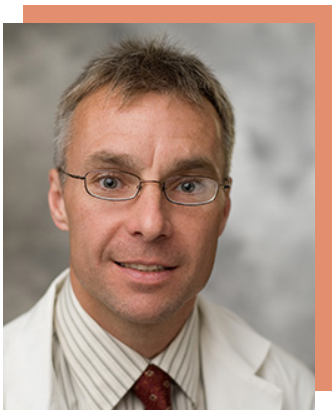
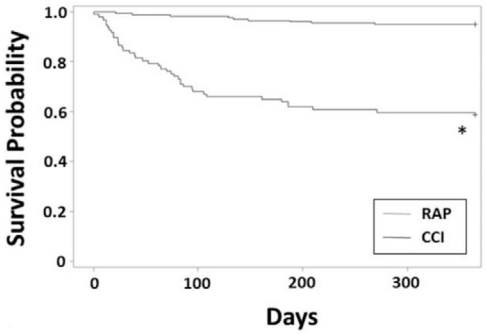
Translational Research Aimed To Understand The Systemic Metabolic Response And To Improve Treatment And Outcomes in Severely Injured Patients



By: Grant O'Keefe, MD, MPH
Professor

With improvements in trauma systems, early management, and critical care, early mortality following severe traumatic injury has declined. However, this has not necessarily translated into improved long-term outcomes. Late mortality remains high and a substantial number of patients are developing what is now referred to as chronic critical illness. It is characterized by prolonged ICU and hospital stays which are punctuated by infection, sepsis, organ dysfunction and marked loss of lean body mass. Chronic critical illness, whether following trauma or sepsis more generally, is a harbinger of poor outcomes in the long term (Figure 1; *Brakenridge et al. Annals of Surgery 2019*). We must focus our efforts on improving treatments

Figure 1: **Post-sepsis follow-up**



in the days to weeks after trauma and critical illness in ways that will improve longer term outcomes. The overarching aims of our research program are threefold:

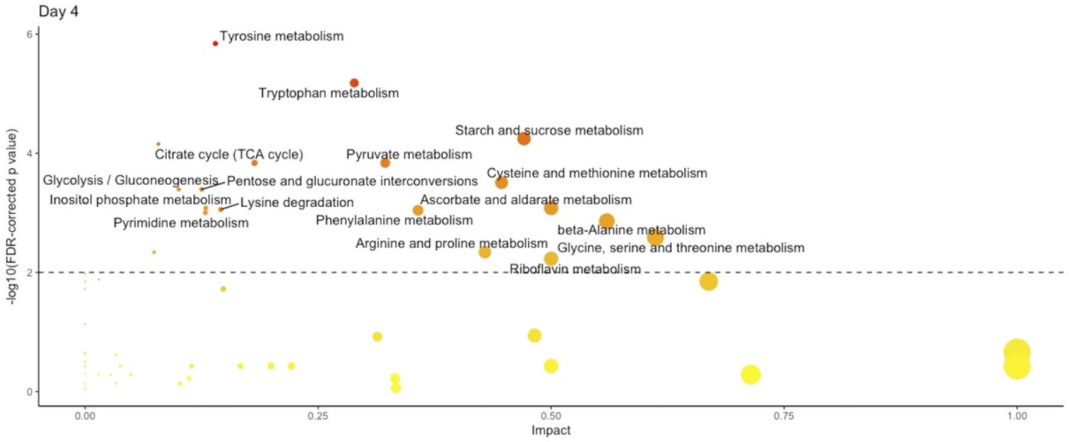
1. Identify physiologic and biologic changes that can be used for early identification of patients likely to develop chronic critical illness.

2. Intervene early (e.g., nutritional support, early treatment for sepsis, etc.) to reduce the risk of complications.

3. Educate trainees in the methods and skills to become surgeon-scientists focusing on translational aspects of severe trauma and critical illness.

With our collaborators, we have applied system wide approaches to studying the metabolic responses to injury. Our approach, referred to as metabolomics, is the study of small molecules, such as amino acids, sugars, lipids, and nucleotides. It provides a quantitative evaluation of multiple metabolic pathways simultaneously. Like genomic and proteomic approaches, metabolomics aims to understand, as broadly as possible, an entire biological system. Analysis of plasma metabolites provide a comprehensive view of a patient's physiology, and has helped us understand the biologic changes related to illness

Figure 2: Day 4 Metabolic Pathways



and recovery. Our initial work demonstrated how metabolic profiles of trauma patients differ from healthy volunteers and change over time, and that metabolites respond differently to enteral and parenteral nutrition *(Parent et al. JAMA surgery 2016 and Parent et al. Journal of Trauma: Acute Care Surgery 2017)*. Recently, we have identified metabolites and metabolic pathways that, as early as four days after traumatic injury, characterize patients who are likely to progress to chronic critical illness. The altered pathways are shown in figure 2. Briefly, the pathways toward the top of the figure, such as tyrosine and tryptophan metabolism, are most strongly associated with chronic critical illness. Of the over 200 metabolites and related pathways tested, those related to amino acid and protein metabolism were heavily represented in our observed differences. These observations indicate the importance of protein catabolism, and therefore efforts to restore protein synthesis in the post-injury period (*Horn et al. Journal of Trauma; Acute Care Surgery 2021*).

Dr. Dara Horn

All of this work has contributed to our efforts to improve patient outcomes and have led to a nearly complete clinical trial where 500 critically ill patients have been enrolled to receive additional protein supplementation aimed to reduce catabolism and improve clinical outcomes. I am thankful for the many collaborators from Harborview Medical Center and across the University of Washington. Experts in metabolomics, clinical nutrition, statistics and complex data analysis are contributing to our work. Future surgeon-scientists such as Dr. Dara Horn, Chief Resident, have been instrumental. We are also grateful to the patients and their families for their participation in these studies and for their trust in our care.

Harborview Research & Training Building

17th David M. Heimbach Visiting Burn Surgery Lectureship

Dr. Leopoldo C. Cancio

In December 2021, the Department of Surgery Division of Trauma, Burn & Critical Care Surgery hosted Dr. Leopoldo C. Cancio as the 17th David M. Heimbach Visiting Burn Surgery Lectureship speaker. Dr. Cancio is the Director of the US Army Burn Center at the US Army Institute of Surgical Research and Professor of Surgery at UT Health San Antonio, TX, and presented his lecture "War and Peace: Recent Advances and Unresolved Problems in Burn Care."

The first Annual UW Burn Center Lectureship was established in 2003 with the first lecturer, Dr. Basil A. Pruitt, a renowned surgeon who had a major impact on the fields of surgery, burns care, trauma, and critical care. In 2008, the event title changed to the David M. Heimbach Visiting Burn Professor Lectureship when Kahill and Jean Gibran, the parents of Dr. Nicole Gibran, Professor Emeritus, created an endowment.

This annual event invites a prominent burn surgeon to speak at the Department of Surgery's Grand Rounds. The event includes a dinner the night before with the guest lecturer, key faculty members, yearly R3s, and key leadership in the Burn Center. After the lecture, the Burn Center hosts between five to eight residents and fellows that present ongoing burn research to the lecturer and all who can attend.

Past Visiting Lecturers

Dr. Basil A. Pruitt | October 2003
Dr. Giulio Gabbiani | October 2004
Dr. David N. Herndon | October 2005
Dr. Ronald Tompkins | September 2006
Dr. Richard L. Gamelli | November 2007
Dr. Mehmet Haberal | September 2008
Dr. Naoki Aikawa | October 2009
Dr. Steven Wolf | December 2010
Dr. Steven T. Boyce | November 2012
Dr. Matthias B. Donelan | September 2013
Dr. Jeffrey R. Saffle | November 2014
Dr. David Auth | September 2015
Dr. Edward E. Tredget | November 2016
Dr. Fiona M Wood | December 2018
Dr. James Chang | December 2019
Dr. David Greenhalgh | December 2020
Dr. Leopoldo C. Cancio | December 2021