Response to Current Pharmacologic Approaches in Painful Bladder Research: An Update

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To the editor,

I read, with great interest, the article “Current Pharmacologic Approaches in Painful Bladder Research: An Update” published by Karl-Erik Andersson and Lori Birder in *Int Neurourol J* on December 2017 [1], and would like to commend on the authors on their review article. The aim of this short review was to summarize the accumulating literature on interstitial cystitis/bladder pain syndrome (IC/BPS) and suggest ways that experimental findings could be applied to preclinical and clinical research. This article discussed several currently developed treatments that focus on systemic and pharmacological intervention and are being used in the clinical setting. I believe that this topic was clinically relevant and the timing was perfect. The recently implemented Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) research network has made great advances in understanding the phenotypes of IC/BPS patients and the molecular basis that underlie this disease [2,3]. There has also been growing interest toward understanding whether symptoms related to IC/BPS are bladder-based, outside the bladder (systemic), or both. However, this remains discrepant. In this review article, the authors discussed a series of research activities and clinical trials that are focused on pharmaceutical blocking of nerve growth factor (e.g., tanezumab and fulranumab), tumor necrosis factor- α (e.g., adalimumab), P2X3 receptor (e.g., AF-219), and α 1-adrenoceptor (e.g., prazosin). The SHIP1 activating drug, AQX-1125, is a known negative regulator of the PI3K network and inflammatory signaling pathways, and has also been considered and tested as a potential systemic treat-

ment for IC/BPS. The authors further provided reasoning on why current systemic pharmacological treatments have shown only limited success. This may be caused by: (1) the lack of current knowledge on how to accurately phenotype and subgroup individual IC/BPS patients for certain treatments, and/or (2) the low efficacy of systemic drug treatments, themselves. Additionally, the writers debated on the important role of local treatment options in overcoming the lower effectiveness of systemic pharmaceutical treatments and concluded that more efforts should be focused on investigating local treatment approaches. Research strategies, including the blocking of toll-like receptor 7 (e.g., hydroxychloroquine) and intravesical liposomes should be tested against IC/BPS in large well-designed cohorts. Successful phenotyping could stratify patient groups who are suffering from localized disease from those suffering from a systemic disorder and provide efficient treatment options. While bladder-specific or systemic-based differences are certainly useful, we would also like to bring up sex differences to the attention of readers. While sex-determined disparities are evident and well-documented in numerous other diseases [4,5], the biological, cellular, and molecular basis of gender biases remain elusive in context of IC/BPS. One potential hypothesis would be that the biological role of sex hormones, such as estrogen, testosterone, et al., create variations in the metabolic rewiring of female and male IC/BPS patients [6]. However, we understand that there are still many areas lacking in this field. Consideration of sex differences in preclinical work and clinical trials will give a better picture of the disease to esteemed readers of

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Submitted: February 1, 2018 / **Accepted after revision:** February 7, 2018

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this article. We hope investigators in this field will continue to conduct studies assessing how to deal with sex disparities and their effects on heterogeneous metabolism in female and male patients. Hopefully, in the near future, merged knowledge will enable us to find the best timing to apply a systemic, local, or combination treatment against IC/BPS to get maximized and synergistic benefits for patients.

• **Grant/Fund Support:** The author acknowledges support from National Institutes of Health grants (1U01DK103260, 1R01DK100974, U24 DK097154, NIH NCATS UCLA CTSI UL1TR000124), Department of Defense grants (W81XWH-15-1-0415), Centers for Disease Controls and Prevention (1U01DP006079), IMAGINE NO IC Research Grant, the Steven Spielberg Discovery Fund in Prostate Cancer Research Career Development Award, the U.S.-Egypt Science and Technology Joint Fund (to J.K.). J.K. is former recipient of Interstitial Cystitis Association Pilot Grant, a Fishbein Family IC Research Grant, New York Academy of Medicine, and Boston Children's Hospital Faculty Development. The funders had no role in the design, data collection and analysis, decision to publish or preparation of the manuscript. In addition, this article is derived from the Subject Data funded in whole or part by NAS and USAID. Any opinions, findings, conclusions, or recommendations expressed in this article are those of the authors alone, and do not necessarily reflect the views of USAID or NAS.

• **Conflict of Interest:** No potential conflict of interest relevant to this article was reported.

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