

# **Overview of Laboratory of Bacterial Polysaccharides**

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Polysaccharides**

# Description of the Laboratory of Bacterial Polysaccharides

- The Laboratory of Bacterial Polysaccharides investigates the biochemistry, biology, chemistry, and immunology of virulence factors of encapsulated bacteria.
- These virulence factors include capsular polysaccharides, lipopolysaccharides, and outer membrane proteins.
- These basic research fields are related to the regulatory activities of the Laboratory of Bacterial Polysaccharides which include, review and approval of BLA and IND submissions related to polysaccharide and polysaccharide conjugate vaccines in addition to non-capsular immunogens of encapsulated pathogens.

# Product Responsibilities

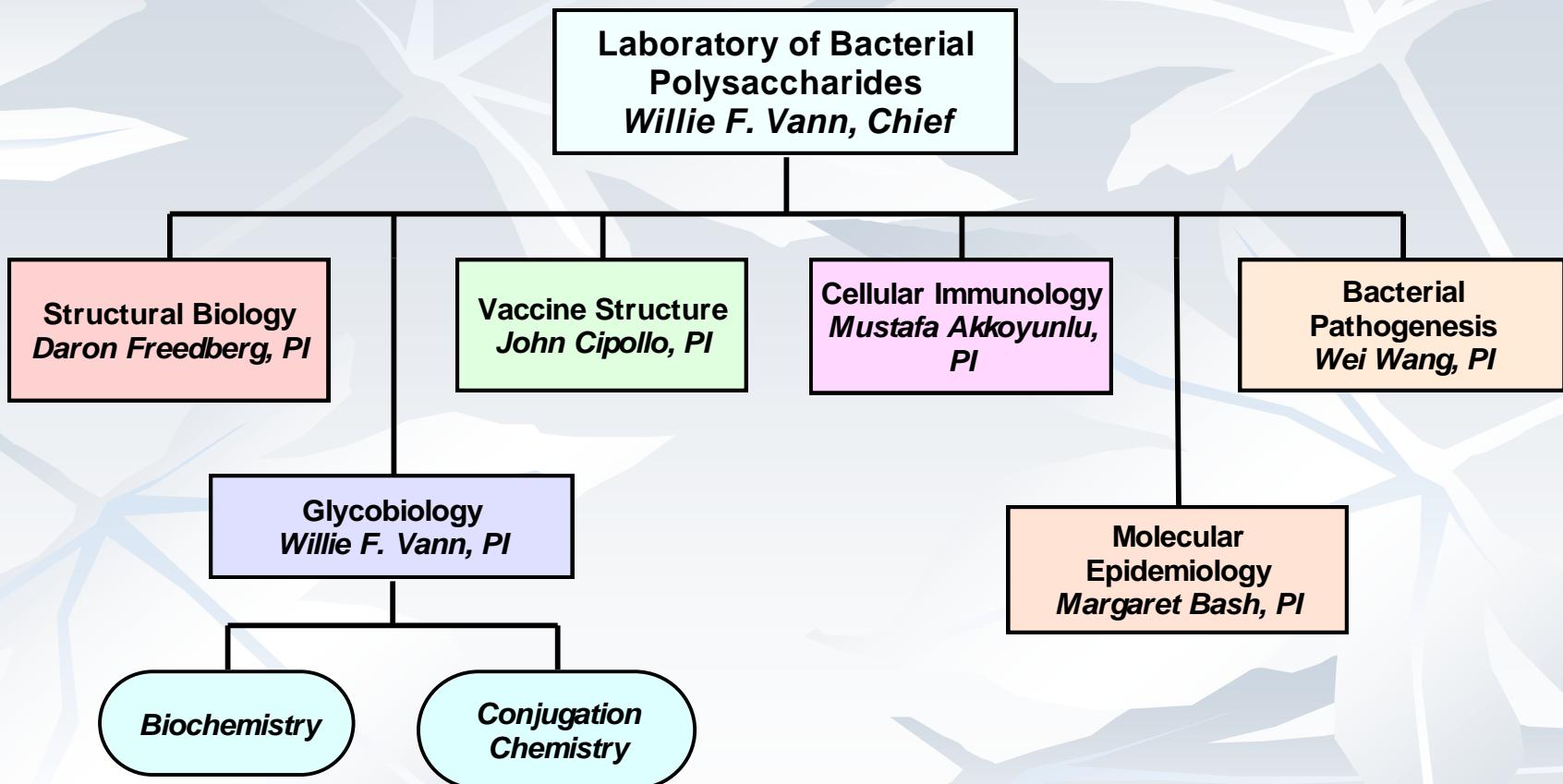
- Licensed Polysaccharide Vaccine
  - 23 Valent pneumococcal polysaccharide
  - Quadrivalent meningococcal polysaccharide
  - Vi polysaccharide
- Licensed Glycoconjugate Vaccines
  - Quadrivalent meningococal-diphtheria toxoid
  - Quadrivalent meningococcal- CRM197
  - 13 valent pneumococcal-CRM197
  - Haemophilus type b –tetanus toxoid (2)
  - Haemophilus type b – outer membrane protein

(BLA supplements, Inspections, Lot release)

# Major Regulatory Accomplishments

Vaccine	Date Submitted	Date Licensed	Manufacturer
<i>Meningococcal tetraivalent ACYW-135 CRM<sub>197</sub> Conjugate</i>	8/28/2008	2/19/2010	Novartis
<i>H. influenzae b Tetanus Toxoid Conjugate</i>	3/17/2009	8/19/2009	GSK
<i>Pneumococcal 13- valent CRM<sub>197</sub> Conjugate</i>	3/6/2009	2/24/2010	Wyeth

# Current Organization of Laboratory of Bacterial Polysaccharides



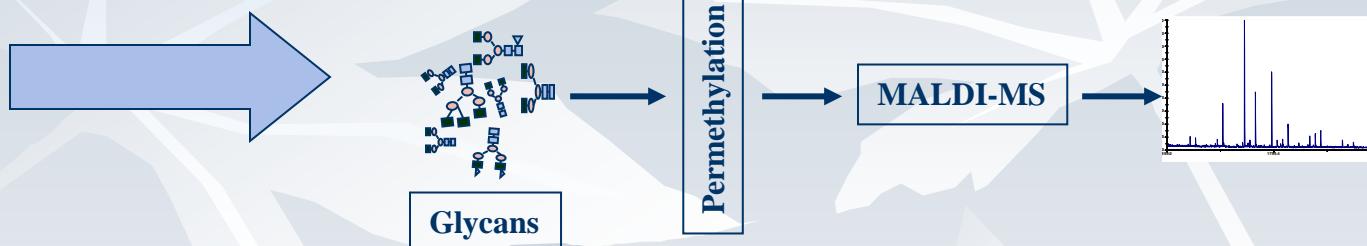
# Major Areas of Research

- **Mustafa Akkoyunlu, PI - Cellular Immunology Group**
  - Immunobiology of the host response to capsular polysaccharides of encapsulated bacteria
- **John Cipollo, PI - Vaccine Structure Group**
  - Mass spectrometry (MS) based strategies to investigate the role and significance of glycoconjugates in infective processes
- **Daron Freedberg, PI - Structural Biology Group**
  - Conformational structure of polysaccharide antigens
- **Margaret Bash, PI - Molecular Epidemiology Group**
  - Outer membrane protein diversification as it relates to vaccine safety and efficacy

- **Wei Wang, PI - Bacterial Pathogenesis Group**
  - Dr. Wang brings a new expertise to the laboratory that is especially relevant to evaluation of vaccines based on genomics.
  - Genetics of *M. catarrhalis* pathogenesis.
- **Willie F. Vann, PI - Glycobiology Group**
  - Biochemistry – Capsular polysaccharide biosynthesis; Targeted design of conjugate vaccines.
  - Conjugation Chemistry – Methodology for preparation of conjugate vaccines.

# **Some Highlights of Research Effort in the Laboratory of Bacterial Polysaccharides**

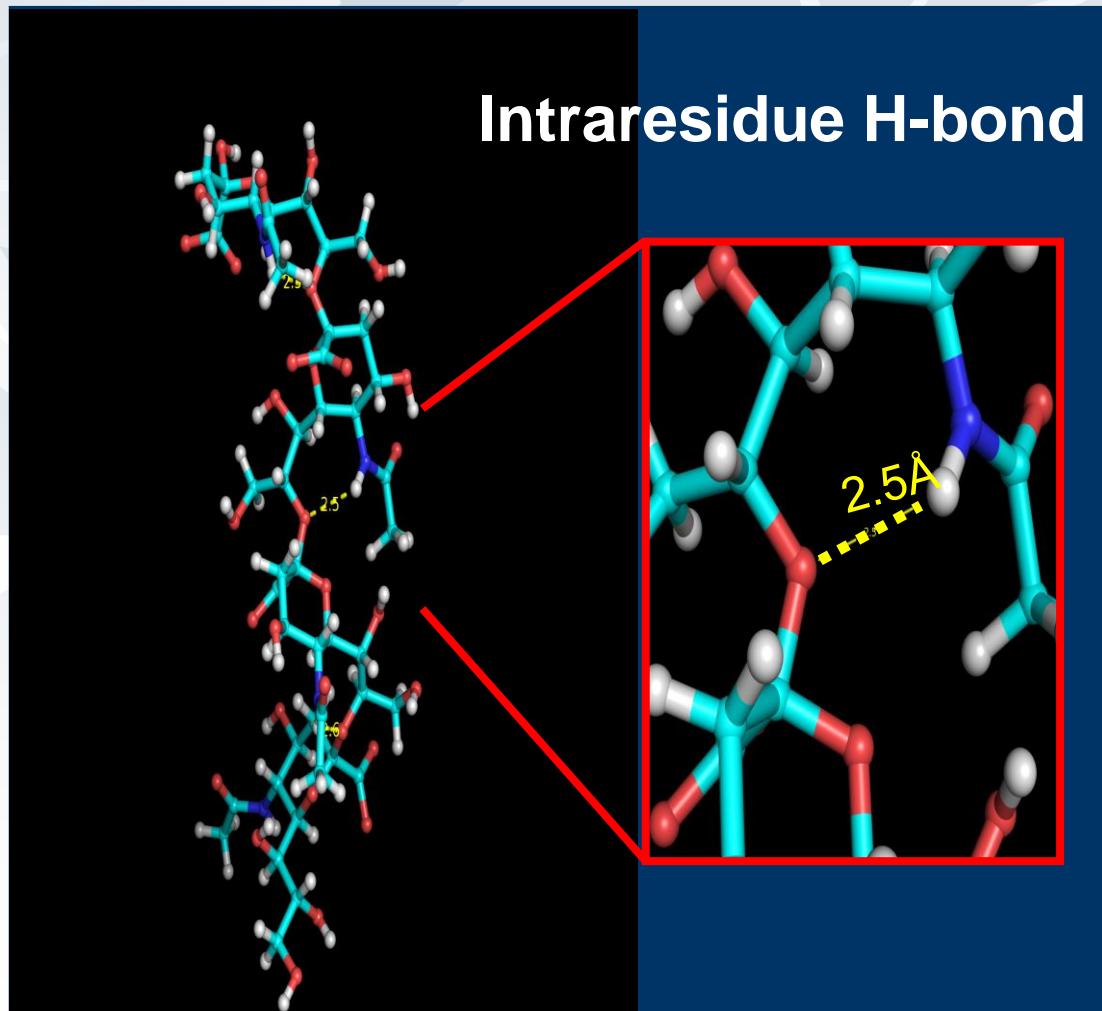
# CIPOLLO: *Caenorhabditis elegans* as a Surrogate Model for Glycan Dependent Host Infection



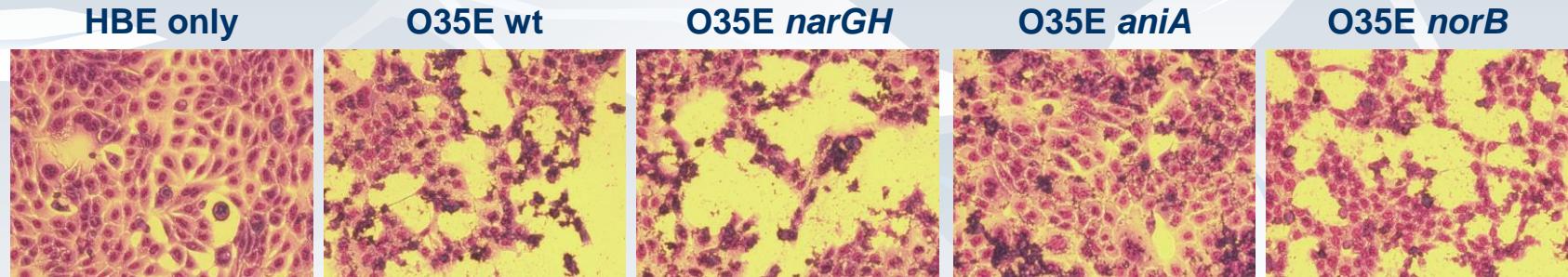
Over 40 microbes infect *C. elegans*: most of which are human pathogens or their close relatives.

- Infectious agents requiring host glycoconjugates to infect *C. elegans* :
  - *Yersinia pestis* and *Y. pseudotuberculosis*
  - *Bacillus thuringiensis*: crystal toxin (Cry5B) binds to glycolipid leading to lethal infection. 'bre' gene family
  - *Coprinopsis cinerea*: fungal pathogen galectin CGL2 binds to the N-glycan core
  - *Staphylococcus aureus*
  - *Microbacterium nematophilum*

# FREEDBERG: Determination of Structural Epitopes in Polysaccharides using High Field NMR Techniques



# WANG: Pathogenic Role of a *Moraxella catarrhalis* Denitrification Pathway



# Relevance of Research Program to CBER Mission

- The Laboratory of Bacterial Polysaccharides has regulatory responsibility for vaccines against encapsulated bacteria and products containing bacterial polysaccharides.
- The overall goal of the research program of the Laboratory of Bacterial Polysaccharides is to understand the virulence factors that are components of vaccines against bacterial pathogens.
- The research program of the Laboratory of Bacterial Polysaccharides is directed toward understanding the physical, chemical, and immunological properties of bacterial polysaccharides, and vaccines against encapsulated bacteria.

**The knowledge and expertise gained  
in this research endeavor provide a  
scientific basis for our decisions  
related to the review of  
manufacturing, purity, potency, and  
safety of carbohydrate containing  
vaccines.**