# An Overview of the Laboratory of Mucosal Pathogens and Cellular Immunology

Scott Stibitz, Lab Chief

# Who we are (CBER-level)?

- Bench scientists who also regulate products under FDA jurisdiction
- What do we mean by regulate?
  - Human clinical trials are done under Investigative New Drug (IND) applications that we review
  - Ultimate licensure upon review of a Biologics License Application (BLA)
  - Lab-based scientists typically review the product
    - Manufacture
    - Testing

# Who we are (LMPCI-level)

- LMPCI is like a typical Microbiology department
  - Microbiologists
  - Immunologists
- Research programs are varied (size-related)
- Research programs relate to the products we regulate
  - Ensure safety and potency (potential to be efficacious)

# Outline

Lab Organization

Lab History

Regulatory Portfolio

Regulatory Challenges

Research Programs

# LMPCI Staff who presented at the Oct. 25, 2017 site visit

- Siobhan Cowley, Ph.D., P.I.
  - Methods to Predict and Improve Efficacy of Vaccines Against Bacterial Pathogens
- Paul Carlson, Ph.D., P.I.
  - Identification of Targets for Development of Vaccines and Biological Therapies Against Gastrointestinal Pathogens
- Scott Stibitz, Ph.D., P.I
  - Safety and Efficacy of Novel Anti-Bacterial Vaccines and Therapeutics
    - Qing Chen, Ph.D. Staff Scientist
      - Genetic analysis of virulence regulatory mechanisms in *Bordetella pertussis*
    - Madushini Dharmasena, Ph.D. Staff Fellow
      - Evaluating *Salmonella*Typhi Ty21a As an Oral Vaccine Delivery Platform for Heterologous Antigens
    - Miranda Oakley, Ph.D. Staff Scientist
      - Characterization of Vaccines and Biomarkers in Preclinical Models of Malaria
    - Steven Derrick, Ph.D., Staff Scientist
      - Characterization of Novel Vaccines and Immunization Strategies Against Tuberculosis
- Karen Elkins, Ph.D, P.I.
  - Advancing Development of Vaccines Against Intracellular Bacteria
    - Roberto De Pascalis, M.D., Staff Scientist
      - Advancing Development of Vaccines Against Intracellular Bacteria

# LMPCI History

- Laboratory of Mycobacterial Diseases and Cellular Immunology (LMDCI)
  - Created to consolidate review of TB vaccine files
  - Research projects added more recently to address issues related to malaria
- Laboratory of Enteric and Sexually Transmitted Diseases (LESTD)
  - Created de novo in 1993
  - Purpose: to review the large number of enteric vaccine files we were receiving
  - STD vaccine files were also included in portfolio
- LMPCI
  - Created by merger upon departure of LMDCI Lab Chief
  - Search to fill that PI position recently completed

# LMPCI Regulatory Portfolio - vaccines

- TB
  - Live attenuated
  - Subunit
- Malaria
  - Subunit
  - Live attenuated
    - Genetic
    - Radiation
- Enterics
  - Live attenuated
  - Subunit
- STDs
  - Subunit

# LMPCI Regulatory Portfolio – Biological Therapeutics

- Live Biotherapeutic Products
  - "Probiotics"
    - Over the Counter or similar
  - "Pharmaceutical grade"
    - Specifically developed for drug indications
- Fecal Microbiota for Transplantation (FMT)
  - Fecal material
  - Defined microbial consortia
- Bacteriophage Therapy
  - Defined phage or cocktails
  - Phage banks for treatment

# CMC Regulatory Challenges (two examples)

- Live Biotherapeutic Products
  - Inherent problem of finding contaminants in a preparation of live bacteria
  - Research Project: Developing improved tests for microbial purity using phage lysins to specifically remove product bacteria.
- Fecal Microbiota for Transplantation
  - Difficult to regulate without a basic understanding of the biological basis of how it works
  - Research Project: Due to effect of MAIT cells in an animal model we have a reliable source of fecal material that works and one that doesn't. Can now investigate functional differences and identify key species.

# LMPCI research programs

- Provide a cadre of scientists to perform regulatory review, who are active in the research fields relevant to products we regulate, and who are free of conflict of interest
- Allow us to speak with scientific as well as regulatory authority
- Provide state of the art, first hand knowledge of the areas we regulate
- Provide expertise to design tests to assess safety, purity, and potency
- Lead to regulatory decisions based on problem solving – not just problem identifying
- Provide for regulatory decision-making based on sound scientific judgment, addressing technical feasibility, and ability to separate “need-to-know” from “nice-to know”