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5R01DK066079-03

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Project Number: 5R01DK066079-03	Contact PI / Project Leader: LUO, YI
Title: BCG IN ENDOGENEOUS AND EXOGENOUS ANTIGEN-INDUCED T CELL	Awardee Organization: UNIVERSITY OF IOWA

Abstract Text:

DESCRIPTION (provided by applicant): The purpose of this project is to create antigen-induced T helper (Th) polarized bladder inflammation models to mimic the postulated pathogenesis of interstitial cystitis (IC) and investigate the potential effect of the Bacillus Calmette-Guerin (BCG) vaccine on treating the disease in these models. The long-term goal is to develop effective treatment strategies to combat IC. Towards achieving these goals, three specific aims will be undertaken: Specific Aim 1: To create an exogenous antigen-induced bladder inflammation model to determine the role of systemic Th1 and Th2 immune polarization in the development of bladder inflammation. To create this model, T helper cells will be isolated from transgenic mice (termed OT-II) that express Th cells specific for the ovalbumin (OVA) antigen. These Th cells will be differentiated in the laboratory into Th1 or Th2 subsets, and adoptively transferred into genetically compatible mice. Cystitis will be induced in the recipient mice by instilling OVA directly into the bladder. This model will particularly lend itself to studies on acute inflammation. Specific Aim 2. To establish a bladder autoimmune disease model by creating a novel transgenic mouse strain that expresses OVA as a "self" antigen via promoter-specific production by the urothelium and to determine the role of the Th immune polarization in the development of this disease. This transgenic mouse strain (termed URO-OVA) will be genetically engineered with DNA containing a bladder-specific promoter and the gene for OVA. An autoimmune form of cystitis will be developed in these URO-OVA mice by adoptive transfer of polarized OT-II Th cells. This model particularly lends itself to studies on chronic inflammation. Specific Aim 3. To assess the therapeutic effect of BCG in antigen-induced bladder inflammation. BCG will be evaluated for its effect on treating Th2 polarized cystitis (the hypothesized type responsible for IC) in both exogenous and endogenous antigen-induced cystitis models. BCG is predicted to shift the diseased Th2 immune state back to a favorable Th1 state. Successful completion of this study will establish the pathological and immunological characteristics for both Th1 and Th2 type cystitis, shed light on BCG's effect on treating this disease, and aid in the future development of prevention and treatment strategies for IC and other painful bladder conditions.

Project Terms:

autoantigens; autoimmune disorder; Bacillus Calmette Guerin vaccine; biotechnology; biotherapeutic agent; disease /disorder model; genetically modified animals; helper T lymphocyte; immunomodulators; immunopathology; immunotherapy; inflammation; interstitial cystitis; laboratory mouse; Mycobacterium bovis; neurogenic urinary bladder disorder; nonhuman therapy evaluation; ovalbumin; transfection; urinary bladder epithelium; urinary tract disorder chemotherapy; urinary tract pharmacology

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