Critical Care Grand Challenge: Sepsis Innovation Portfolio

A comprehensive innovation portfolio comprised of therapeutics, diagnostics, devices and digital health solutions to transform the way we diagnose, treat and monitor SEPSIS to improve patient care and outcomes, enhance the clinician experience, and reduce healthcare costs.

Sepsis is a body-wide response to infection that can cause organ failure and death.
What is Sepsis?

Sepsis is a life-threatening medical condition caused by an extreme immune response to an infection. Chemicals released into the blood to fight the infection trigger widespread inflammation that becomes uncontrolled and leads to multiple organ damage. Think of it as “friendly fire” within the body caused by an infection or other insult. Sepsis has devastating consequences, including long hospital stays, recurring complications, and a high death rate.

ANNUAL STATISTICS: A DEADLY TOLL
- 19 million cases worldwide
- 1 million cases in the U.S.
- #1 global killer, especially children
- 250,000 deaths in the U.S.
- #1 U.S. hospital cost at $20.3 billion

SURVIVING SEPSIS
- 75% of survivors may have long-term problems
- Higher risk of sepsis reoccurrence
- Increased risk of ICU-derived post-traumatic stress syndrome
- Little support available for the vast number of survivors that struggle with substantial post-recovery challenges

“New” Sepsis Survivors by Year

Total Number of Sepsis Survivors

≥ 3 Year Sepsis Survivors  637,867

With Cognitive Impairment  106,311
(95% CI: 79,692, 133,930)

With Functional Disability  476,862
(95% CI: 455,026, 498,698)

Symptoms & the “Art” of Diagnosis

- High fever
- Low body temperature
- Chills with body shaking
- Confusion or changes in mental status
- Rapid breathing (hyperventilation)
- Rapid heartbeat (tachycardia)
- Low urine production

Current Treatment

- Hospitalization is necessary to treat sepsis successfully.
- Blood culture tests are performed to identify the causative pathogenic bacteria.
- While the test results are pending, intravenous antibiotic therapy is administered to the patient consisting of a broad-spectrum (kills a variety of bacteria) antibiotic or multiple antibiotics.
- When the test results become available, the treatment can then be tailored to combat the causative pathogenic bacteria.
- Further testing may be done to identify the source or originating site of the infection.
- Supportive therapy with oxygen, intravenous fluids, and medications to restore normal blood pressure, is also important for recovery.

Treatment Gaps

NO HOSPITAL “LAB TEST” EXISTS TO DIAGNOSE SEPSIS

- Initial diagnosis relies on clinical suspicion, physical exam, and vital signs
- Diagnosis confirmation depends on blood cultures that may take up to 48 hours or more
- Test results/cultures may be inconclusive
- Improved outcomes if therapy starts within first 30-90 minutes of sepsis recognition

= Need for rapid, bedside diagnostics

LACK OF RAPID DIAGNOSTICS LEADS TO USE OF BROAD-SPECTRUM ANTIBIOTIC OR MULTIPLE ANTIBIOTICS

- Contributes to antibiotic resistance
- Opportunistic infection resulting from compromised immune system
- Life-threatening side effects like kidney and liver failure
- Under-treatment of critically ill patients

= Need for personalized management of immune system

NO GOOD MECHANISM TO MONITOR PATIENT IMMUNE STATUS AND THERAPEUTIC INTERVENTIONS

- Poor, slow, unreliable and invasive measures of fluid responsiveness from rigorous hydration
- Unable to measure inflammatory cascade
- Uncertain when to start, add or stop prescribed therapies
- Poor markers of liver and brain organ dysfunction

= Need better solutions for “front-line” patient management

MCIRCC Sepsis Innovation Portfolio:

SOLUTIONS FOR IMPROVED PATIENT OUTCOMES AT REDUCED HEALTHCARE COSTS

POTENTIAL CLINICIAN BENEFITS:

- Identify and respond to sepsis conditions earlier
- Deliver targeted, evidence-based and personalized treatment
- Monitor and gauge effectiveness of therapeutic interventions

POTENTIAL PATIENT BENEFITS:

- Accelerate recovery
- Reduce duration in ICU
- Improve survival
- Lessen risk of sepsis reoccurrence
- Decrease chronic complications

Ebola leads to death from sepsis with multi-organ failure
Portable Monitoring System for Early Detection of Sepsis

A continuous, low-power, non-invasive monitoring system for early detection of sepsis both inside and outside the hospital

- Produces results faster than current lab tests which can take up to 24 hours
- Untethered monitoring sensor with wireless communication
- Captures high resolution, real-time vascular dynamics information >> early indicators of septic shock
- Technology uses a “sensing ring” worn on the finger
- Sensor is small, simple, inexpensive + physically robust

Collaborators
- Rodney Daniels, MD
  Pediatric Critical Care Medicine
- Kyle Gunnerson, MD
  Emergency Medicine
- Ashwin Belle, PhD
  Biomedical Image & Signal Processing
- Sardar Ansari, PhD
  Biomedical Image & Signal Processing
- Kayvan Najarian, PhD
  Computational Medicine & Bioinformatics

Potential Partners
- Apple
- IBM
- AirStrip
- Phillips
- GE Healthcare
- Siemens Healthcare

SPEED
PORTABLE
SPECIFICITY
NON-INVASIVE
SIZE

Optimize mechanical structure of sensor ring
Finalize portable data collection unit
Conduct in-lab tests with predefined experiments
Initiate data collection in ICU
Optimize computational methodology using in-lab test data
Start analysis of data collected in ICU

Month 1
Month 2
Month 3
Month 4
Month 5
Month 6

Technology
Competitive Advantage
Commercialization Roadmap

Sensor
Signal Processing
Algorithms extract biomarkers indicative of sepsis

Heart rate + variability
Peripheral vascular resistance
Pulse pressure variation

Principal Investigators
Kenn Oldham, PhD
Mechanical Engineering

License Technology
Class II Device
501(k) regulatory pathway

Government

PROJECT MILESTONES
**Sepsis Endotheliopathy Assessment Panel**

Rapid detection and analysis of endothelial cells and coagulation/inflammation biomarkers in blood to diagnose and monitor sepsis

**Team**

- **Principal Investigators**
  - Xudong Fan, PhD, Biomedical Engineering
- **Collaborators**
  - Maung Khaing Oo, PhD, Biomedical Engineering
  - Daniel Myers, DVM, MPH, Vascular Surgery
  - Kevin Ward, MD, Emergency Medicine
  - Rodney Daniels, MD, Pediatrics-Intensive Care

**Competitive Advantage**

- **SPEED**
  - 15-minute rapid, bedside diagnostic
- **MULTI-USE**
  - Diagnose sepsis and severity + monitor therapeutic intervention
- **PORTABLE**
  - Laptop-size for use in hospital, ambulatory and long-term care facilities
- **COMPATIBLE**
  - Utilizes standard syringe and tubing equipment
- **COST**
  - Lower equipment and operational cost compared to competition

**Technology**

- Detects endothelial cell damage >> Linked to sepsis + sepsis severity
- Tests for blood biomarkers
- Detects inflammation/coagulation biomarkers >> Linked to sepsis
- Replaces traditional ELISA reader

**Commercialization Roadmap**

- **Potential Partners**
  - Enzo Lifesciences
  - Abbot
  - Optofluidic Bioassay
- **Class II Device**
  - 501(k) regulatory pathway
- **License Technology or New Startup Company**

**PROJECT MILESTONES**

- **MONTH 1**
  - Fabricate multi-hole capillaries
- **MONTH 2**
  - Assemble entire optical detection and microfluidic systems
- **MONTH 3**
  - Benchmark against current standard test (ELISA)
- **MONTH 4**
  - Evaluate accuracy of endothelial cell detection in standard solution of cells
  - Complete detection of 6 biomarkers using blood
- **MONTH 5**
  - Complete detection of 6 biomarkers in buffering agent
  - Begin endothelial cell detection
- **MONTH 6**
  - Test endothelial cell detection & benchmark against current standard (FACS)
**Real-Time Ultrasound Lung Strain Measurement Device**

Device to monitor fluid volume status and manage mechanical ventilation with sepsis patients.

**PROJECT MILESTONES**

- **MONTH 1 - In-Vitro**
  - Test tidal volume & FRC estimates of ventilated lung phantoms

- **MONTH 2 - In-Vitro**
  - Test ultrasound scanner with ventilated phantoms

- **MONTH 3 - In-Vitro & In-Vivo**
  - Perform matched ultrasound/CT scans with ventilated phantoms
  - Perform lung ultrasound scans on ventilated patients: 1 normal + 1 abnormal

- **MONTH 4 - In-Vitro & In-Vivo**
  - Repeat Month 4 to demonstrate reproducibility and refine methodology

- **MONTH 5 - In-Vitro & In-Vivo**
  - Repeat Month 3 & 4 with ventilated phantoms, doubling experiments
  - Repeat Month 5 with ventilated patients

**Collaborators**

- Kyle Gunnerson, MD
  - Emergency Medicine

- Jamie Hamilton, PhD
  - CTO, Epsilon Imaging

- Jonathan Rubin, MD, PhD
  - Radiology

- Cheri Deng, PhD
  - Biomedical Engineering

**Technology**

- “Speckle track” lung’s surface using 2D ultrasound transducers
- Calculate local lung strain/stiffness
- >> Indicates hydration status
- >> Determines point of optimal ventilation

**Team**

- **SPEEED**
  - Real-time, minute-to-minute updates

- **NON-INVASIVE**
  - Safe, bedside application using ultrasound technology

- **MULTI-USE**
  - Monitor hydration + manage ventilation

- **SPECIFICITY**
  - Quantitative evaluation of lung function

- **EASY**
  - Requires little expertise to operate
Point-of-Care Platform Using Redox as a Sepsis Biomarker

Redox microfluidic diagnostic device that detects sepsis severity and gauges response to therapy

5-minute bedside diagnostic using redox as a biomarker

Detect sepsis severity + monitor therapy + prognostic measure

Hand-held device for use at hospital, ambulatory and long-term care facilities

Technology maintains sensitivity for accurate & precise redox measurements in whole blood

Enables new therapies for sepsis treatment that target redox

MONTH 1
- Test platform via swine shock model
- Optimize electrode for microfluidic integration

MONTH 2
- Test platform via swine shock model
- Further optimize electrode for microfluidic integration

MONTH 3
- Test prototype in critical care setting
- Refine prototype design

MONTH 4
- Finalize prototype
- File patent disclosure

SPEED

MULTI-USE

PORTABLE

SENSIVITY

NEW BIOMARKER

Principal Investigators
Mark Meyerhoff, PhD
Chemistry

Principal Investigators
Mark Meyerhoff, PhD
Chemistry

Shuichi Takayama, PhD
Biomedical Engineering

Rodney Daniels, MD
Pediatrics-Intensive Care

Collaborators

COMPETITIVE ADVANTAGE

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Technology

Commercialization Roadmap

SPEеноd CARTRIDGE

MICROFLUIDIC DEVICE

NANOPOROUS GOLD ELECTRODE SENSOR

Non-permeable to oxygen/air

Measures whole blood redox
Resists biofouling
Maintains sensitivity

Potential Partners
Abbott
Werfen Group
Epocal

Class II Device
510(k) PMA regulatory pathway

License Technology or New Startup Company

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Immunotherapy & Immunophenotyping for Sepsis Treatment

Therapeutic to boost patients’ immune response using Interleukin-15 (IL-15) to stimulate T cell production to combat the underlying cause of sepsis.

- Prolonged treatment at reduced IL-15 quantities >> boosts immune response + reduces side effects and toxicities
- Therapeutic + diagnostic + prognostic system to treat and manage patients
- Real-time status updates to monitor therapeutic interventions
- Requires very small blood volumes for safe use with neonates and infants
- Single application, pharmaceutical-grade injectable delivered bedside

Potential Partners
- PerkinElmer
- Vedantra Pharmaceuticals

Investigational New Drug (IND) regulatory pathway

License Technology/Therapy

PROJECT MILESTONES

- **MONTH 1**: Produce nanoparticles and conduct dose response study
- **MONTH 2**: Conduct delayed treatment study and data analysis for biomarkers
- **MONTH 3**: 
- **MONTH 4**: 
- **MONTH 5**: 
- **MONTH 6**: 

Delivery + prolonged release of IL-15

Phenotypes T cells >> sepsis biomarker

Monitors efficacy of IL-15 therapy

TEAM

- **James Moon, PhD**, Pharmaceutical Sciences and Biomedical Engineering
- **Jean Nemzek, DVM, MS**, Laboratory Animal Medicine
- **Jianping Fu, PhD**, Biomedical Engineering

COMPETITIVE ADVANTAGE

- DELIVERY
- MULTI-USE
- SPEED
- BLOOD
- EASY

TECHNOLOGY

- MICROFLUIDIC PLATFORM
- IL-15 THERAPEUTIC
- ICMV NANOPARTICLE

COMMERCIALIZATION ROADMAP

- Principal Investigators
- Collaborators

LICENSE TECHNOLOGY

- Delivery + prolonged release of IL-15
- Phenotypes T cells >> sepsis biomarker
- Monitors efficacy of IL-15 therapy

POTENTIAL PARTNERS

- PerkinElmer
- Vedantra Pharmaceuticals

INVESTIGATIONAL NEW DRUG (IND) REGULATORY PATHWAY

- FDA
Rapid Determination of Bacteremia & Antibiotic Resistance in Sepsis

Direct detection of microbial DNA allows physicians to quickly identify the right drug for the right bug, to treat sepsis patients.

**Team**

- **Principal Investigators**
  - J. Scott VanEpps, MD, PhD
  - Nicholas Kotov, PhD
- **Institution**
  - University of Michigan Medical School

**Technology**

- **Competitive Advantage**
  - **SPEED**: Rapid 3-hour bedside diagnostic vs. 24-72 hour blood culture
  - **MULTI-USE**: Bacterium identification + antibiotic resistance profile
  - **SPECIFICITY**: Narrow antibiotic regimen for personalized treatment and improved care
  - **SENSITIVITY**: Identify bacteria at low concentrations and without prior culture growth
  - **EASY**: Reliable and easy to perform test

- **Potential Partners**
  - Airstrip
  - Nico Technologies
  - Genetech
  - Nanosphere

- **Class II Device**
  - PMA regulatory pathway

- **License Technology**

**Commercialization Roadmap**

**PROJECT MILESTONES**

- **MONTH 1**
  - Design & synthesize PCR primers for target bacteria
- **MONTH 2**
  - Confirm efficacy of PCR primers & synthesize gold nanorods
- **MONTH 3**
  - Modify & couple nanorods to PCR primers
- **MONTH 4**
  - Test nanorod-primer couples in whole human blood
- **MONTH 5**
  - Determine limits for bacteria detection & accuracy of test with whole human blood
About MCIRCC

The U-M Center for Integrative Research in Critical Care (MCIRCC) is one of the world’s first comprehensive research enterprises devoted to transforming critical care medicine by accelerating science and moving it from bench to bedside. To do this, MCIRCC brings together integrative teams comprised of world-class U-M scientists, clinicians, and engineers with industry partners and funding sources to develop and deploy cutting-edge solutions that elevate the care, outcomes, and quality of life of critically ill and injured patients and their families.

CRITICAL CARE GRAND CHALLENGE

MCIRCC is currently utilizing the Accelerant Cycle funding program outlined below with its inaugural Critical Care Grand Challenge targeting sepsis. Designed to support high-impact proposals for milestone driven research over a six-month timeframe, the Grand Challenge targets the most pressing problems in critical care and rewards bold solutions created by teams working together to move these solutions into the critical care ecosystem.

ACCELERANT FUND

A mechanism to accelerate science and move it from bench to bedside, the Accelerant Fund unites researchers, business experts, philanthropists, and disease foundations to develop critical care solutions and deploy them to market faster:

- A panel of experts from research and industry screen applications from MCIRCC teams and select projects with the greatest transformational promise.
- Mentors from the top ranks of business, venture capital, and the healthcare industry work with the scientists to translate their discoveries into marketable technologies.
  - Pioneering philanthropic partners—U-M alums, corporate and foundation partners, and individuals with a passion for great research—provide funding for proof-of-concept work, helping researchers to create spin-off companies and tap licensing opportunities.
- Once a technology successfully moves forward, MCIRCC reinvests its share of all royalties and license fees from the resulting intellectual property into the Accelerant Fund, increasing future support capabilities and continuing the cycle of innovation.

The goal is to find “game-changers” that demonstrate the greatest potential to transform critical care and elevate patient outcomes at reduced costs.
GOAL:
To accelerate disruptive science and move it from bench to bedside

Partners Defined
• Disease Foundations
• Key Opinion Leaders
• Industry

License Royalty
Minimally Viable Product Commercialization Plan
Ideation Plan
• MVP Plan
• Rapid Iterative Testing
• Prototype Build & Test

Evaluation Group Review
Projects Selected
• Novel/disruptive
• Clear path to commercialization

Accelerant Screen
Project Strengthening
• Workflow
• Business Model Canvas
• Value Proposition & Verification

Spin Out Company
Mentor Coaching
Funding Sources

Accelerant Fund
Funded by Donors

Proposal from MCIRCC Research Team

CATALYST TEAM
Accelerant Cycle
INFLUENCE SCIENCE AND DISCOVERY FOR HIGH-IMPACT, REAL WORLD SOLUTIONS
Sepsis is a complex public health problem that affects over one million Americans per year, results in 250,000 annual deaths, and represents the highest annual treatment cost in U.S. hospitals at $20.3 billion. Sepsis does not discriminate, but attacks the young and elderly, the sick and the healthy. Despite its debilitating effects and huge economic burden, only three out of 10 Americans know the word sepsis.

Recognizing the need to revolutionize sepsis care and treatment, the U-M Center for Integrative Research in Critical Care’s Grand Challenge program integrates medical and engineering experts to develop and deliver transformative solutions that elevate patient outcomes at reduced costs.

“If we can make something that works well for the septic patient given all its complexities, those technologies could easily translate to other settings such as trauma, cardiac arrest, and traumatic brain injury, to name a few. The Grand Challenge gives us the opportunity to build platform technologies and approaches.”

— KEVIN WARD, MCIRCC EXECUTIVE DIRECTOR