Overview of the Laboratory of Mucosal Pathogens and Cellular Immunology

LMPCI Site Visit

February 15, 2024

A brief history of the Laboratory of Mucosal Pathogens and Cellular Immunology (LMPCI)

- LMPCI was formed in 2014 by the merger of:
  - Laboratory of Enteric and Sexually Transmitted Diseases
    - Scott Stibitz, PI and Lab Chief
  - Laboratory of Mycobacterial Diseases
    - Sheldon Morris, PI and Lab Chief
    - Karen Elkins, PI
    - Siobhan Cowley, acting PI

LMPCI Principal Investigators

- Initial principal investigators (2014):
  - Scott Stibitz, PI and Lab Chief
  - Karen Elkins, PI
  - Siobhan Cowley, PI (closed lab in 2023)

- Current principal investigators (2024):
  - Scott Stibitz, PI and Lab Chief
  - Karen Elkins, PI
  - Paul Carlson, PI (hired in 2015)
  - Heather Painter, PI (hired in 2019)

LMPCI Research/Regulatory Portfolio Stibitz Lab

Selected Research Topics:

- Improved microbiological testing of live biotherapeutic products (LBPs)
- Bacterial host/bacteriophage interactions: MRSA
- Extensive genetic analysis and modification of *B. pertussis*

Product Review:

- Live biotherapeutic products for a wide range of infectious and non-infectious clinical indications
- Bacteriophage therapy proposals
- Genetically engineered bacterial vaccines and LBPs

LMPCI Research/Regulatory Portfolio – Carlson Lab

Selected Research Topics:

- Identifying targets for development of vaccines and therapeutics against *C. difficile*
- Understanding and improving Fecal Microbiota for Transplantation (FMT) production
- Development of assays for LBP characterization
- Bacteriophage therapy against Vancomycin Resistant *Enterococcus* (VRE)

Product Review:

- FMT for a wide range of infectious and non-infectious clinical indications
- LBPs for a wide range of infectious and non-infectious clinical indications

Research and Regulatory Portfolio – Elkins Lab

Selected Research Areas:

- Determine innate immune responses to live attenuated vaccines that impact safety and efficacy
- Understand critical adaptive immune responses that inform correlates of vaccine-induced protection against *Francisella tularensis* and can serve as biomarkers of effective immune response
- Understand critical adaptive immune responses that inform correlates of vaccine-induced protection against *Mycobacterium tuberculosis* and can serve as biomarkers of effective immune response

Product Review

- Vaccines against intracellular pathogens (*F. tularensis* and *M.* tuberculosis)
- Vaccines against Lyme disease
- Vaccines against multicellular parasites (worms)

LMPCI Research/Regulatory Portfolio – Painter Lab

Selected Research Areas:

- Molecular mechanisms of malaria gametogenesis (critical for disease transmission)
- Develop improved molecular diagnostics based on CRISPR activities.

Product Review

- Vaccines against malaria
- Human challenge studies with malaria
- Biomarker qualification for molecular methods of parasite detection for use in human malaria challenge models

LMPCI - notable regulatory accomplishments

FDA licensing of two first-in-class biologic products:

- Rebyota
  - Minimally processed human stool for fecal microbiota transplantation (FMT)
  - Indication: prevention of recurrence of *C. difficile* infection
  - Licensed November, 2022
  - Primary product manufacturing reviewer – Paul Carlson
- VOWST
  - Bacterial spores derived from human stool by ethanol treatment
  - Indication: prevention of recurrence of *C. difficile* infection
  - Licensed April, 2023
  - Primary product manufacturing reviewer – Siobhan Cowley

Biomarker Qualification – Malaria

- RT-PCR 18S rDNA/rRNA assay for earlier detection of parasitemia in human challenge studies
- For use in challenge studies performed in non-endemic regions
- Primary subject matter expert and assay reviewer – Heather Painter

LMPCI regulatory outreach

Workshops and Symposia

- Live Biotherapeutic Products (2018) - FDA workshop
- Microbiome and Cancer Immunotherapy (2019) – FDA mini-symposium
- Bacteriophage Therapy (2021) – workshop together with NIAID/NIH
- Malaria (2023) – symposium at ASTMH – also planned for 2024
- Valley Fever Vaccines – workshop together with NIAID/NIH (2024)

Publications

- Bacteriophage Therapy (2019)
- Human Challenge Studies (2019)
- Fecal Microbiota for Transplantation (2020)

Speaking engagements

- Bacteriophage Therapy – several in review period
- Live Biotherapeutic Products and FMT – too many to list

Thank-you