New Frontiers in Therapies for Autoimmunity
Preview

• Discuss spectrum of autoimmune research at MUSC
• Identify some of the key investigators in basic and clinical research at MUSC
• Discuss specific areas of research interest in autoimmunity at MUSC
• Identify potential areas of collaboration
Autoimmunity/Inflammation Research at MUSC

- Basic Mechanisms
- Genetics
- Translational
- Clinical
- Outcomes
- Epidemiologic
- Environmental
- Community
**Basic Researchers**

Jim Oates – Associate Professor of Rheumatology  
John Zhang – Associate Professor of Rheumatology  
Tamara Nowling – Assistant Professor of Rheumatology  
Melissa Cunningham – Assistant Professor of Rheumatology  
Paula Ramos – Assistant Professor of Rheumatology  
Gary Gilkeson – Professor of Rheumatology

**Bench Research**

Zihai Li – Professor of Microbiology and Immunology  
Wei Jiang – Assistant Professor of Microbiology and Immunology  
Chenta Vasu – Associate Professor of Microbiology and Immunology  
Steve Tomlinson – Professor of Microbiology & Immunology
Clinical Research

**Public Health**
John Vena – Professor of Public Health Sciences
Paul Nietert - Professor of Public Health Sciences
Edith Williams - Assistant Professor of Epidemiology

**College of Health Professions**
Hazel Breland - Assistant Professor of Health Professions

**Lupologists**
Gary Gilkeson - Professor of Microbiology and Immunology
Diane Kamen - Associate Professor of Rheumatology
Jim Oates - Associate Professor of Rheumatology
Melissa Cunningham – Assistant Professor of Rheumatology
Genetics/Epigenetics

Progress
- Nearly a hundred gene linkages associated with lupus
- Epigenetic differences noted in key immune genes
- Rare single gene mutations

Future
- Whole genome sequencing
- Combining genomic sequencing with epigenetics, gene expression
- Long non-coding RNAs

Opportunities at MUSC
- Gullah population
- MCRC repository of samples with extensive clinical data
TLRs and other pattern recognition receptors

Progress
- Clear evidence they are important in the pathogenesis of lupus in mice with corroborative evidence in humans
- Key pathway mediators identified

Future
- Identifying a successful therapeutic strategy

Opportunities at MUSC
- Dr. Li’s studies of gp96 and GARP as modulators of TLR pathways
- Dr. Cunningham’s studies of the role of sex hormones and sex hormone receptors in TLR signaling
- Dr. Jiang’s studies of gut permeability
Interferons

Progress

Clear evidence of Type 1 interferon overexpression in a number of autoimmune diseases.
Two trials of anti-IFNα antibodies failed.
Are Type 1 IFN pathogenic or an indication of disease?

Future

Identifying which Type 1 interferon is pathogenic- alpha, beta or lambda?
Identifying which cells are producing it- pDCs, PMN?

MUSC opportunities

Expertise in type 3 interferons
Clinical trial expertise
Animal model expertise
Agnostic screens- AMP

Progress
  Urine Proteomics
  Microarrays
  Some Metabolomics
Future
  Lipidomics
  Microbiome
  Single cell analyses
Concerns
  Tons of data in each? How do we integrate it all? How do we prove pathogenicity?
MUSC opportunities
  Leader in lipidomic analyses
  Patient samples
  Microbiome expertise
  AMP pilot projects
Cell specific targeting

**Progress**
Multiple cell types shown to be involved in pathogenesis of disease
New techniques allow identification and isolation of rare subsets

**Future**
Identifying specific subsets of cells that are pathogenic in specific individuals
Develop targeted therapies to eliminate/modulate those cells

**Opportunities at MUSC**
Dr. Vasu is submitting a grant to obtain a CyTOF analyzer
Cellular therapies

**Progress**
Cellular therapy has shown impressive efficacy in mice:
- Tregs
- MSCs
- Bregs

**Future**
Performing the clinical trials in humans to prove efficacy

**Opportunities at MUSC**
- GMP Clean Cell Facility
- One MSC trial in progress
- Second MSC trial at 3rd base
Disease prevention

Progress
In Type I diabetes, lupus and rheumatoid arthritis individuals at increased risk can be identified.

Environmental factors are being identified that can be changed.

Future
Devising clinical trials to demonstrate disease can be prevented either by medication or environment risk reduction.

Opportunities at MUSC
MCRC patient core has samples from first degree relatives and unrelated controls.
Extensive environmental assessments on patients with lupus and scleroderma
Department of Public Health Sciences has expertise in environmental assessments including GPS localization.
Key Unanswered Questions?

• Why women? Estrogen, X chromosome
• Why African Americans/Hispanics? Socioeconomics, genetic environmental
• Is incidence/prevalence increasing? Hygiene hypothesis
• Can we induce tolerance when we do not know what the antigen is? Is the antigen the same for everyone?
Opportunities at MUSC

• We have the patient populations
• We now have a growing cadre of investigators, both clinical and basic, allowing program and core grant submissions
• We have the clean cell facility and about to be newly refunded CTSA
• We have a growing academic/industry partnership