Infectious Disease Technologies at the University of Chicago

April 2017

POLSKY Center for Entrepreneurship and Innovation
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Subunit and Live Vaccines

Subunit and Live Vaccines

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.

Schneewind UCHI 1239

Clinical-Grade Non-Immunosuppressive Vaccine for Plague

- The use of wild-type LcrV-based *Yersinia pestis v*accines has been hindered due to the antigen's dual immune stimulatory and suppressive activities.
- Dr. Olaf Schneewind's lab has engineered the LcrV protein, V10, which lacks the immunosuppressive properties of wild-type LcrV but retains its antigenicity to protect against multiple plague strains.
- The broad-spectrum single subunit vaccine provides 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 optimized for GMP manufacture and will next be validated in preclinical settings

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Antibody-Based Therapeutics and Vaccines

Antibody-Based Therapeutics and Vaccines

Schneewind and Missiakas UCHI 1306, 1727, 1734
Protective Staphylococcus aureus Protein Antigens

- 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 formatin.
  - 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.

Wilson UCHI 1835
Cross-Reactive Antibodies Neutralize H1N1 Influenza Virus

- Hemagglutinin (HA), is an attractive target for treating influenza, but the variability of HA among influenza strains presents a challenge for designing effective antibody therapies.
- Dr. Patrick Wilson has generated humanized monoclonal antibodies that recognize conserved stalk epitopes of HA on H1N1 strains of influenza.
- The therapeutic antibodies provide a treatment for patients suffering from severe H1N1 influenza infections, such as the highly pathogenic 1918 and avian flu strains.
- The broad-neutralizing capacity against antigenically distinct H1N1 strains has been validated against 4 distinct H1N1 strains in mouse models of influenza infection.
- Issued patents and pending applications have been filed broadly on H1N1 neutralizing antibodies.
- Researchers are seeking commercial partners for therapeutic development.

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Antibody-Based Therapeutics and Vaccines

Wilson UCHI 2365
Broad-Spectrum, Neutralizing Influenza Antibodies

- 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.
- Researchers are seeking commercial partners for therapeutic development.

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Resistance-Evading Small Molecule Anti-Infectives

Resistance-Evading Small Molecule Anti-Infectives

Alverdy UCHI 2152
PEG-phosphate Compound for the Prevention of Anastomotic Leaks after Gastro-Intestinal Surgery

- 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.
- A PEG-Pi pre-surgery solution would be administered to a patient prior to gastrointestinal or esophageal surgery.
- In a rat anastomotic leak model, administration of PEG-Pi significantly diminished the rate of anastomotic leakage incidence and severity by suppressing Pseudomonas aeruginosa and Serratia marcescens pathogenicity.
- A US patent application is pending for methods of preventing and treating anastomotic leaks. A provisional has been filed on new compositions of PEG-Pi.
- Dr. Alverdy is interested in seeking commercial partners to help move this technology to the clinic.

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.

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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 to 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 the required antibiotic dosage by about ~30 times or more.
- Nationalized applications are pending in multiple territories for methods of treating bacterial infections, with claims allowed in the US.
- The compounds will be tested for effectiveness in soft-tissue models of MRSA and for inhibition of resistance development through serial passage studies.

Roizman UCHI 2161

Inhibition of Herpes Simplex Virus Recurrences

- 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 *ex-vivo* model of latency using infected ganglia, treatment with the p300/CBP inhibitor, curcumin, effectively blocked reactivation of viral LAT and viral activation genes.
- An issued US patent on methods of modulating latent virus reactivation using HAT inhibitors
- The investigators are interested in identifying and testing additional novel compounds that can inhibit HATs associated with HSV reactivation.

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UChicago's Unique Infectious Disease Capabilities

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.

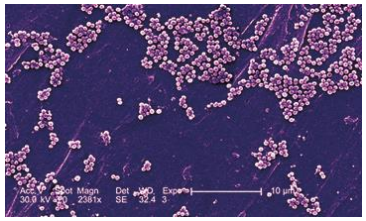
- Provides state of the art Level 3 biocontainment facilities for laboratory and animal research
- HTRL mission is the creation of novel therapeutics for biodefense and emerging infectious diseases.

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.

How to Partner with the University of Chicago

Contact the Polsky Center for Entrepreneurship and Innovation Technology Commercialization and Licensing team and speak to anyone on the project management team.

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