

VISCERAL PAIN RESPONSE IN BALB-C MICE IMMUNIZED WITH UROPLAKIN UP3B AS A MURINE MODEL FOR INTERSTITIAL CYSTITIS

Hypothesis / aims of study

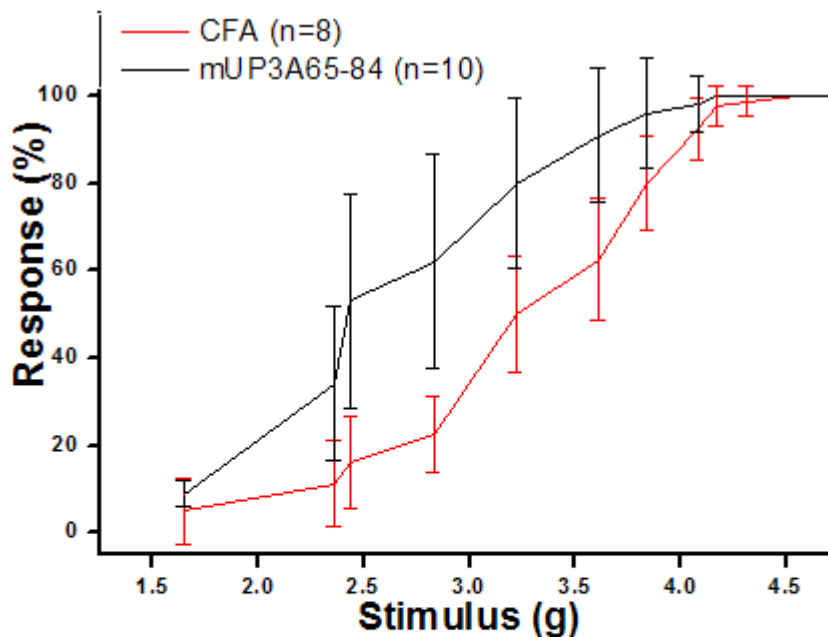
Interstitial cystitis/painful bladder syndrome (IC/PBS) is an elusive disease with irritative voiding symptoms and pelvic pain. Little progress has been made in elucidating the pathophysiology or treatment of IC/PBS. We recently reported a method of inducing bladder-specific autoimmunity that manifests IC/PBS symptoms. The aim of this study was to induce autoimmunity in murine bladder with uroplakin UP3b peptide and to examine its phenotype.

Study design, materials and methods

We used a database of major histocompatibility complexes (MHCs) and their recognized peptide motifs (<http://www.syfpeithi.de/>) to predict immunogenic peptides of known sequences for bladder-specific uroplakins. At 6-8 weeks of age, female BALB-C mice were injected with an emulsion of water and CFA comprised of 400 µg of TB H37RA with (n=10) or without (n=8) 200µg of UP3b peptide. Peptides were made from the known sequence of UP3b and were selected based on having the binding motif for H2-D MHC II molecules expressed in BALB-C mice. At 7 weeks, we assessed abdominal and paw visceral pain response using calibrated von Frey monofilaments and measured levels of antibody to UP3b by ELISA. We also assessed 24-hour urinary frequency-volume charts.

Results

We identified a motif from UP3b that was strongly recognized by MHC type H2-D and that correlated with increased antibody against UP3b. Increased micturition frequency and decreased output per micturition were observed in immunized mice compared to control (p<0.05). Visceral pain response to von Frey monofilament stimulus was statistically heightened in UP3b immunized mice compared with controls (p<0.05). Similarly, visceral pain response measured by paw stimulus was statistically heightened in immunized mice versus controls (p<0.05) (figure).



Visceral Pain Measurement on Hind Paw by Von Frey

Filaments At 7 Weeks After Injection of BALB/C

Female Mice With mUP3b 65-84

Interpretation of results

A peptide motif of UP3b is recognized by MHC H2-D. Immunization of BALB-C mice with UP3b induces an immunogenic response that phenotypically manifests as increased visceral pain response, increased micturition frequency, and decreased output per micturition.

Concluding message

This phenotype is similar to that observed in IC/PBS patients and thus may qualify this animal model as a candidate model for IC/PBS.

<i>Specify source of funding or grant</i>	This research was made possible through funding by the department of urology, Case Western Reserve University.
<i>Is this a clinical trial?</i>	No
<i>What were the subjects in the study?</i>	ANIMAL
<i>Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?</i>	Yes
<i>Name of ethics committee</i>	IACUC #2009-0131