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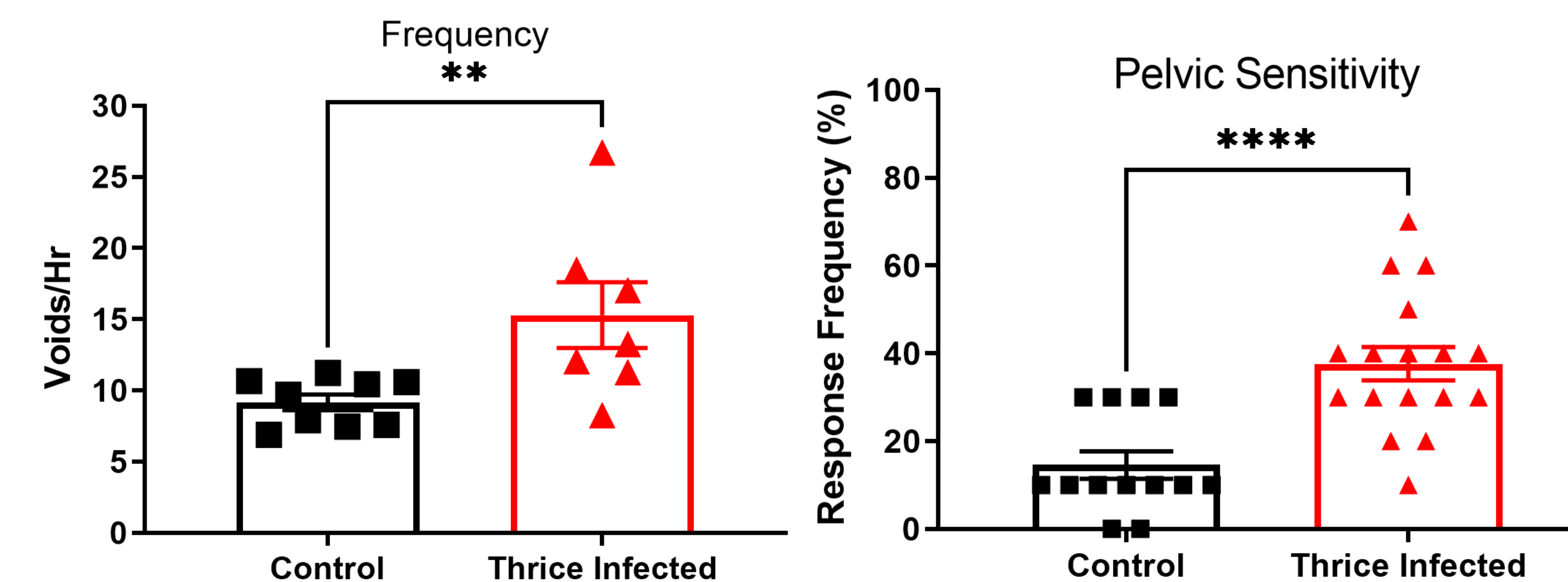
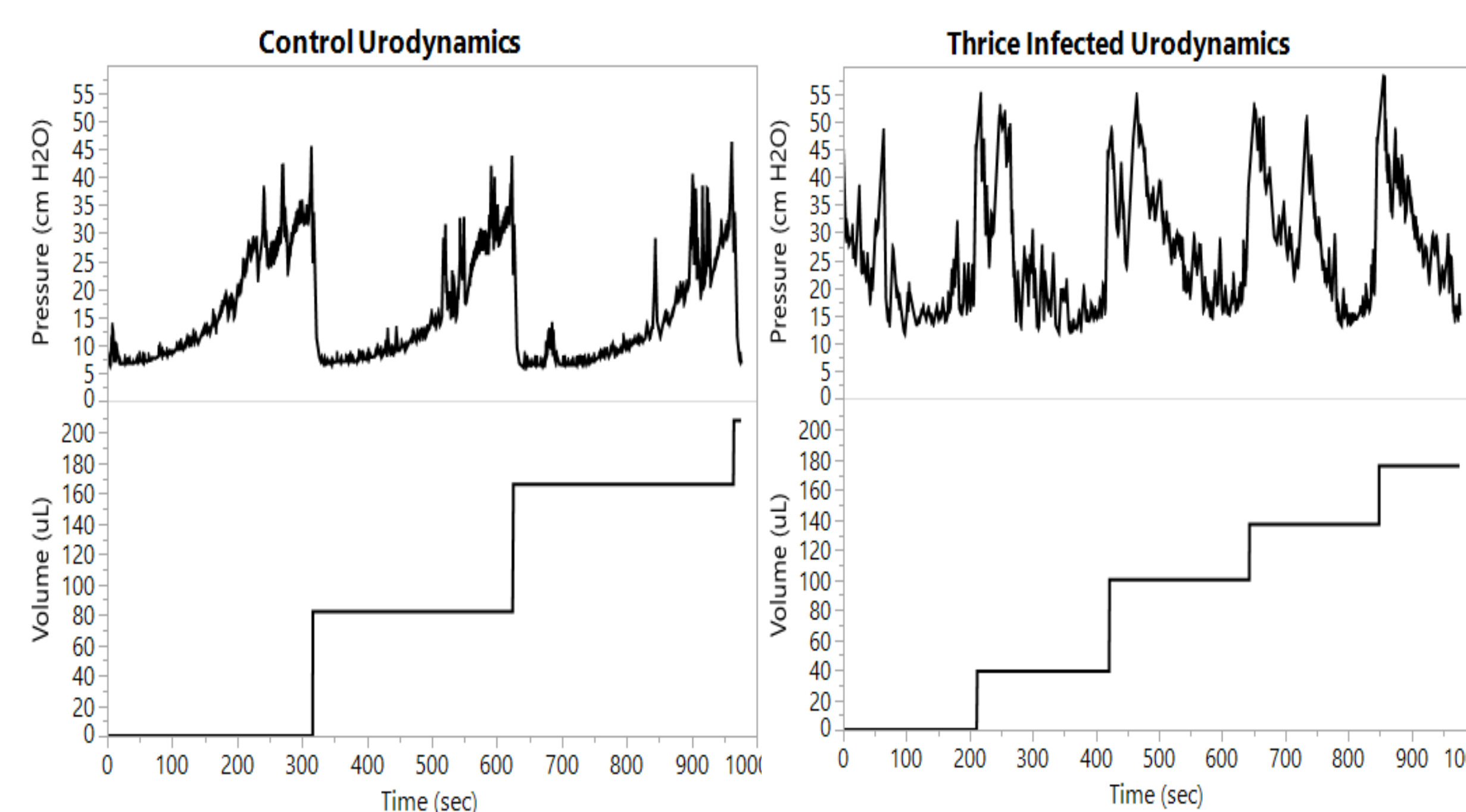
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## Introduction

- Bladder Pain Syndrome (BPS) is a broad-spectrum pelvic pain disorder characterized by pain and one or more underlying lower urinary tract symptom (i.e. frequency)
- Current animal models are insufficient in presenting disease pathogenesis and progression
- Clinically, mast cell (MC) mediators such as histamine is found in patient urine
- Patients often report history of urinary tract infections (UTIs)

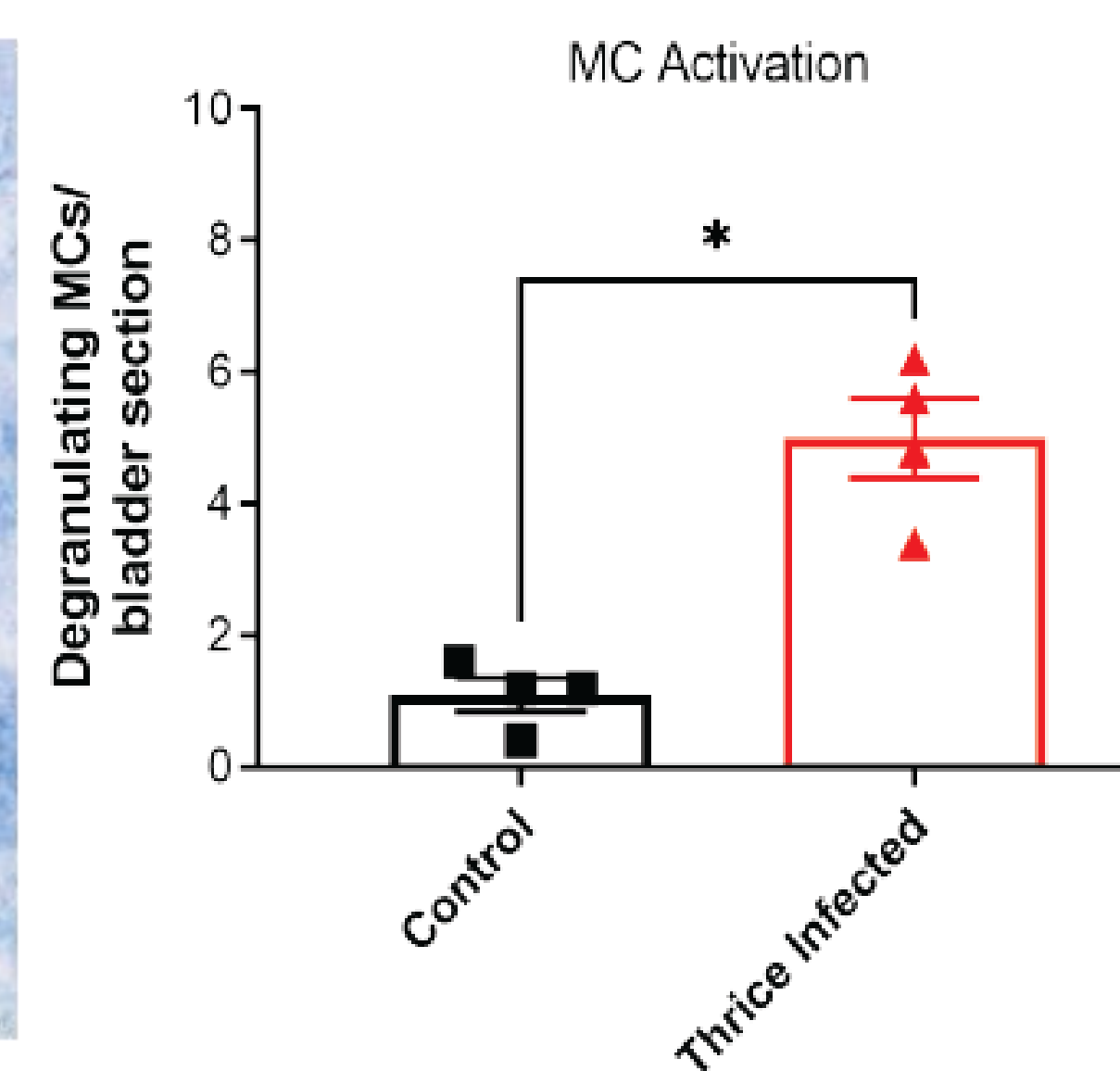
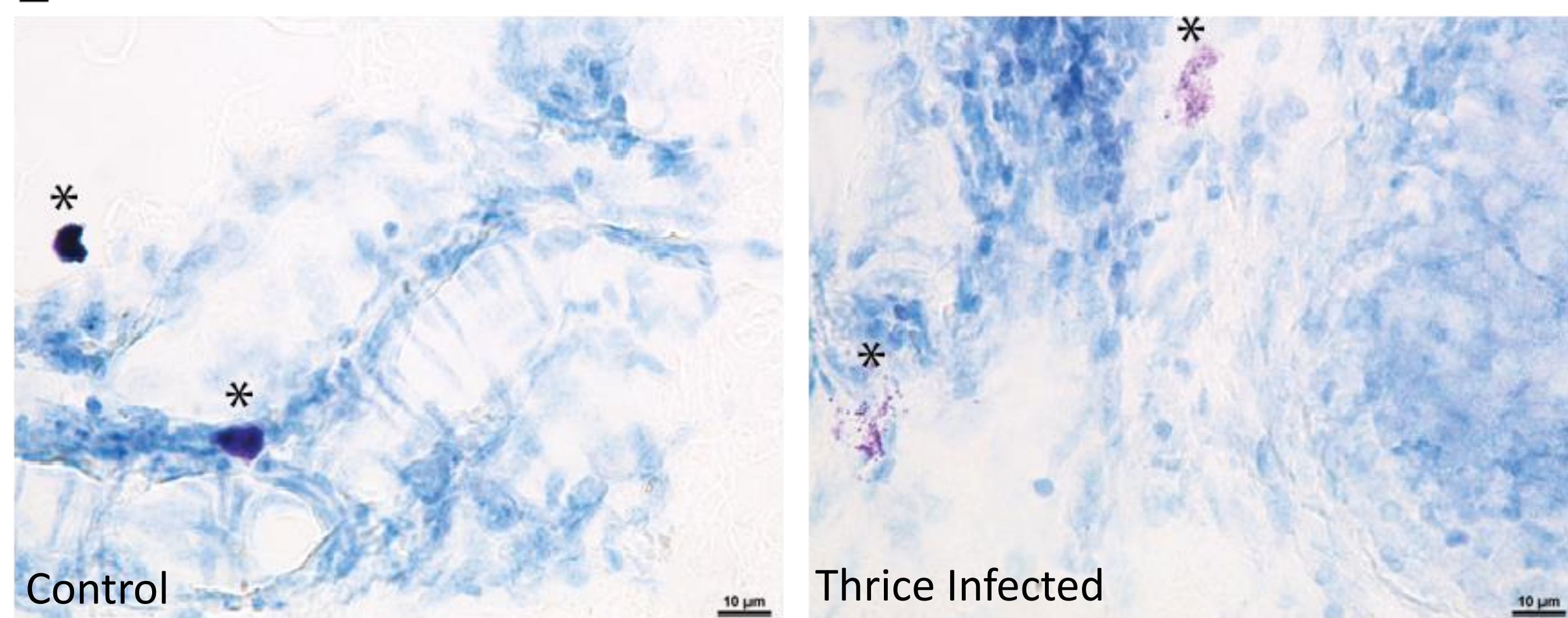
**Based on these clinical observations, we sought to determine the underlying mechanism linking these clinical observations utilizing our murine model of BPS**

## BPS Mouse Model – 3 once-a-week instillations of E.coli in the bladder



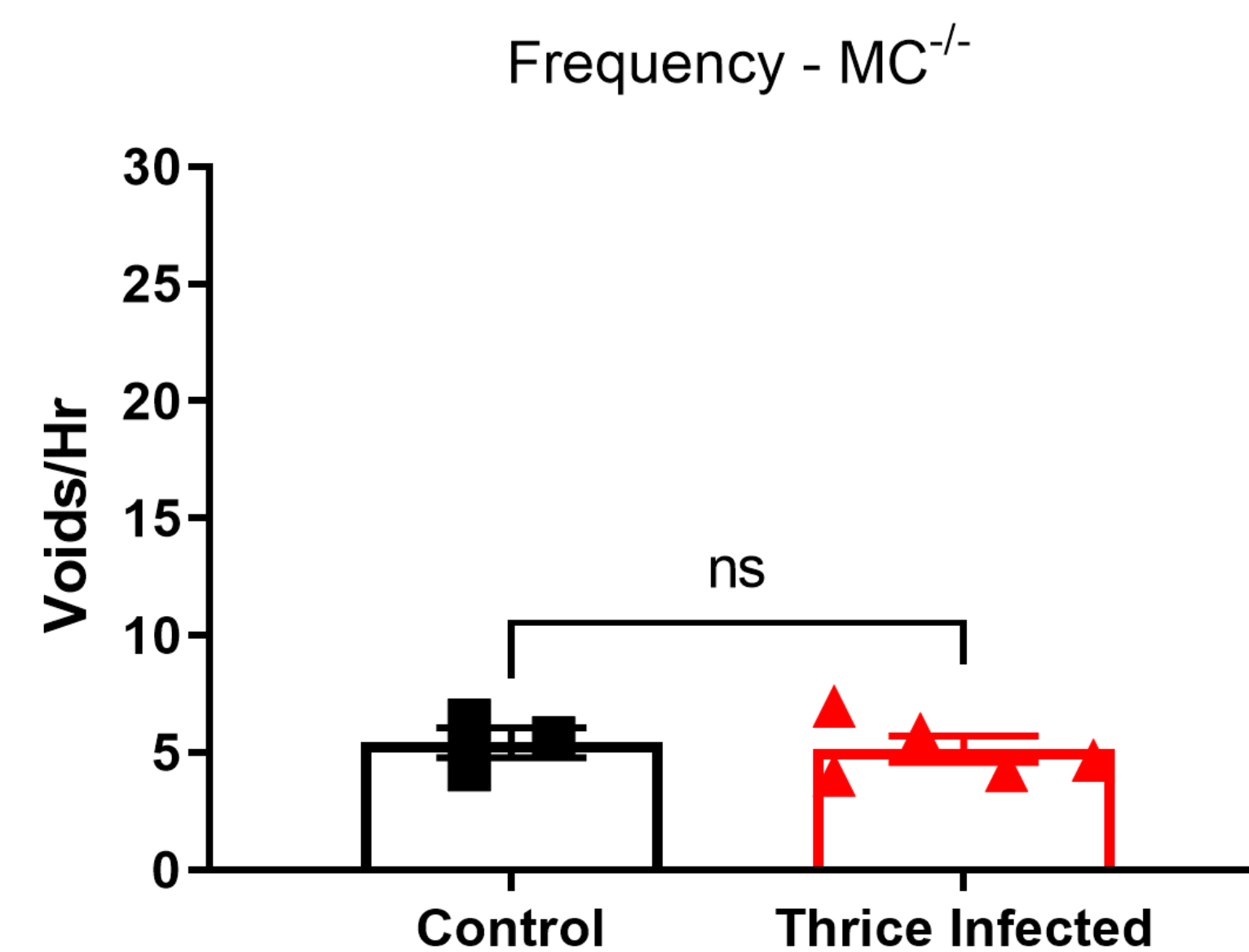
**Mice with a history of UTIs void more frequently and experience pelvic pain**

## Persistent MC and Nociceptor Activation in Bladder Lamina Propria 2 weeks after infection

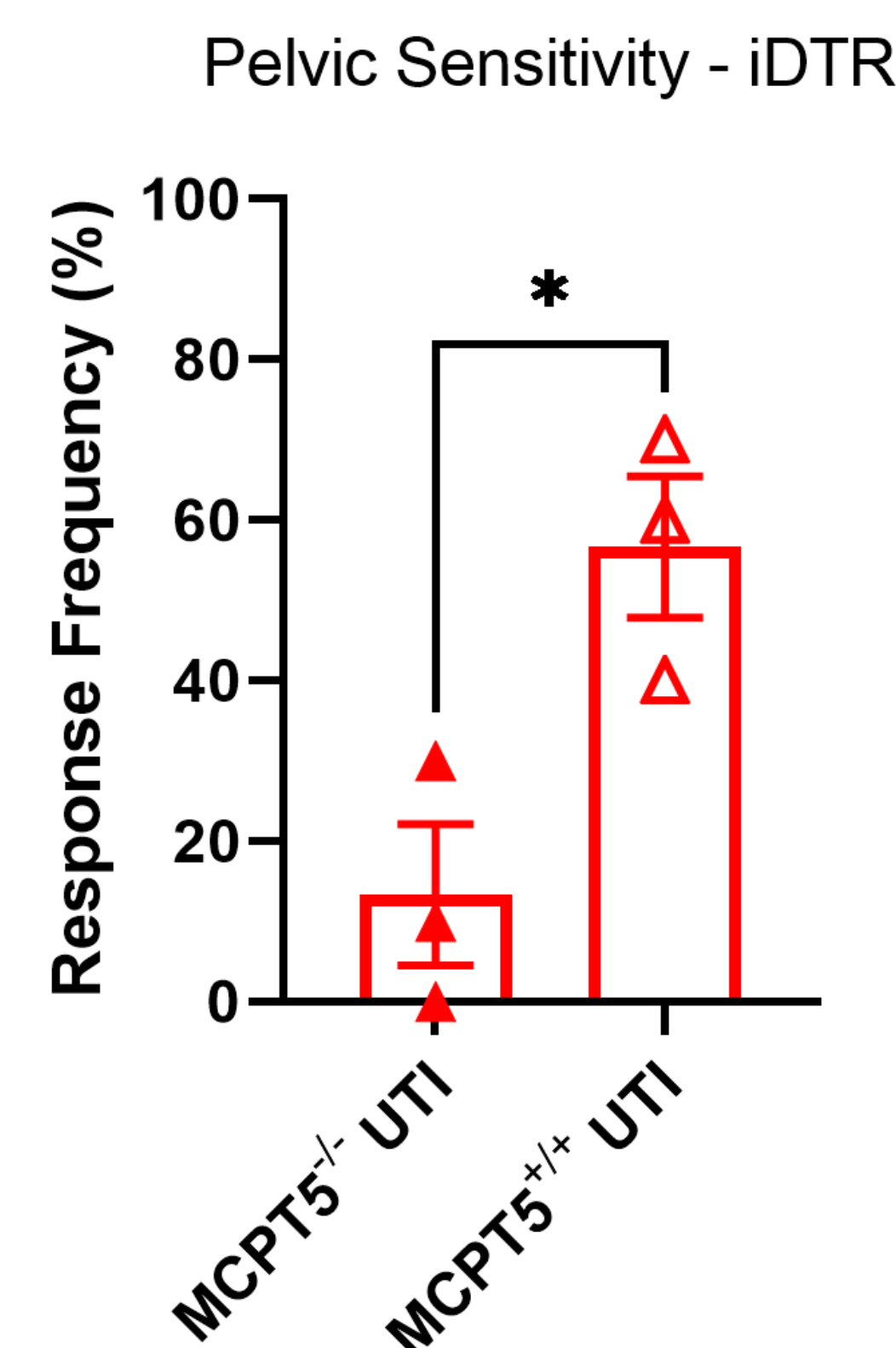


**Toluidine Blue stain of bladder sections display dispersal of granules, signifying MC degranulation (activation)**

## MCs are Required for UTI induced BPS

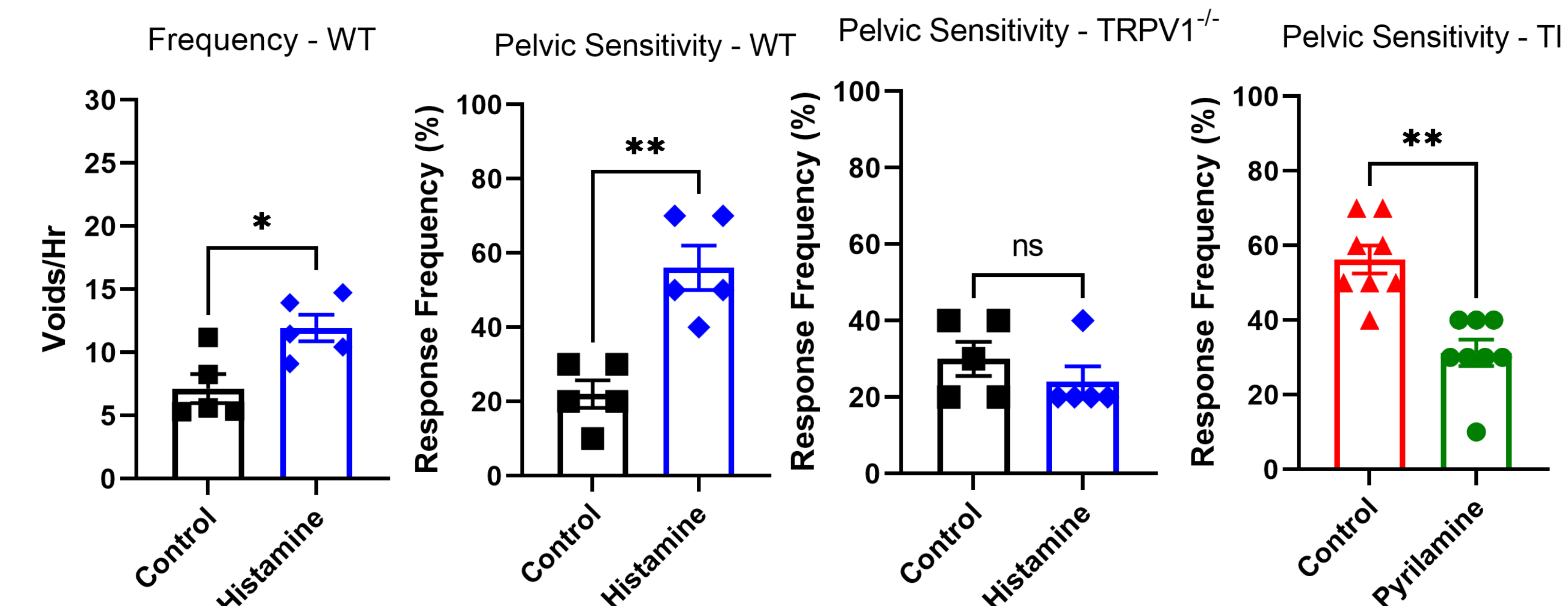


**Constitutive MC<sup>-/-</sup> model targeting Kit**



**Inducible MC depletion model targeting MCPT5**

## Histamine Mediates BPS symptoms after UTI



**Histamine receptor antagonism reduces pain in TI mice**

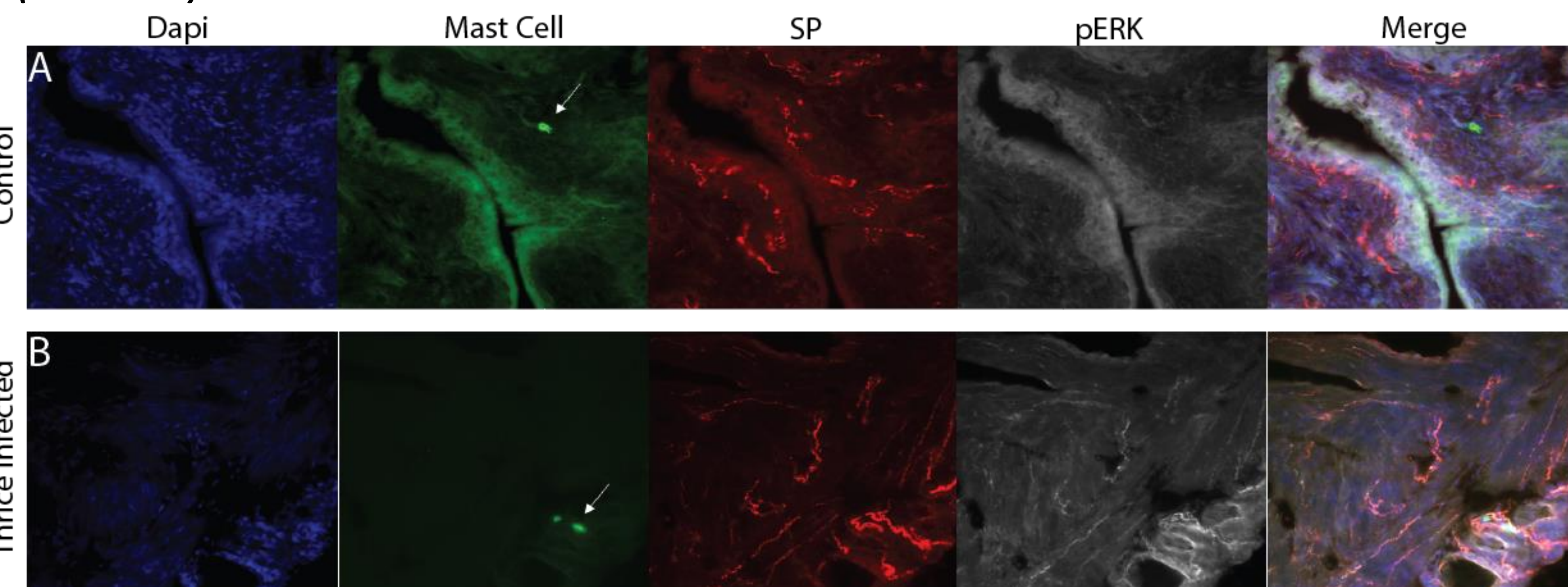
## Conclusion

- Our murine model of BPS recapitulates phenotypes observed in human patients, including prolonged MC activity.
- Pathology was dependent on nerve mediated signaling of MC-derived histamine in the bladder.

**As our model was based on bladder UTIs, a common bacterial infection in humans, these findings demonstrate a possible etiology of BPS, and define the underlying basis for the observed BPS symptoms. Furthermore, these findings present a potential lasting impact of UTIs on bladder sensation and relevant cell types that may be involved.**

## Acknowledgements

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**pERK colocalization with Substance P (SP) nociceptors display nerve activation near MCs in bladder sections of thrice infected (TI) mice**