

MCIRCC

CENTER FOR INTEGRATIVE
RESEARCH IN CRITICAL CARE

PIECING TOGETHER TRAUMATIC BRAIN INJURY

A CRITICAL CARE GRAND CHALLENGE
INNOVATION PORTFOLIO

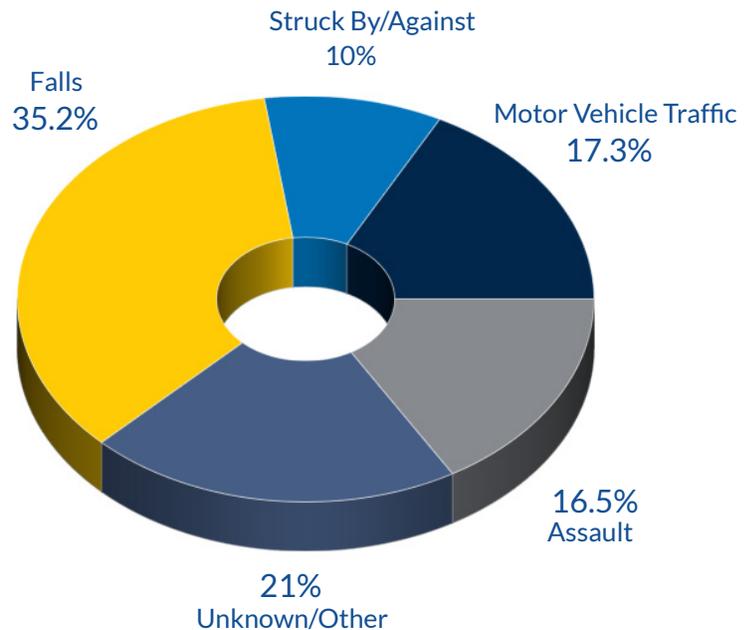


WHAT IS TRAUMATIC BRAIN INJURY (TBI)?



TBI is a disruption in the normal function of the brain that can be caused by a bump, blow, or jolt to the head, rotational force, sudden acceleration and deceleration, shock from an explosive blast, or a penetrating head injury. Acute neurologic injuries in the brain and spinal cord are amongst the hardest injuries to treat. Even when they aren't fatal, the ability to recover is limited.

COMMON TBI CAUSES*



TBI STATISTICS

1.7M

People sustain a traumatic brain injury in the U.S. each year

47%

of all TBI-related ED visits, hospitalizations, and deaths in the U.S. were due to falls

30%

of all injury deaths are due in part by TBIs

75+

Age of highest rated TBI-related deaths and hospitalizations

9

Number of years life expectancy decreases following a TBI

57%

of people who sustain a TBI are moderately or severely disabled five years later

Sources: Center for Disease Control and Prevention -
*<http://www.cdc.gov/traumaticbraininjury/>
https://www.cdc.gov/traumaticbraininjury/get_the_facts.html
https://www.cdc.gov/traumaticbraininjury/pdf/Moderate_to_Severe_TBI_Lifelong-a.pdf

THE MCIRCC SOLUTION

We have the recipe for success.

The Center for Integrative Research in Critical Care is the innovation hub for more than 170 critical care researchers across the University of Michigan. As one of the first comprehensive enterprises devoted to transforming critical care medicine, we foster multidisciplinary collaborations between our members – unifying scientists, clinicians, engineers and industry partners – to accelerate science and deploy cutting-edge solutions that elevate the care, outcomes, and quality of life of the critically ill and injured.

The Massey TBI Grand Challenge aims to support researchers to find these new solutions. Researchers are tasked with the goal of developing the most innovative diagnostic, device, therapeutic, and health information technology solutions that target the ‘golden hours’ of care after severe TBI. Treatment administered during this critical time frame can determine patient survival and have a significant effect on long-term function and disability

With MCIRCC at the helm, many promising research projects have been funded through the Grand Challenge. Since 2015, 24 teams have received funding, going on to publish their work in peer-reviewed journals, present at national conferences, or obtain follow-on funding through other sources. Some projects have made it all the way to commercialization, spinning off four new companies.

This program is made possible thanks to a generous donation from the Joyce and Don Massey Family Foundation.



A Partnership with the DEPARTMENT OF DEFENSE

Department of Defense (DoD) service members and families represent the largest U.S. population suffering from the impact of TBI. Through a collaborative partnership, the U.S. Army’s Combat Casualty Care Research Program brings expertise and resources to MCIRCC helping to accelerate the movement of translational research outputs into the field. DoD Neurotrauma leadership members form part of the Massey TBI Grand Challenge panel, assisting in reviewing proposals for funding, and providing mentoring to each of the funded teams. In addition, this partnership provides our TBI researcher community with invaluable resources and opportunities.

- Educational seminars
- Early notification of DOD funding opportunities
- Increased national awareness of U-M’s TBI research program
- User feedback to help fine-tune research
- Collaborations with leading TBI experts
- Access to DoD research database

Funded projects that drive toward proof of concept and human testing have the potential to receive follow-on funding from the DoD for solutions, therapies and products that can be used by DoD medics in the field.

The following are samples of a comprehensive portfolio comprised of therapeutics, diagnostics, devices, and digital health solutions to transform the way we diagnose, treat, and monitor traumatic brain injuries to improve patient care and outcomes and enhance the clinician experience.

Intracranial pressure monitor enhancement for cerebral hemodynamic monitoring

AWARD AMOUNT: \$104,433

THE TEAM

Hakam Tiba, MD, MS
Co-Investigator

Kevin Ward, MD
Co-Investigator



Craig Williamson, MD
Co-Investigator

Kenn Oldham, PhD
Co-Investigator

THE PROBLEM

Many TBI interventions are currently performed to prevent secondary injury due to restricted blood flow to the brain.

However, there is currently no method to continuously track changes in blood flow, or arterial response within the brain to interventions, that might help guide therapies.

Continuously monitor changes in blood flow and vascular reactivity

Replicate hemodynamic monitoring capabilities for TBI through alteration of an existing intraparenchymal catheter used for ICP monitoring

- ✓ No increased invasiveness
- ✓ Differential beat-to-beat arterial waveform comparison rejects slow-varying disturbances
- ✓ Continuous blood flow measurement may be measurable
- ✓ Continuous cerebral arterial autoregulation may be measurable
- ✓ Low cost

THE SOLUTION

Added to the exterior of a traditional intracranial catheter, are smart materials allowing real-time tracking of changes in arterial diameter and other properties to provide feedback on responsiveness to clinical interventions and an estimate of blood flow trajectory.

Fine optical fibers measure volume >
Piezoelectric polymer thin-films sense pressure and create arterial waveforms >



THE TECHNOLOGY

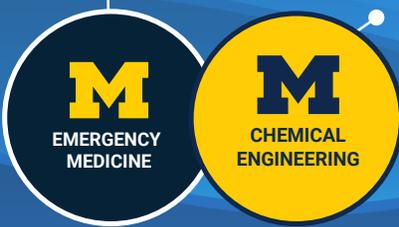
A Point-of-Care Microfluidic Device for High Frequency and Real-Time Measurement of Biofluid Markers

AWARD AMOUNT: \$115,800

THE TEAM

Frederick Korley, MD, PhD
Lead Investigator

Mark Burns, MD
Co-Investigator



Developing a
proof-of-concept
device for
high-frequency,
real-time
monitoring

Real-time monitoring via microfluidics will provide clinicians with objective data on the amount of brain cells that are dying and determine whether the treatment being administered is decreasing that number.

- ✓ Hand-held device that sends test results directly to a smartphone
- ✓ Portable
- ✓ Can be used in austere medical environments

THE SOLUTION

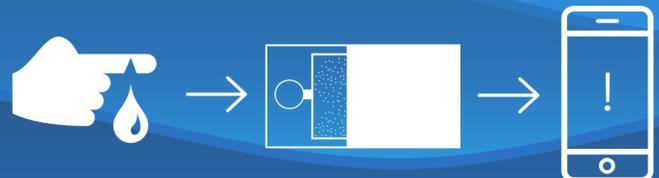
THE PROBLEM

Severely injured TBI patients are usually in a coma which limits the ability for clinicians to monitor individual patient response to treatment in real-time. There are currently no diagnostics for monitoring response to neuroprotective treatments.

Severe TBI is a heterogenous disorder but patients with this condition are treated uniformly

Failure of new therapy clinical trials for TBI is partly due to the lack of objective ways to titrate treatments to individual patient response

Blood-based biomarkers can be used to monitor individual patient response to TBI treatment with neuroprotective agents. A microfluidic device for performing repeated measurements of identified blood-based biomarkers at the point-of-care will be developed.



THE TECHNOLOGY

Diagnostic tool for coagulation abnormalities in Traumatic Brain Injury

AWARD AMOUNT: \$120,000

THE TEAM



Kevin Ward, MD
Co-Investigator



Mark Burns, MD
Principal Investigator

Sarah Mena, PhD
Research Investigator

**Developing
a point-of-care
diagnostic tool to
measure coagulation
abnormalities**

A microfluidic device that can detect coagulation process in minutes. Early detection will help determine the best course of treatment. The device is inexpensive to fabricate and easy to use allowing for repeated measurements throughout treatment.

- ✓ Point-of-care technology
- ✓ Use microliters of blood in analysis (fingertprick)
- ✓ Disposable one-time used chips costing less than \$10

THE SOLUTION

THE PROBLEM

The mortality of patients suffering TBI induced coagulopathy is as high as 50.45% vs. a mortality of 17.3% for patients without coagulopathy.

The current standard of coagulopathy diagnosis relies on expensive benchtop equipment not widely used in intensive care or emergency rooms.

High cost of coagulopathy diagnosis equipment 

Need for trained personnel for data collection and analysis 

Technology not widely available 

The coagulation process involves a blood change of state from liquid to a solid gel. The viscosity of the blood changes due to the coagulation cascade.

Forms droplets, blood viscosity determines size ➤

Smaller droplets = Larger viscosities (and vice versa) ➤

Characteristic points detected in coagulation curves including the gel point, the time-to-gel-point and the maximum clot viscosity ➤



THE TECHNOLOGY

Mesenchymal Stem Cell-Derived Exosomes as a Neuroprotective and Neurorestorative Treatment Strategy for Traumatic Brain Injury

AWARD AMOUNT: \$110,570

THE TEAM

Ben Biesterveld, MD
Co-Investigator

Aaron Williams, MD
Co-Principal Investigator

Hasan Alam, MD
Co-Principal Investigator

Gerry Higgins,
MD, PhD
Co-Investigator



Benjamin Buller, PhD
Co-Principal Investigator

Successful transition of exosomes into clinical use as an early treatment for TBI

Depending on the timing of administration, mesenchymal stem cell (MSC)-derived exosomes may play a substantial and multifaceted role in providing neuroprotection and/or neuro-restoration:

- ✓ High efficacy
- ✓ Safe + easy to administer
- ✓ Use in military and austere settings
- ✓ Reduction in associated multi-organ injuries
- ✓ Low-cost
- ✓ Potential for large scale production

THE SOLUTION

THE PROBLEM

Despite recent improvements in supporting and rehabilitative care for TBI, no pharmacological agents exist that are able to:

Reduce TBI-associated mortality



Improve neurologic outcomes following injury



The data generated from large animal model studies will advance MSC-derived exosome development and testing as an early TBI treatment.

Test earlier administration strategies

Assess the therapeutic effects of early administration

Identify exosomes' protective mechanisms of action in the brain

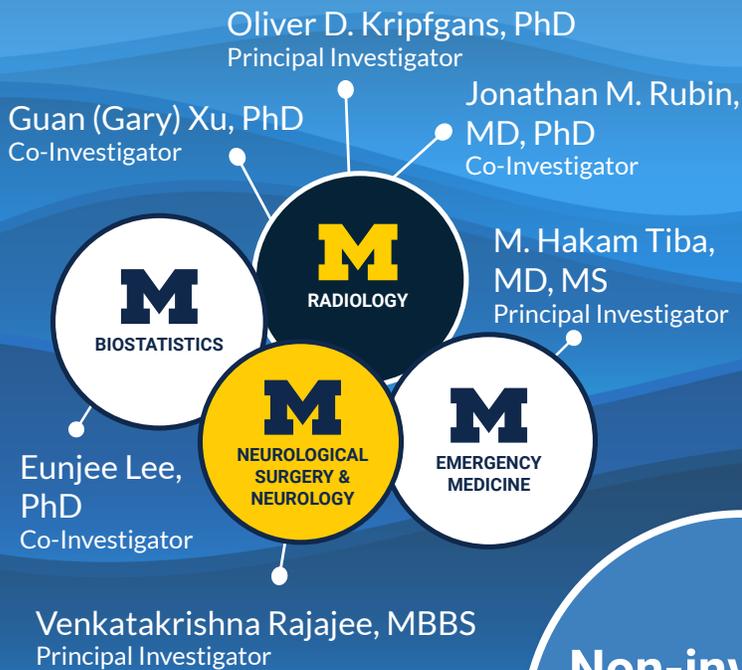


THE TECHNOLOGY

Real-Time, Non-Invasive Brain Metabolism

AWARD AMOUNT: \$118,666

THE TEAM



**Non-invasively
measure brain
blood flow and
oxygen use**

Bedside quantitative monitoring of cerebral oxygen consumption

- ✓ Tell intensivists how much blood is actually entering the brain
- ✓ Provide feedback to therapeutic hyperventilation and use of vasopressors
- ✓ Validate in pre-clinical model where (invasive) absolute reference measurements are available

THE SOLUTION

THE PROBLEM

Though it is a vital predictive sign of secondary injury, clinical diagnosis of absolute brain blood flow and oxygen consumption at the bedside is currently not possible. Available techniques are either severely flawed, pose significant risks to the patient's condition or are otherwise impractical.

- Blood pressure does not reflect blood flow ✗
- CT, PET, or MRI require transport ✗
- Blood Velocity \neq Blood Flow ✗

Develop and validate an ultrasound-based non-invasive, portable, inexpensive device that measures two critical physiological parameters:



- Quantify blood flow using three-dimensional ultrasound ➤
- Use photoacoustic visualization to quantify oxygen consumption ➤

THE TECHNOLOGY

Barreleye: A Decision Support Tool for TBI Care

AWARD AMOUNT: \$83,489

THE TEAM



Craig Williamson, MD
Principal Investigator

Krishna Rajajee, MD
Co-Investigator



Ashwin Belle, PhD
Principal Investigator

Mark Salamango
Principal Investigator

Bryce Benson, PhD
Co-Investigator

**Real-time,
continuous
decision support
software for
traumatic brain
injury (TBI)
care**

Barreleye collects physiological data from various monitors, such as EKG and blood pressure, in order to gauge patient trajectory and predict potential adverse events.

- ✓ Integrates with existing monitors and systems
- ✓ Novel technology ensures quality data
- ✓ Applications beyond TBI

THE SOLUTION

THE PROBLEM

There are currently no tools capable of visualizing physiological trends or predicting when a patient will “crash.” This means that caregivers can only react to a rapid decline in patient condition instead of intervening beforehand.

Sporadic collection of patient data 

Too much data to analyze manually 

Lack of continuous monitoring 

Barreleye continuously calculates clinically-relevant measures such as Shock Index and Pressure Reactivity Index, which gives caregivers an overall picture of patient condition.

The software also leverages a machine learning model that calculates hemodynamic trends to help clinicians reduce the risk of secondary brain injury.



THE TECHNOLOGY

Digital External Ventricular Drain with Data Analytics Integration

AWARD AMOUNT: \$81,804

THE TEAM



Rodney Daniels, MD
Principal Investigator



Ashwin Belle, PhD
Principal Investigator

Mark Salamango
Principal Investigator

Hakam Tiba, MD
Co-Investigator

Brendan McCracken, MS
Co-Investigator

**Automated
monitoring device
integrates with
data analytics to
diagnose and
treat TBI**

The DEVD automatically quantifies, monitors, and regulates ICP and CSF drainage in real-time. It also streams data, which can be utilized in predictive modeling for advanced TBI diagnosis and treatment.

- ✓ Automatically adjusts to patient position/condition
- ✓ Alerts caregivers in real-time
- ✓ Stores patient data across all phases of care
- ✓ Integrates into current workflows

THE SOLUTION

THE PROBLEM

Using an external ventricular drain to monitor intracranial pressure (ICP) after TBI can help improve survival, yet current archaic systems are not able to take real-time digital measurements, and require manual adjustments by caregivers.

Not suitable in challenging environments 

No integrated alarm systems 

Prone to user error 

No digital readouts 

A flow meter and pressure sensor is used to continuously monitor CSF flow rate and total volume output, allowing caregivers to dial the target pressure/flow based on patient needs.



The device will report data and graphs wirelessly to portable devices, allowing control of the DEVD remotely.

THE TECHNOLOGY



JOYCE MASSEY TBI GRAND CHALLENGE 2016 Funded Research Projects

Funding was awarded based on the potential to impact the way traumatic brain injury is diagnosed and treated during the initial "golden hours" of care.

GENOMIC & PROTEOMIC TECH TO DISCOVER VPA MECHANISM

THE TEAM



Hasan Alam, MD
Acute Care Surgery



Brian Athey, PhD
Computational Medicine
and Bioinformatics



Patrick Georgoff, MD
General Surgery

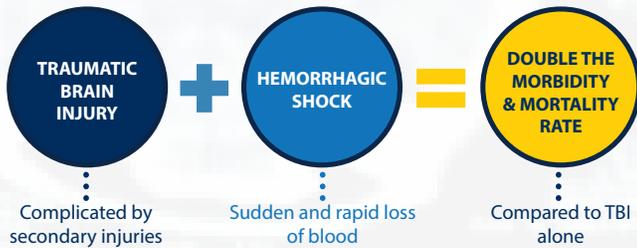


Gerald Higgins, MD, PhD
Computational Medicine
and Bioinformatics

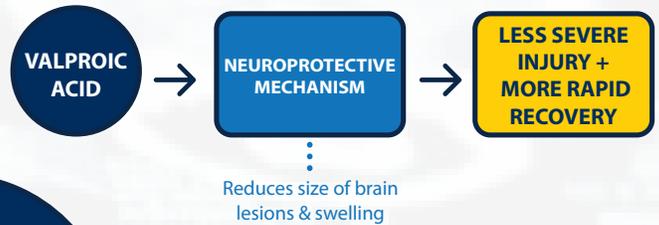


Vahagn Nikolian, MD
General Surgery

THE NEED



THE TECHNOLOGY



Using genomic & proteomic tech to identify how valproic acid decreases the severity of TBI.

COMPETITIVE ADVANTAGE

COMMERCIALIZATION ROADMAP

- PROVEN DATA**
The team's preliminary data suggest that early administration of VPA can decrease the severity of TBI.
- PORTABLE, LOW VOLUME, & EASY TO ADMINISTER**
Can be widely incorporated into trauma resuscitation protocols, including on the battlefield where TBI is the "signature injury."
- NOVEL TBI THERAPY**
There are currently no effective therapies for TBI patients. Valproic acid is well positioned to be the first.



PROJECT MILESTONES





JOYCE MASSEY TBI GRAND CHALLENGE 2016 Funded Research Projects

Funding was awarded based on the potential to impact the way traumatic brain injury is diagnosed and treated during the initial "golden hours" of care.

PROTECTING INJURED BRAIN CELLS WITH IMATINIB

THE TEAM



Daniel Lawrence, PhD
Cardiovascular Medicine

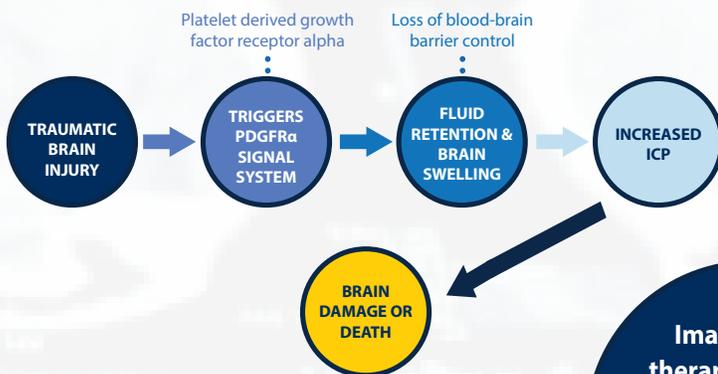


E. Joe Su, PhD
Cardiovascular Medicine

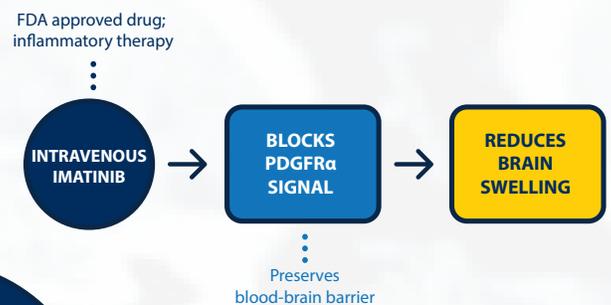


Geoffrey Murphy, PhD
Molecular & Behavioral
Neuroscience

THE NEED



THE TECHNOLOGY



Imatinib drug therapy preserves the blood-brain barrier to reduce fluid retention and brain swelling in TBI patients

COMPETITIVE ADVANTAGE



FAST TRACK

Utilizing FDA approved drugs with well-established safety profiles that block PDGFRα signals could rapidly transition into a clinical trial.



PROVEN DATA

The team's preliminary data has shown that Imatinib treatment reduces brain fluid retention and improves outcomes after TBI in animal models.



NOVEL TBI THERAPY

There are currently no effective therapies for TBI patients. Imatinib could be a new therapy for TBI.



EXPANDED DRUG DELIVERY

Allowing for intravenous delivery of Imatinib would expand treatment options for unconscious TBI patients.

COMMERCIALIZATION ROADMAP



PROJECT MILESTONES





JOYCE MASSEY TBI INNOVATION FUND 2015 TBI Funded Research Projects

Funding was awarded based on the potential to impact the way TBI is diagnosed and treated during the initial "golden hours" of care.

REAL-TIME HEMODYNAMIC MONITORING SYSTEM

THE TEAM



Ashwin Belle, PhD
Emergency Medicine



Kayvan Najarian, PhD
Emergency Medicine

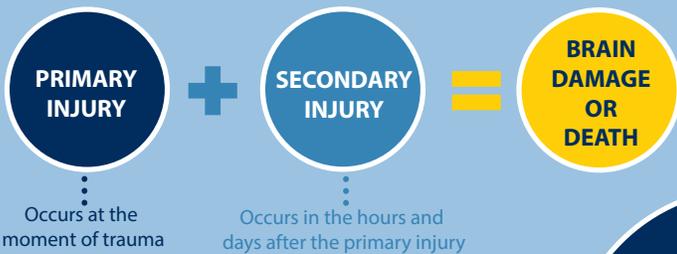


Venkatakrishna Rajajee, MBBS
Neurological Surgery

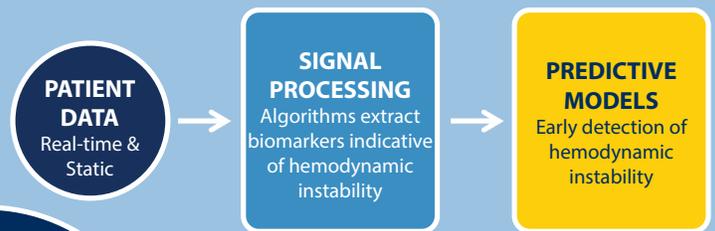


Kevin Ward, MD
Emergency Medicine

THE NEED



THE TECHNOLOGY

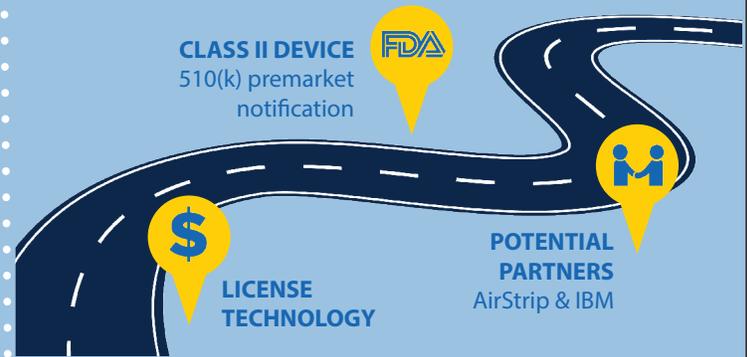


A continuous monitoring and real-time analytics tool that detects the early onset of hemodynamic instability to prevent TBI patients from suffering from secondary brain injuries

COMPETITIVE ADVANTAGE

- REAL-TIME STREAMING DATA**
Uses high resolution, real-time waveform data unlike other approaches that rely on single source static data.
- PRECISION MEDICINE**
Comprehensive, personalized data portfolio determines patient's unique neurological and systemic physiology.
- NON-INVASIVE**
Technology does not rely on invasively captured patient data.
- SPEED**
Continuous real-time bedside monitoring provides relevant physiological endpoints for timely intervention.

COMMERCIALIZATION ROADMAP



PROJECT MILESTONES





JOYCE MASSEY TBI INNOVATION FUND 2015 TBI Funded Research Projects

Funding was awarded based on the potential to impact the way TBI is diagnosed and treated during the initial "golden hours" of care.

EARLY ADMINISTRATION OF PLASMA & VALPROIC ACID

THE TEAM



Yongqing Li, MD, PhD
Trauma Surgery Research



Ihab Halaweish, MD
Traumatology



Hasan Alam, MD
Acute Care Surgery

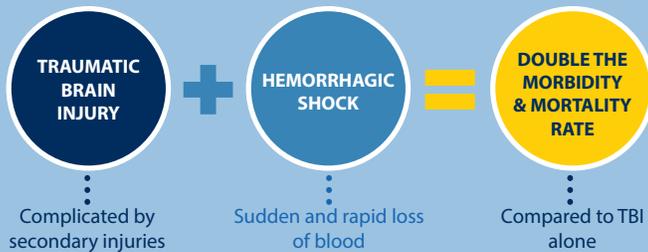


Patrick Georgoff, MD
General Surgery



Vahagn Nikolian, MD
General Surgery

THE NEED



THE TECHNOLOGY



Early administration of plasma & valproic acid to decrease brain injury & complications from hemorrhagic shock, to improve TBI patient outcomes & recovery speed

COMPETITIVE ADVANTAGE

- ONE-OF-A-KIND LARGE ANIMAL MODEL**
Funded by the DoD, U-M has the only TBI model in existence to identify and test promising new treatments.
- PROVEN DATA**
The team has verified that early treatment with plasma and valproic acid can significantly improve outcomes in hemorrhage patients.
- PORTABLE & COMPATIBLE**
Can be widely incorporated into trauma resuscitation protocols, including on the battlefield where TBI is the "signature injury."
- NOVEL TBI THERAPY**
There are currently no effective therapies for TBI patients. Plasma and valproic acid could be a new therapy for intracerebral hemorrhage.

COMMERCIALIZATION ROADMAP



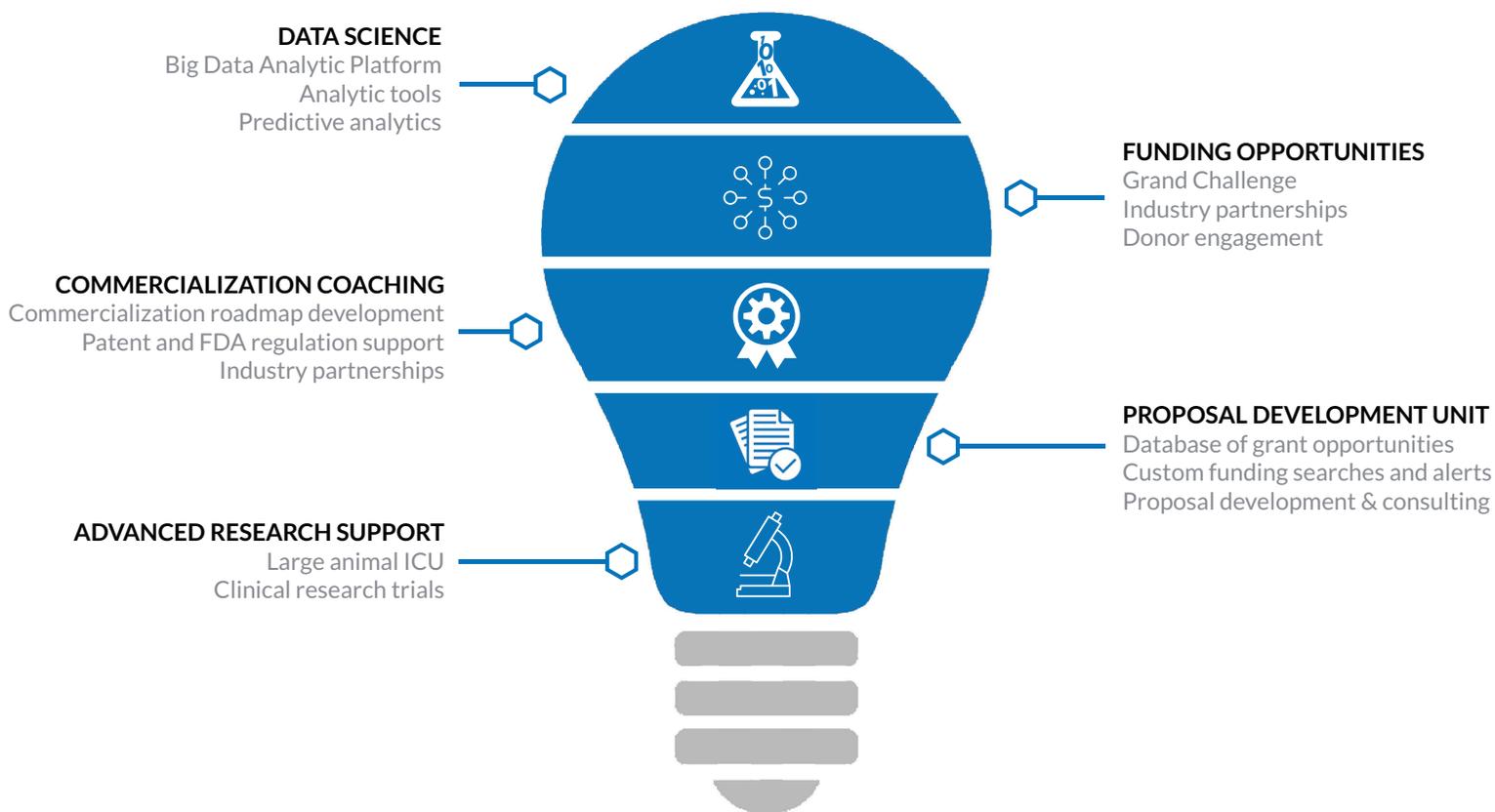
PROJECT MILESTONES





CENTER FOR INTEGRATIVE
RESEARCH IN CRITICAL CARE

WE CAN GET YOUR IDEAS TO MARKET.



WHO WE ARE

The Michigan Center for Integrative Research in Critical Care is the hub for critical care researchers across the University of Michigan.

We foster multidisciplinary collaborations between our members and provide them with tools and resources to accelerate their research from bench to bedside.

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INNOVATION INTEGRATION ENTREPRENEURSHIP



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