VISCERAL PAIN RESPONSE IN BALBc/J MICE IMMUNIZED WITH UROPLAKIN UP3a AS A MURINE MODEL FOR INTERSTITIAL CYSTITIS

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Introduction

- Interstitial cystitis/painful bladder syndrome (IC/PBS)
  - Is an elusive disease
  - Associated with irritative voiding symptoms and pain in the bladder or pelvis

- Little progress has been made in elucidating the pathophysiology of IC/PBS
  - Animal models that mimic the phenotype of IC/PBS are lacking

- We recently reported a method using uroplakin to induce bladder-specific autoimmunity in mice with a phenotype similar to IC/PBS (Lin et al, 2008)

Specific Aims
1. To identify immunogenic motifs within the known sequences of the murine uroplakin family
2. To induce autoimmunity in murine bladder with these immunogenic peptide sequences
3. To characterize the resultant phenotype

Methods

1. Searched 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
2. Synthesized peptides from the known sequence of UP3a and were selected based on having the binding motif for MHCII H2-D expressed in BALBc/J mice
3. Subcutaneous injection of female BALBc/J mice with (n = 10) or without (n = 8) 200 μg of UP3a peptide (Figure 1)
4. Seven-week measurements included
   - Abdominal and paw visceral pain response using von Frey monofilaments (Figure 2)
   - Levels of antibody to UP3a by ELISA
   - 24-hour urinary frequency-volume charts

Results

- A motif from UP3a is strongly recognized by MHCII H2-D correlating with increased antibody production against UP3a
- Increased micturition frequency and decreased output per micturition were observed in immunized mice (P < 0.05) (Figures 3 and 4)

Conclusions & Future Directions

- A peptide motif of UP3a is recognized by MHCII H2-D
- Immunization of BALBc/J mice with UP3a induced an immunogenic response that phenotypically manifested as
  - Increased micturition frequency
  - Decreased output per micturition
  - Increased visceral pain response
- This phenotype is similar to that observed in IC/PBS patients and may qualify this animal model as a candidate model for IC/PBS

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