## Available Infectious Disease Technologies

### Subunit and Live Vaccines

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Subunit and Live Vaccines

**Schneewind UCHI 2137**
Staphylococcus aureus Live-Attenuated Vaccine Prevents Infection

- *Staphylococcus aureus* infections recur without eliciting protective immunity due to Protein A (SpA), which contributes to the bacteria's immune evasion tactics.
- Dr. Olaf Schneewind's group has engineered a strain of *S. aureus* expressing mutant Protein A (SpA) that protects against lethal challenges of virulent *S. aureus* strains.
- The live-attenuated vaccine strain dampens the bacteria's immune evasion capabilities, enabling the host immune system to generate protective antibodies against virulence factors, such as alpha-toxin, coagulase, and iron-binding proteins.
- In a mouse model of infection, the vaccine protected against a lethal challenge with USA300 (a community-acquired, multi-drug resistant strain of *S. aureus*).
- A US application is pending on Staphylococcus live cell vaccines.
- The investigators are currently developing attenuated bovine-relevant strains with applications for bovine mastitis and animal health.

**Schneewind UCHI 1239**
Clinical-Grade Non-Immunosuppressive Vaccine for Plague

- LcrV-based *Yersinia pestis* vaccines have hindered its use in humans due to the antigen's dual immune stimulatory and suppressive activities.
- Dr. Olaf Schneewind's lab has engineered the LcrV protein, V10, that lack the immunosuppressive properties of wild-type LcrV but retains its antigenicity to protect against multiple plague strains.
- The broad-spectrum single subunit vaccine can provide protection against both bubonic and pneumonic plague.
- In mice and guinea pigs models of infection, vaccination with V10 demonstrated protection against lethal doses of *Y. pestis*.
- A US patent application has been issued for methods and compositions involving LcrV proteins.
- The vaccine has been GMP-optimized and will next be validated in preclinical settings.

BACK
Subunit and Live Vaccines

**Schneewind UCHI 2055**
Capsule-Based Vaccine (PDGA-D4) Protects Against Toxigenic and Non-Toxigenic Forms of Anthrax

- Bacterial surface structures, such as capsules, are attractive vaccine antigens, but often stimulate weak or no immune response.
- Dr. Olaf Schneewind's group has designed a new antigen conjugation method to boost immune responses to low immunogenic antigens.
- The group has engineered a homogeneous anthrax capsule-toxin conjugate vaccine that induces robust antibody response against both toxin and capsule, providing immunity against multiple anthrax strains.
- In mice and guinea pig models of infection, vaccination with the capsule-conjugate showed protection against virulent B. anthracis Ames spores.
- A US application is pending for immunogenic protein conjugates and method for making and using the same.
- The investigator is interested in commercializing the vaccine in the biodefense space.

**Collier UCHI 1877**
Synthetic Peptide Adjuvant Produces Robust Immune Response without Provoking Excess Inflammation

- There is a need for an effective adjuvant system capable of eliciting a robust and specific immune response to the target antigen.
- Dr. Joel Collier has developed a heat-resistant, fibrillizing peptide (Q11), which can be fused to any antigen to enhance its immunogenicity.
- Assembled Q11-based vaccine can display single or multiple antigens on the surface of the fibril and prepared immediately prior to administration.
- Mice administered Q11-S. aureus antigen or Q11-ovalbumin antigen showed enhanced antibody generation without inflammation at the site of injection.
- There are two issued patents, as well as pending continuations, for compositions and methods involving fibrillizing polypeptides.
- The investigators are currently seeking partners for adjuvant and vaccine development.
Antibody-Based Therapeutics and Vaccines

Schneewind UCHI 2056
MRSA Antibody Therapeutic Simultaneously Treats and Vaccinates against Reinfection

- Staphylococcus aureus infections recur without eliciting protective immunity due to Protein A (SpA), which contributes to the bacteria’s immune evasion tactics.
- Dr. Olaf Schneewind’s lab has developed a monoclonal antibody (mAb) against S. aureus the highly-conserved envelope protein, SpA.
- The mAb neutralizes SpA activity to treat and protect against S. aureus infections.
- In a neonatal mouse model of infection, passive immunization with SpA mAb demonstrated protection against several S. aureus strains.
- Nationalized applications are pending in multiple territories for compositions and methods related to antibodies against SpA.
- The mAb is currently being validated in other immunocompromised models, and pre-clinical studies are underway.

Wilson UCHI 1835
Cross-Reactive Antibodies Neutralize H1N1 Influenza Virus

- There is a need to develop therapeutic approaches that are broadly effective against H1N1 influenza strains in order to decrease the development of viral resistance against current therapies.
- Dr. Patrick Wilson and colleagues have generated human monoclonal antibodies which recognize conserved epitopes across several H1N1 influenza strains, thereby providing broad protection against the disease.
- The H1N1 monoclonal antibodies provide prophylactic protection against several antigenically distinct H1N1 strains, as well as serve as a therapeutic.
- In a mouse model of influenza, pre-treatment (prophylactic) or treatment (therapeutic) with the antibodies improved survival when challenged with highly pathogenic H1N1 influenza.
- Nationalized applications are pending in multiple territories for antibodies directed against influenza.
- The antibodies are available as research reagents, and researchers are seeking commercial partner for diagnostic/therapeutic applications.
Pneumonia is among the most prominent S. aureus-mediated diseases, accounting for approximately 15% of documented invasive staphylococcal infections. Staphylococcal pneumonia concomitant with influenza infection is often a lethal complication. Up to one-half of staphylococcal pneumonia isolates are classified as methicillin-resistant S. aureus (MRSA), confounding the delivery of appropriate treatment and resulting in reported mortality as high as 56%.

Dr. Julie Bubeck Wardenburg has developed monoclonal antibodies (mAb) against Alpha-hemolysin (Hla), a secreted pore-forming toxin, an essential virulence factor of MRSA in a mouse model of S. aureus pneumonia.

The mAbs antagonize toxin activity, preventing human lung cell injury in vitro and protecting against lethal S. aureus pneumonia in animal models.

In addition, active immunization with the first 50 amino acids of the toxin also conferred protection against S. aureus pneumonia.

Nationalized applications are pending in multiple territories for compositions and methods related to active and passive immunization against Hla.

The researchers are seeking a commercial partner for therapeutic applications.

Staphylococcus aureus is the most common cause of nosocomial infections with significant morbidity and mortality.

Dr. Schneewind’s group has developed a large number of protein antigens that display protective immunity in animal models.

These antigens include:

- **Emp** - an envelope-associated protein associated with abscess formation.
- **EsxA and EsxB** – small, secreted proteins
- **EsaC** - an effector molecule important for host pathogen interaction

All antigens are effective in active immunization animal models, singly or in combination.

Nationalized applications are pending and issued in multiple territories for compositions and methods related to active immunization against the antigens.

The researchers are seeking a commercial partner for therapeutic applications.
Current antibodies are ineffective in recognizing strain variants of influenza, thereby increasing the probability of developing influenza escape variants.

Dr. Patrick Wilson and his team have generated broadly neutralizing antibodies that recognize the conserved hemagglutinin (HA) protein across several H7 (avian) and Group 1 influenza strains.

The H7N9 monoclonal antibodies provide prophylactic protection against several antigenically distinct H7N9 strains, and are effective across a broad therapeutic window.

In a mouse model of influenza, pre-treatment or treatment with the antibodies showed marked protection when challenged with H7N9, and neutralized multiple Group 1 influenza strains in in vitro neutralization studies.

Nationalization is pending for compositions and methods for neutralization of influenza.

The investigators are testing antibody efficacy in combination with other influenza therapies.
 Resistance-Evading Small Molecule Anti-Infectives

**Daum UCHI 2145**
Small Molecule Potentiators of Antibiotics for Treatment of Methicillin-resistant Staphylococcus aureus (MRSA)

- Methicillin-Resistant Staphylococcus aureus (MRSA) are becoming more resistant towards beta-lactam antibiotics due to bacterial adaptation of cell wall stress.
- Dr. Robert Daum and colleagues have identified compounds which inhibit the vraSR operon, which is responsible for sensing cell wall stress and modulating antibiotic resistance.
- Dr. Daum has designed a small-molecule approach to inhibit the operon, potentiating the efficacy of currently available antibiotics and reducing the likelihood of resistance to beta-lactam antibiotics.
- In an in vitro assay, lead anti-MRSA compounds enhanced oxacillin- and vancomycin-mediated inhibition of bacterial growth and inhibition of gene expression of the vraSR operon while decreasing antibiotic dosage by about ~30 times or more.
- Nationalized applications are pending in multiple territories for methods of treating bacterial infections.
- The compounds will be tested for effectiveness in soft-tissue models of MRSA and for inhibition of resistance development through serial passage studies.

**Missiakas UCHI 2102**
Small molecule Inhibitor of Lipoteichoic Acid Synthesis as a Narrow-Spectrum Gram-Positive Antibiotic

- There is a need for identifying new targets against Gram-positive bacterial infections, which can decrease the development of bacterial resistance.
- Dr. Dominique Missiakas’ group has identified a small-molecule inhibitor against lipoteichoic acid synthase (LtaS), an essential component of Gram-positive bacterial cell walls.
- The LtaS inhibitor has narrow-spectrum activity against intractable resistant Gram-positive bacteria, and inhibits their growth by preventing the synthesis of lipoteichoic acid.
- In a mouse model of S. aureus sepsis, treatment with the LtaS inhibitor was shown to prolong mice survival when compared to the untreated group.
- A US patent application is pending on methods and compositions for inhibiting Gram-positive bacteria.
- The antibiotic will next be lead-optimized using iterative medicinal chemistry efforts.
Resistance-Evading Small Molecule Anti-Infectives

**Bubeck Wardenburg UCHI 1971**
Small Molecule Treatment for Staphylococcus aureus Lung or Skin and Soft Tissue Infections

- Staphylococcus aureus secretes a pore-forming toxin, alpha-Hemolysin (Hla), which is responsible for causing injury to epithelial cells and leads to lung or skin and soft tissue infections (SSTIs).
- Dr. Julie Bubeck Wardenburg has developed a novel strategy for the treatment of SSTIs caused by S. aureus, which utilizes inhibitors of the host metalloprotease, ADAM10, which is the Hla receptor involved in establishing infection.
- ADAM10 inhibitors reduce S. aureus infection severity and recurrence, and promote tissue healing.
- In mouse models of pneumonia and dermonecrosis, intranasal or topical administration of an ADMA10 inhibitor showed protection against Hla-induced SSTIs.
- A US patent has been issued, and additional applications are pending in the US and Europe for methods of using ADAM10 inhibitors to treat bacterial infections.
- Dr. Bubeck-Wardenburg is interested in collaborating with commercial partners to identify, test, and optimize ADAM10 inhibitors suitable for use against S. aureus infection.

**Alverdy UCHI 2152**
High Molecular Weight PEG Derivatives for the Treatment of Anastomotic Leak

- Anastomotic leakage is the most significant complication that develops after a patient has undergone intestinal resection.
- Dr. John Alverdy has demonstrated that anastomotic leaks are caused by the in vivo transformation of non-pathogenic bacteria to a pathogenic form, and application of a polyethylene glycol and phosphate (PEG/Pi) solution can prevent this transformation to reduce anastomotic leaks.
- Application of high molecular weight (HMW) PEG/Pi solution suppresses Pseudomonas aeruginosa pathogenicity and prevents accumulation at anastomotic sites.
- In a rat anastomotic leak model, administration of HMW PEG/Pi significantly diminished the rate of anastomotic leakage incidence and severity.
- A US patent application is pending for methods of preventing and treating anastomotic leaks.
- Dr. Alverdy is interested in finding partners to help move this treatment to the clinic.
• Current HSV antiviral therapies lessen the extent of the viral infection, but do not protect against reactivation of dormant HSVs.

• Dr. Bernard Roizman’s group has discovered that histone acetyltransferase (HAT) inhibitors can suppress the reactivation of HSV and help prevent recurring infections.

• HAT inhibitors suppress the reactivation of latent HSV by decreasing the levels of LAT (latency-associated transcript) in a dose-dependent manner, thereby providing a therapeutic target against which HAT inhibitors can be screened.

• In an *in vitro* model of latency using infected ganglia, treatment with the p300/CBP inhibitor, curcumin, effectively blocked reactivation of viral LAT and viral activation genes.

• A US patent application is pending for methods of modulating latent virus reactivation using HAT inhibitors

• The investigators are interested in identifying and testing novel compounds that can inhibit HATs associated with HSV reactivation.
UChicago’s unique access to infectious disease facilities, clinical research centers, and world-renowned leaders in the fight against pathogens ensures maximum investment return for industry collaborators.

**Howard T. Ricketts Laboratory (HTRL)**
- UChicago’s HTRL located at Argonne National Laboratory is one of 13 regional biocontainment facilities in the US
  - Provides state of the art Level 3 biocontainment facilities for laboratory and animal research
  - HTRL mission is the creation of novel therapeutics for biodefense and emerging infectious diseases.

**Great Lakes Regional Center of Excellence (GLRCE)**
- NIAID named the University of Chicago as the lead institution for the GLRCE and awarded the center more than $35 million in research funding
- GLRCE combines the research excellence of inter-disciplinary scientists at 27 member institutions in the Great Lakes region
- Research focus on biodefense & emerging disease vaccines/therapeutics
- Regional resource for providing expertise, rapid diagnosis, support and advice about containment and treatment in the event of a bioterror event or the emergence of new disease-causing agents.

**MRSA Research Center**
- MRSA Research Center is a consortium of 20 members at UChicago who collaborate on studying the spread and progression of MRSA disease
  - Center’s MRSA strain bank receives patient-derived MRSA strains daily from the UChicago Medical Center, stores them and warehouses molecular/clinical info from these isolates
  - Collaborative research to further the understanding of resistant strains for the development of novel antibiotics
  - Engaging worldwide to delineate the changing epidemiology of community-associated MRSA
  - A Nature news feature “Man vs. MRSA” highlights Dr. Robert Daum’s efforts and the groundbreaking work being done at UChicago on attacking resistance mechanisms
Contact UChicagoTech, the Center for Technology Development & Ventures, to learn more.

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