analyze how regulatory T cells regulate antigen-specific CD8⁺ T cells.*

Response: We thank the reviewer for his/her effort and favorable comments. The role of Treg cells in the control of antigen-specific CD8⁺ T cells is certainly an interesting topic that we are considering exploring in our future research.