

AORTIC RESEARCH CONSORTIUM



By: Matthew Sweet,
MD, MS
Associate Professor
& Section Chief



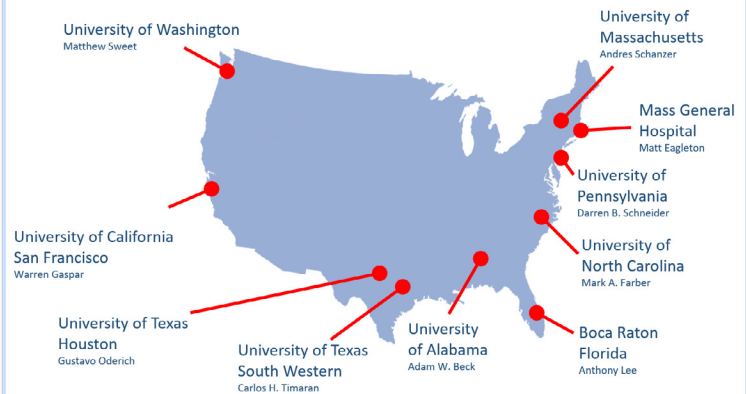
By: Sara Zettervall,
MD, MPH
Assistant Professor

Aortic aneurysms involving the thoraco-abdominal aorta (TAAA) pose a threat to life if they rupture. TAAA are one of the most difficult surgical conditions to treat due to the high morbidity and mortality associated with the complex procedures needed to treat them. Open operation requires opening the chest and abdomen, various strategies for distal aortic perfusion, aortic cross-clamping, viscero-renal ischemia-reperfusion, and significant blood loss. This is a major undertaking with significant stress to the patient. Endovascular treatment using branched stent grafts provides the opportunity to treat patients who otherwise would not be candidates for open repair and has been found to be safer in the short term than open operation, but it is technically complex and has less well-defined long-term durability.

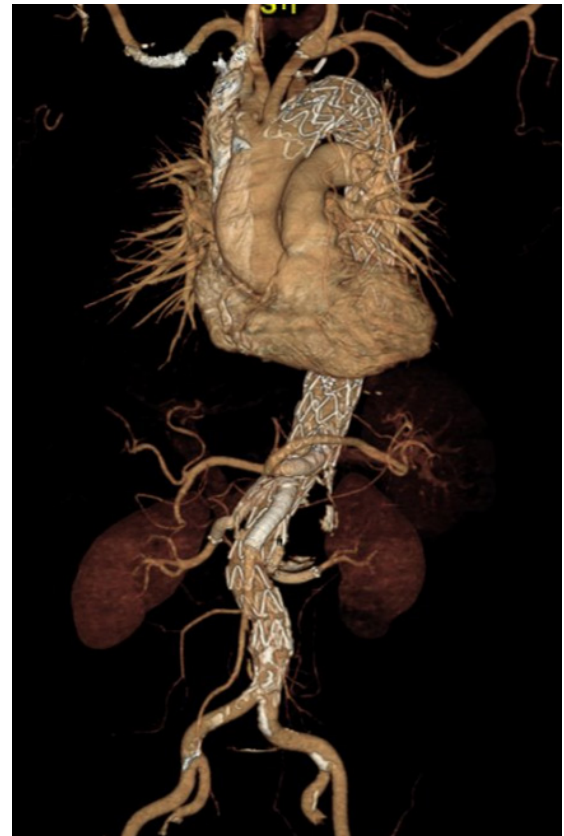
Branched stent grafts are not currently commercially available in the United States. To date, the University of Washington is one of only 10 sites in the U.S. with access to these devices through a Physician-Sponsored Investigational Device Exemption (IDE) study. Under the direction of Dr. [Matthew Sweet](#), Associate Professor, the study opened in 2012 here at UW and now has expanded with the addition of Dr. [Sara Zettervall](#), Assistant Professor, Division of Vascular Surgery. In 2016, these 10 sites began collaborating on the Aortic Research Consortium (ARC), a multi-center study using the data from the 10 IDE studies. These data are prospective, standardized and audited for completeness. The studies are monitored by each hospital's Institutional Review Board and the U.S. Food and Drug Administration.

Over the ensuing years, the study has continued to grow and the dataset now includes in excess of 2,000 treated patients.

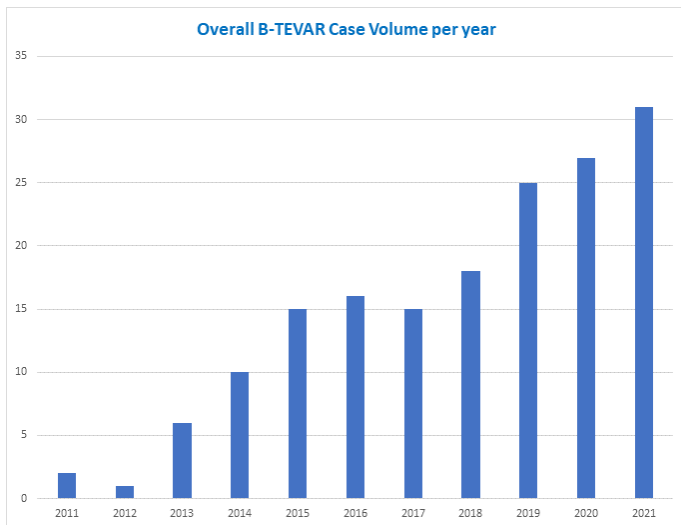
United States F/BEVAR Aortic Research Consortium (ARC)



This project offers us a unique opportunity to study a complex surgical procedure with analytic power far beyond what any single site could achieve, and with better long-term follow-up data and clinical granularity than is currently available in any administrative quality improvement database. Thus far, seven separate research projects have been completed looking at various topics such as treatment of patients with post-dissection TAAA, how outcomes differ for women and

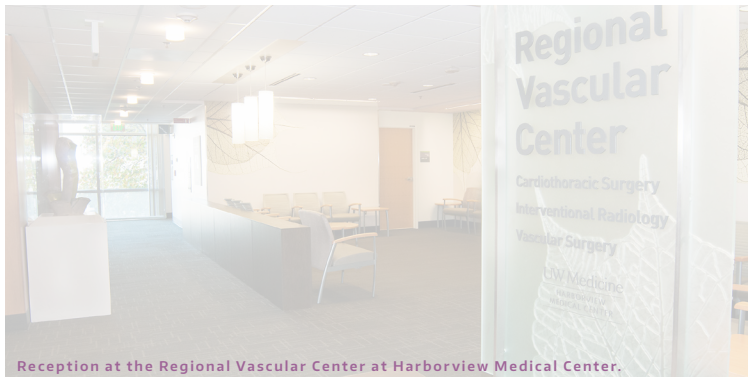


3D reconstruction of a B-TEVAR case



men, use of pre-loaded systems, strategies for spinal cord injury prevention and treatment of failed prior endovascular repair. The most recent publication was led by our UW team. Dr. Zettervall examined the frequency and clinical impact of reintervention on patient survival. In the process, she helped demonstrate that the standardized reporting scheme for reinterventions fails to fully discriminate between high and low physiologic stress reinterventions and determined that reinterventions improve long term survival in these medically complex patients.

The ARC is a powerful tool for studying a complex surgical procedure. Thus far, we have focused on answering clinically relevant questions using the data in a retrospective fashion. The greater power of the study, however, lies in the ability to use it in a prospective way in two areas. First, the structure is in place to conduct prospective randomized clinical trials (RCT). This provides the exciting opportunity as the heavy lifting of RCT study infrastructure and implementation is already complete. Second, these data can be used to establish objective performance goals of safety and effectiveness. As the branched endografts become clinically available, these data will serve to set standards that can guide the broader use of this technology, hopefully improving the safety of these procedures in the years to come.



RESEARCH STAFF HIGHLIGHTS

Heidi Kenerson

Research Scientist/Engineer III
HPB Surgical Oncology Lab



How did you get into this line of research?

From a young age I had the desire to work in the field of cancer research. Upon completion of my MS in Bioengineering at the UW, I was looking for an opportunity to gain experience in molecular and cancer biology and joined Dr. Raymond Yeung's lab.

What does your typical workday look like/what do you do?

My typical day consists of a variety of tasks such as collecting, processing, and distributing tumor tissue procured from liver resections, running experiments utilizing collected tumor tissue and cell culture lines, managing the laboratory and the liver research biorepository, as well as supporting rotating research residents and our multiple research collaborations.

What has been your most significant accomplishment/finding?

The set up and development of the Tissue Slice Culture (TSC) platform in our laboratory. TSCs are established from solid tumors and are an effective in vitro model for studying human cancer that preserves the tumor microenvironment. We have standardized this method to assess and compare human cancer growth ex vivo across a wide spectrum of tumors. Tumor slices cultures can be utilized for short-term studies including experiments using drugs and cell-based therapies and response can be assessed using multiple readouts.^{1,2}

¹Protocol for tissue slice cultures from human solid tumors to study therapeutic response.

²Tumor slice culture as a biologic surrogate of human cancer.

VA PUGET SOUND SURGICAL ONCOLOGY RESEARCH GROUP: THERAPY-INDUCED SENESCENCE AND COLORECTAL CANCER



By: Peter C. Wu, MD, FACS

Associate Professor

Director, VISN20 TeleTumor Board Program

WA State Chair, American College of Surgeons

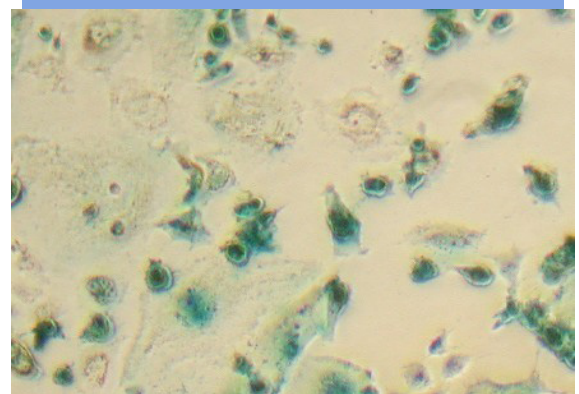
Commission on Cancer

Advanced gastrointestinal (GI) cancers are infrequently cured by chemotherapy or radiation, and surgery continues to be the mainstay treatment for most patients resulting in significant impacts on quality of life and survival. Furthermore, the variable responses to cancer treatment and apoptosis markers suggest alternative cell death pathways exist. Our collaborative research group at the VA Puget Sound has been studying and characterizing therapy-induced senescence over the course of several funded projects. Cellular senescence is defined as prolonged cell cycle arrest associated with signs of cell aging. The sentinel work of Hayflick and Campisi revealed that cells will continue to divide until they encounter mortality restrictions at M1/M2 resulting from telomere shortening and activation of p53 and p16/RB pathways. Either or both p53 and p16/RB must be inactivated for immortalization which explains why over 50% of solid tumors harbor mutations at these sites. Malignant cells can be induced into a state of cell cycle arrest following exposure to chemoradiation, termed therapy-induced senescence (*Figure 1*). Evidence suggests that therapy-induced senescence is a prominent solid tumor response to therapy, and subsets of senescent cells can “escape” and re-enter the cell cycle eventually leading to tumor progression. We observed that massive telomere loss occurs in senescent colorectal cancer cells exposed to chemotherapy. Interestingly, senescent cells able to escape replicative arrest were able to partially recover their telomere loss. We hypothesized that modulation of telomerase activity regulates escape from therapy-induced

senescence in colorectal cancer. One of the goals of our lab is to define the role of telomerase in regulating therapy-induced senescence and senescence escape in colorectal cancer. This project is a key component of an ongoing effort to elucidate molecular mechanisms of therapy-induced senescence and identify markers that can reliably predict treatment response and reveal key checkpoints that could be targeted to block senescence escape. A serendipitous finding in our lab of differential adenovirus transfection in senescent cells led to the discovery that coxsackie adenoviral receptor (CAR) expression could be used as a novel marker to quantitate senescence profiles, and a funded pilot study with Nuclear Medicine colleagues to create new radioligand conjugates to detect in vivo senescent tumors with small animal PET imaging. Using CAR as a surrogate biomarker for senescence, we have shown that senescence response can be detected in rectal cancer patients treated with neoadjuvant chemoradiation (*Figure 2*).

Another project examining CAR expression in archival resected rectal tumor specimens was able to identify nodal micrometastases by routine immunohistochemistry which correlated with patient survival. Recently,

A



B

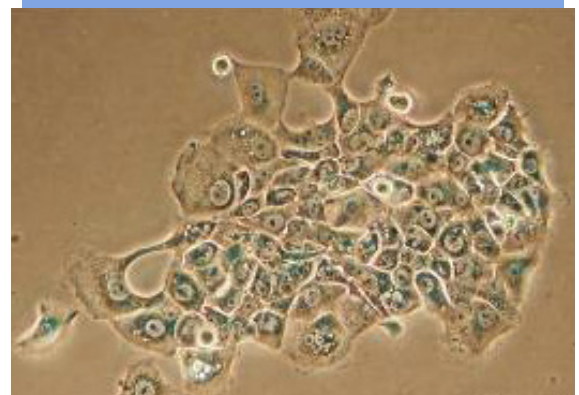


Figure 1. Light microscopy of blue senescent tumor cells in replicative arrest characterized by enlarged and flattened cell shape, increased cytoplasmic granularity, nuclear polyploidy, and expression of pH-restricted SA-beta-galactosidase (A) H1299 lung carcinoma cells. (B) Bx-PC3 pancreatic carcinoma cells.

exosomes have been shown to have potential application as cancer biomarkers with increased sensitivity and specificity compared to traditional protein or nucleic acid markers. Exosomes are 40-50 nm extracellular vesicles released by cells which can embed proteins, lipids and nucleic acids from the parent cell and circulate in human serum. In cancer patients, exosomes are shed from cancer cells and we have been able to measure CAR in tumor-specific exosomes from VA colon cancer patients receiving chemotherapy which allows us to examine cellular events in human patients while undergoing treatment. Our collaborative research group strives towards gaining a better understanding of cancer treatment response, leverage technology to examine cellular events, and develop rational novel targets for clinical testing. An IRB-approved GI Tumor Tissue and Blood Repository is also maintained by the lab group and has accumulated over 250 VA patient samples for research study purposes. Numerous clinical trials are also managed within the group and supported by clinical trial coordinators. Most recently, we received a generous quality improvement grant from the American Cancer Society to improve colorectal cancer screening rates at the VA Puget Sound impacted by the COVID-19 pandemic through the introduction of screening navigators.

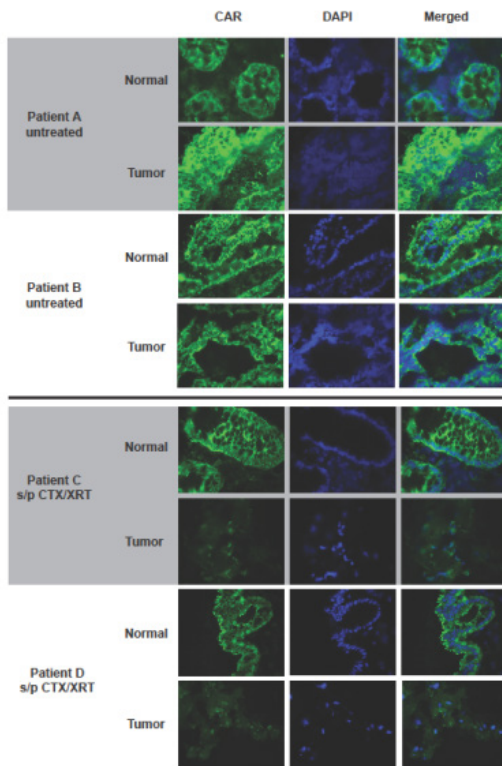


Figure 2. CAR expression and senescence in colorectal cancer. Human tumor and adjacent normal tissue specimens were obtained from colorectal cancer patients undergoing curative resection treated with or without preoperative chemoradiotherapy. Freshly frozen specimens were stained with CAR primary antibody followed with FITC-conjugated secondary antibody or with DAPI. Immunofluorescence micrographs (40X) of CAR, DAPI and merged images are shown.

RESEARCH STAFF HIGHLIGHTS

Laura Hennessy, RN

Research Nurse Supervisor
Division of Trauma, Burn & Critical Care



How did you get into this line of research?

I was working as a flight nurse with Airlift Northwest and looking for a change. I wanted something that would allow me to learn, teach me a different side of medicine, but allow me to maintain some autonomy. My background has always been trauma and critical care, so it was a pretty easy fit.

What does your typical workday look like/what do you do?

My team and I review all critical care and trauma admissions daily for possible enrollment in our studies. I also am responsible for the regulatory part of research, specifically working with Institutional Review Boards and helping residents and attendings with study designs and submissions. Our studies are either government supported or sponsor supported, so much of my time is working with the budgets and communicating with other sites or sponsors. I also perform research procedures such as blood draws, drug infusions, etc., as well as talk with families and patients about the research.

What has been your most significant accomplishment/finding?

I was once told that as a clinical nurse, I was helping one patient at time, but as a research nurse, I'm contributing to helping the population at large. I hope that the science that has come from our studies will do that for generations to come.

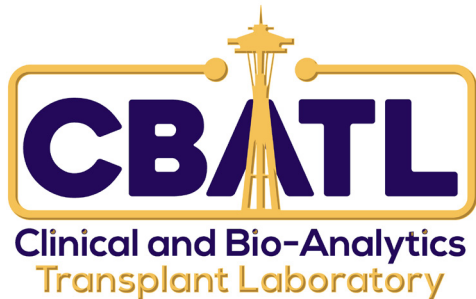
Advice for others looking to get into this field?

I just had my 35th anniversary here at Harborview. I continue to learn from some of the smartest people on the planet. If you want to stay intellectually stimulated and want to feel like you are part of the scientific world, this is the best place to be.

CLINICAL AND BIO-ANALYTICS TRANSPLANT LABORATORY



By: James D. Perkins,
MD, MSDS
Professor



Transplant surgeons, fellows, residents, medical students, and other healthcare professionals use the services of the **Clinical and Bio-Analytics Transplant Laboratory (CBATL)** to research ideas to improve patient care. The services of CBATL include a “think tank” of individuals to provide analytical and interpretative expertise to researchers. The multiple technical modalities of CBATL include microsimulation using Markov models, mathematical optimization to optimize resources, genomic evaluation, data mining of large clinical repositories, text analytics with natural language processing, and many machine learning algorithms for classification and survival analysis.

CBATL was organized in 2010 by Dr. **James Perkins**, Professor, Division of Transplant Surgery, to help extremely busy clinical transplant surgeons, fellows, and residents conduct research to improve transplant patient care. CBATL has now expanded to help many others with a need in their research efforts. Dr. Perkins completed a Master's in Data Science in 2015 to expand the technical modalities available from CBATL. In 2019, CBATL started a fellowship in operational healthcare analytics to help with the many research projects.



Dr. Jorge
Reyes



Dr. Christopher
Little

Since 2017, CBATL has provided support for 30 published articles, over 20 national and regional oral abstract presentations, and three international invited presentations. Dr. **Jorge Reyes**, Professor & Chief, Division of Transplant Surgery, recently gave an invited international presentation at the American Association for the Study of Liver Diseases with a title, “Split Liver Transplant: Should we push for it?” This presentation resulted from a publication in *Transplantation* in June 2019 entitled, “**New Evidence Supporting Increased Use of Split Liver Transplantation.**” This work encourages liver transplant centers to utilize splitting donor livers to transplant two waiting candidates instead of only one candidate, thus saving lives. Dr. Reyes used CBATL’s resources of data mining a large data repository and machine learning algorithms while working with UW surgical resident Dr. **Christopher Little**, Research Resident, to publish, “**Livers From Pediatric Donation After Circulatory Death Donors Represent a Viable and Underutilized Source of Allograft**” in *Liver Transplantation*, September 2020. This research also expanded the donor pool allowing transplantation of more liver candidates.

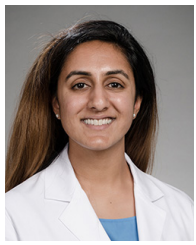


Dr. Catherine
Kling



Dr. Lena
Sibulesky

Dr. **Catherine Kling**, Assistant Professor, as a transplant fellow working with Dr. **Lena Sibulesky**, Associate Professor, Division of Transplant Surgery, was able to conduct cutting-edge research with CBATL’s resources and published, “**Utilization of organs from donors according to hepatitis C antibody and nucleic acid testing status: time for change**” in the *American Journal of Transplantation*, in November 2017. She followed this with a publication in *Surgery* July 2019 titled, “**Listing practices and graft utilization of hepatitis C-positive deceased donor in liver and kidney transplant**” and another publication in the *American Journal of Transplantation* in November 2019 titled, “**Three-year follow-up of aviremic hepatitis C-positive kidneys.**” This work expanded the pool of donor organs allowing more transplant candidates around the world to be transplanted. She is now using mathematical optimization to research a new liver allocation model to improve graft survival following liver transplantation.



Dr. Mohini Dasari

Dr. Sibulesky, with CBATL's resources, expanded the prior work on using HCV positive donors and published, "[Can we mitigate the effects on simultaneous liver-kidney transplantation through increased utilization of HCV-positive donors?](#)" in the *American Journal of Transplantation*, October 2018. Working with Dr. [Mohini Dasari](#), Chief Resident, and using CBATL's microsimulation technology, Dr. Sibulesky was accepted for a recent publication in *Experimental and Clinical Transplantation* entitled, "[Prescriptive Analytics Determining Which Patients Undergoing Simultaneous Liver-Kidney Transplants May Benefit From High-Risk Organs.](#)" These studies helped improve the organ shortage for both liver and kidney transplant candidates.



Dr. Andre Dick

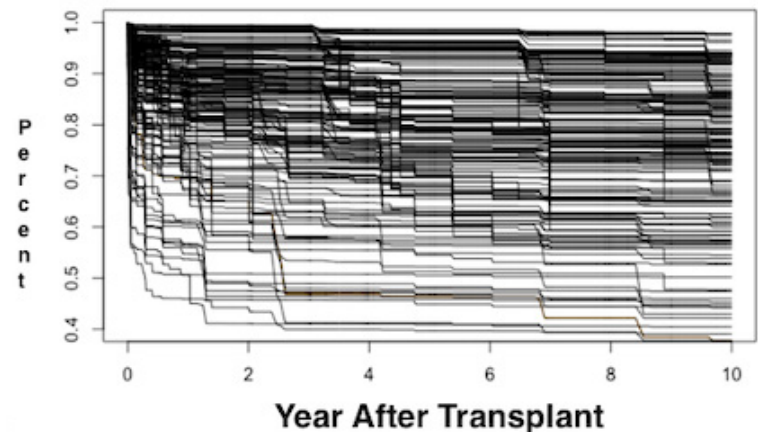
Dr. [Andre Dick](#), Associate Professor, Division of Transplant Surgery, using CBATL's resources had a presentation at the American College of Surgeons annual meeting October 2019 and a publication entitled, "[Does the Funding Source Influence the Long-term Patient Survival in Pediatric Liver Transplantation](#)" in *Pediatric Transplantation*, March 2021. Dr. Dick is currently conducting research on the cutting-edge topic of how the area deprivation index (community resources) of transplant candidates influence their post-transplant survival in liver and kidney transplantation with Dr. James Hendele, a recent graduate of the Transplant Fellowship at UW. These research efforts help programs study the socioeconomic support needed by transplant candidates and recipients to provide the best long-term survival.



Dr. Mark Sturdevant

Presently, CBATL is supporting 15 different research projects with our UWMC and Seattle Children's Hospital transplant surgeons, hepatologists, nephrologists, fellows, residents, medical students, general surgeons, and vascular surgeons. The goal for these projects is to improve patient care. There are too many other research projects to mention but one very exciting project led by Dr. [Mark Sturdevant](#), Associate Professor, Division of Transplant Surgery, and our hepatology colleagues, is exploring many different new machine learning survival algorithms to find an evidence-based system to allocate nondirected, anonymous living liver donor hepatic grafts (Figure 1). These donors are heroes in that they give up a part of their liver so a person unknown to them can live. This allocation model will honor these donors by providing a model that predicts long-term graft survival.

Figure 1



DR. ANDRE DICK IS APPOINTED SEATTLE CHILDREN'S SENIOR VICE PRESIDENT (SVP) AND SURGEON-IN-CHIEF



On January 26, 2022, [Seattle Children's announced Dr. André Dick was appointed Seattle Children's senior vice president \(SVP\) and surgeon-in-chief](#). Dr. Dick has served at Seattle Children's since 2008, first as a surgeon in the Division of Transplant Surgery, then in 2016 as surgical director of Kidney Transplantation. In 2017 he became clinical director for the surgical inpatient unit, and in 2020 was appointed associate surgeon-in-chief. Dick accepted the role of interim SVP and surgeon-in-chief in April 2021. He is also an associate professor of surgery at the University of Washington (UW).

A champion of addressing racism and promoting an inclusive culture, Dick is an inaugural co-DEI (diversity, equity and inclusion) advisor to the American Society of Transplant Surgeons executive council and is also co-leading Children's Health Equity, Diversity and Inclusion (HEDI) Education and Leadership Committee which is focused on providing anti-racism education and training opportunities for our workforce.

He brings this vital lens to his role as surgeon-in-chief, where he is responsible for Seattle Children's surgical operations, ensuring all aspects of operative care function safely, equitably and efficiently. André will also focus on addressing the impact of Social Determinants of Health (SDOH) to deliver more equitable care to the patients and families we serve, as well as expanding our clinical capacity.

MYTHBUSTING IN PLASTIC SURGERY



By: Raymond
Tse, MD
Associate Professor



By: Ezgi
Mercan, PhD
*Director,
Craniofacial Image
Analysis Laboratory*



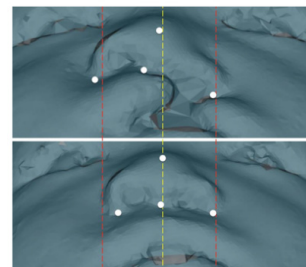
By: Russell
Ettinger, MD
Assistant Professor

Cleft lip and palate occurs in 1 in 750 newborns due to failure of fusion of embryologic components of the face. The degree of clefting can be variable in its involvement of lip, alveolus, hard palate, and soft palate, and the impacts include impairments in feeding, speech, hearing, hygiene, dental health, and appearance. The [Craniofacial Center at Seattle Children's Hospital](#) (SCH) serves the Washington, Alaska, Montana, and Idaho regions and provides comprehensive multidisciplinary care to children with these and other facial differences. Plastic Surgery is at the core of the team, providing surgical care from birth to adulthood and balancing patient needs with impacts of treatment on growth and development. While the clinical team is the largest and most comprehensive in North America, the research team continues to make strides in our understanding of cleft deformities.

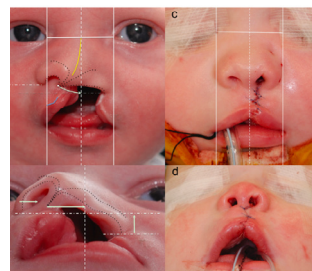
One of the fundamental principles of any reconstruction is a clear understanding of the deformity and the “normal ideal.” Until now, descriptions of the cleft lip nasal deformity have been based upon subjective observations and, in turn, those descriptions have formed the basis of surgical goals that have been passed along as dogma for decades. With the use of 3D imaging, computer vision techniques, and collaboration with researchers in the Department of Computer Science and Engineering, the Plastic Surgery team at SCH has produced an objective model of the deformity. Their data-driven model has revealed misperceptions in previous descriptions and has revealed that previous goals of surgery have been misleading. Not only does their model re-define treatment objectives, it also provides insights into the cause of the deformity. The combination of a gap, an uncoupled growth center, and changes that occur in opposing manner can explain everything. With this newfound knowledge, the team is now redefining the objectives of surgery which will allow surgeons to improve outcomes for children with clefts.

The work is the product of a long-time collaboration of Drs. [Raymond Tse](#), Associate Professor, Division of Plastic Surgery, Ezgi Mercan, Director, Craniofacial Image Analysis Laboratory and [Russell Ettinger](#), Assistant Professor, Division of Plastic Surgery, the latest addition to the team. Their work has most recently been conducted as part of the SCH [Craniofacial Image Analysis Laboratory \(CranIAL\)](#). The collaboration with Dr. Mercan started when she was a PhD student and continued with her addition to the Craniofacial Team as a dedicated researcher. Dr. Mercan is supported through donated funds and now manages and runs a diverse spectrum of projects involving multiple investigators in the broader Craniofacial Team.

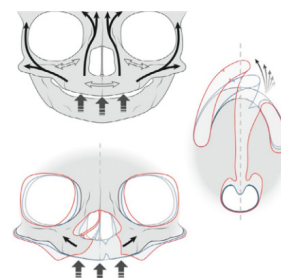
Although Dr. Tse and other members of the Craniofacial Team are involved in other NIH supported projects, funding via donations provides the means to conduct more free-form investigations. The lack of constraints affords freedom and creativity to engage in research in innovative and practical ways. The surgeon-engineer collaboration would not have been possible without this funding. The SCH team values the support they receive from the UW and other donors. They continue to strive to improve care here and abroad through the discovery of truths that impact care globally.



3D surface image analysis.



Correction of cleft lip and nose deformity with references to guide surgical objectives.



Conceptual model of the underlying pathology.

THE RECONSTRUCTIVE PELVIC MEDICINE CLINIC AT SEATTLE CHILDREN'S HOSPITAL AND QUALITY IMPROVEMENT EFFORTS FOR PATIENTS WITH HIRSCHSPRUNG DISEASE



By: Caitlin Smith,
MD, MS
Assistant Professor



By: Samuel Rice-
Townsend, MD, MPH
Assistant Professor

Drs. [Caitlin Smith](#), Assistant Professor, and [Samuel Rice-Townsend](#), Assistant Professor, Division of Pediatric General Surgery, are pediatric colorectal surgeons at Seattle Children's Hospital (SCH), and are actively involved in the multidisciplinary [Reconstructive Pelvic Medicine \(RPM\)](#) Program, which Dr. Smith also directs. The RPM Program represents one of the few multidisciplinary pediatric colorectal and reconstructive pelvic surgery programs in the United States, offering a comprehensive approach to patients with complex surgical problems such as anorectal malformations, cloaca, and Hirschsprung disease (HD). The clinical and translational research they perform reflects the RPM Program's mission, aiming to improve the quality of life for patients affected by these conditions.

These conditions are rare and their management specialized, and for these reasons, their research often leverages collaboration with the Pediatric Colorectal and Pelvic Learning Consortium (PCPLC), an international consortium of surgeons and other specialists to facilitate multi-institutional studies. SCH was one of the founding centers for this collaborative.

In an example of this work, they recently examined practice patterns of botulinum toxin (Botox-BT) use in patients with Hirschsprung disease. Infants and children with Hirschsprung disease may struggle with obstructive symptoms after pullthrough procedure in up to 30% of cases. While injection of BT is widely accepted as a therapeutic option, its described use and patient selection varies. Using the PCPLC multi-institutional registry,

Drs. Smith and Rice-Townsend sought to characterize patterns of BT use across these referral centers as a step toward the development of consensus guidelines.

A total of 494 pediatric patients with Hirschsprung disease were included in the study between 2017 and 2021. About a quarter of patients received BT during the time period. Most patients underwent a pullthrough procedure alone while about 10% underwent a primary and redo pullthrough procedure.

Patients who had a redo pullthrough were more likely to receive BT and also received it more frequently. This was expected. Interestingly, however, patients who underwent primary pullthrough at a younger age were less likely to receive BT. While most of the patients who received BT were male and white, patients with Hispanic ethnicity were statistically less likely to receive BT when compared to non-Hispanic patients.

No significant difference was seen otherwise for the patients who received BT compared to those that did not in terms of sex, race, ethnic status, insurance status, or a diagnosis of Trisomy 21.

Looking at variability of BT use across centers, a wide range was seen. Percentage of HD patients receiving any BT varied significantly among hospital sites ranging from 8%-50% of HD patients. Frequency of BT also varied significantly by hospital site.

In summary, Drs. Smith and Rice-Townsend found that at referral centers, patients with Hirschsprung disease who required revisional surgery received more BT, while Hispanic patients received less. Additionally, there was a significant association between timing of pullthrough procedure and use of BT. These findings warrant further investigation. The wide variation in practice patterns across institutions also justifies ongoing efforts within the consortium to clarify best practice protocols for BT administration in patients with Hirschsprung disease.

Age and Timing of Botox Use in Hirschsprung Patients

	Patient ever received a Botox injection		Overall (N = 494)	P-value
	Yes (N = 118)	No (N = 376)		
Age in years at data lock (May 3rd, 2021)				0.406 ¹
< 5	48 (40.7%)	177 (47.1%)	225 (45.5%)	
≥ 5 and < 12	55 (46.6%)	150 (39.9%)	205 (41.5%)	
≥ 12	15 (12.7%)	49 (13.0%)	64 (13.0%)	
Endorectal pullthrough history				<.001 ¹
Only a primary pullthrough on record	83 (70.3%)	282 (75.0%)	365 (73.9%)	
A primary pullthrough and a revision on record	26 (22.0%)	23 (6.1%)	49 (9.9%)	
Age at primary endorectal pullthrough (months)				0.021 ²
N	109	305	414	
Median (Q1, Q3)	3.8 (1.5, 11.4)	2.9 (0.5, 7.8)	3.4 (0.7, 8.5)	
Age at primary endorectal pullthrough				0.019 ¹
< 1 month	22 (18.6%)	98 (26.1%)	120 (24.3%)	
1 month to 3 months	19 (16.1%)	58 (15.4%)	77 (15.6%)	
> 3 months to 6 months	28 (23.7%)	48 (12.8%)	76 (15.4%)	
> 6 months to 1 year	13 (11.0%)	49 (13.0%)	62 (12.6%)	
> 1 year	27 (22.9%)	52 (13.8%)	79 (16.0%)	

THE LONG GAME



By: David Marko Hananel
*Director, Center for Research in Education
 and Simulation Technologies
 Assistant Teaching Professor, Division of Healthcare
 Simulation Science*

By many measures, the United States military is the world's largest educational institution. They train service members in everything from basic language skills to the management and leadership of very complex organizations. Because of their educational mission, they also have been at the forefront of developing new tools and techniques and support many modalities of education, including simulation. One could easily argue that this simulation focus has given us flight simulators, the gaming industry, and head-mounted displays, amongst other innovations. For many years, they have been the only government agency to invest in research and development in healthcare simulation, including several projects undertaken by the UW [Center for Research in Education and Simulation Technologies \(CREST\)](#).

One of these projects, the Advanced Joint Airway Management Simulator (AJAMS), is now in its final phases of assembly and testing before going into a training effect study and a prolonged field test. AJAMS is a manikin-based physical trainer supported by a physiology engine that drives vital signs and allows physicians and medics to practice the management of patients with compromised airways. It is also the first such manikin to have both a female and male instance developed from the very beginning. The manikin goes well beyond technical skills training; it allows for complex scenarios to be implemented that require the provider to first identify what is wrong, then practice increasingly invasive techniques until the airway is secured. AJAMS is the perfect example that highlights the capabilities of CREST, and it has been a truly transdisciplinary team effort (creating a unity of intellectual frameworks beyond the disciplinary perspectives), driving forward the science of healthcare simulation.

In addition to its role in military education, our trainer will also go into service with our very own King County Medic One organization, the very same people we all depend on in case of a healthcare emergency. The acquisition of these systems by the Medic One program has been made possible by direct funding from the Washington State Legislature.

The CREST team has been following a long-term research agenda that ensures every new project we take builds upon our previous efforts, gradually building up a platform that allows us to tackle ever more complex projects. This would not be possible if we did not follow a well thought out roadmap. We not only pursue funding opportunities and collaborations that move the needle in the right direction, but we also seek out the best new team members that add to our overall capabilities.

The AJAMS project brought together all capabilities of our team, starting with human tissue characterization, moving into 3D anatomic modelling from real patient scans, followed by educational design, sculpting, molding, 3D printing, software development, closed loop electromechanical system design and educational research. Core team members have now been working together for over ten years and continue to follow the passion that brought us together from the very beginning.



So, what is next? As part of the [Division for Healthcare Simulation Science](#), with our sister organization The [WWAMI Institute for Simulation in Healthcare \(WISH\)](#), we are hard at work launching a Master's program in Healthcare Simulation Science to train the next generation of researchers, engineers, developers in our field.

RESEARCH STAFF HIGHLIGHTS

Jason Speich

*Research Scientist, Simulated Anatomy Team
Healthcare Simulation Science - CREST Lab*

**How did you get into this line of research?**

My background is in fine art. I studied ceramics and sculpture at a small school in Wisconsin. I had amazing mentors, and I became passionate about my studio classes. It absorbed my time and thoughts and I loved learning about manipulating materials and processes. This included clay, cast metal, woodworking, and electronics. Sculpture was a catch-all for diving into multiple skills. I then taught and ran a sculpture studio at an art school in Colorado. When I moved back to the Midwest I saw a posting for a temporary position at the **CREST** lab, a medical simulation group led by Dr. Rob Sweet, which at that time was in Minneapolis. Eventually, the position became permanent, and the group grew. It was an unexpected pairing for me, but my background helped me create our physical simulators and I learned about the medical procedures we were representing through collaboration. Our projects ranged from tabletop endoscope models with fine details to train scope navigation, a simulated C-Arm to help users safely learn needle guidance, to large, immersive trauma scenarios to train military medics. We build these simulators but also research what is important to simulate accurately during that training.

The CREST lab then moved to UW and I was lucky enough to be invited by Dr. Sweet to come to Seattle to continue the work for the past six years.

What does your typical workday look like/ what do you do?

My days are always dynamic. We often meet with clinicians to better understand a procedure and distill the necessary parts to recreate through simulation. This may be a tissue characteristic or a difficult step. We want to allow a user to correctly perform a procedure, but also allow for common errors that they can learn from. We create a setting where mistakes can happen without consequences. Quality training on simulators translates to improved patient care. I commonly use some very traditional techniques of molding and casting parts that represent patient anatomy. We are also finding innovative ways to combine these processes with new technology and materials. 3D-printing is a new interest of mine. Because the members in our lab have very different backgrounds, we teach each other about the possibilities of our specialties. My days include a mix of observing clinicians, researching procedures, design discussions, testing materials, and prototyping approaches.

What has been your most significant accomplishment/finding?

I find my work very fulfilling as it often has the creative and productive energy of a personal art practice. I am still creating a physical object that requires attention to detail and is setting up an interaction between a user/viewer, but what we are creating is serving a need through improving medical training. I know that I am doing my job well when I see students fully engaged in a procedure on a simulator or a clinician says that they felt their heart rate increase when they were stopping the bleeding in a trainer that we have built. It's an ongoing discussion and a large thrust of our research to better understand what amount of detail is needed to accurately represent a patient or procedure.

Advice for others looking to get into this field?

I wish I would have known about possible jobs like this earlier. I always had an interest in fabrication, engineering, and medicine, but never had formal training in any of these. I now have a job that gets me in the orbit of all these specialties, and it is my background that helped me get here. It was an unlikely path, but I have a unique position in a growing field. I try to encourage people with an art background to not be limited in their scope for finding jobs. Every forward-thinking group is looking for creative problem-solvers. The skills you have learned in your art practice can find a home in exciting and unlikely places.

TOWARD NEW PARADIGMS IN GLOBAL BURN CARE



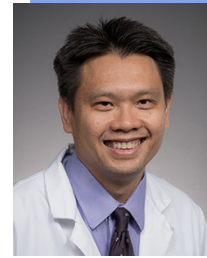
By: Barclay Stewart, MD, PhD, MPH
Assistant Professor

Dr. **Barclay Stewart**, Assistant Professor, Division of Trauma, Burn & Critical Care Surgery, at Harborview Medical Center and core faculty within **Harborview Injury Prevention and Research Center's (HIPRC)** Global Injury Section, is working to reduce preventable death and disability after burn injury. The vast majority of burn injuries happen in low- and middle-income countries (LMICs) due to energy poverty, unsafe cooking arrangements, and insufficient policies and regulations around specific hazards. People living in LMICs and in other austere settings (e.g., frontline military environments, remote and rural communities, etc.) commonly lack access to organized trauma and burn care systems. As a result, most people who sustain a major burn injury do not receive immediate, goal-directed fluid resuscitation, which leads to preventable death and disability from shock, acute kidney injury, lung injury, compartment syndromes, and progression of the burn injury.

Delays in resuscitation stem from resource limitations (e.g., lack of crystalloid solutions, central venous access devices, and monitoring equipment), stressful operational environments and limited burn care expertise. These issues can be overcome, in part, by an operationally advantageous method of resuscitation that can be done by patients themselves, their family or friends, lay and medical first responders, and by hospital-based providers. Enteral resuscitation - drinking fluid or having it administered through a nasogastric tube - is simple, operationally advantageous, safe and has proven efficacy for large volume resuscitation (e.g., cholera). Additionally, enteral resuscitation may promote intestinal blood flow and mitigate pathologic changes in gut immune function and shifts of microbiomes. The latter have known implications on the risk of developing acute respiratory distress syndrome (ARDS), sepsis and multiple organ dysfunction after major injury. Despite the potential utility of enteral resuscitation, controlled study of enteral resuscitation compared to intravenous (IV) resuscitation has not been performed.



Dr. Charles
Mock



Dr. Tam
Pham



Dr. Monica
Vavilala



Dr. Adam
Gyedu



Dr. Shankar
Man Rai

With outstanding mentorship from Drs. Charles Mock, Professor and HIPRC Global Injury Section Lead, **Tam Pham**, Professor & Chief, Burn Center, Division of Trauma, Burn & Critical Care Surgery, Monica Vavilala, HIPRC Director, Adam Gyedu and Shankar Man Rai, Dr. Stewart has received funding from the Department of Defense, NIH/Fogarty Center and institutional grants to study the effectiveness, implementation and gut-related impacts of enteral resuscitation with studies in:

1. Ghana (funded, seeking approvals) – cluster-randomized effectiveness trial at 24 hospital country-wide
2. Nepal (enrolling) – single-center randomized trial with focus on implementation
3. Harborview (data being collected) – multi-center observational study of enteral fluid administration and resuscitation outcomes
4. Harborview and Nepal (enrolling) – microbiome science projects to understand impacts of enteral resuscitation on the relative abundance of taxa within the gut and wounds of burn-injured patients.

Our goal is to determine who should receive enteral resuscitation, how to deliver it to maximize safety and effectiveness, and if it is operationally and/or physiologically advantageous compared to IV resuscitation. Stay tuned for data, implications and implementation toolkits from these projects in the months and years to come!

In addition to advancing the science of burn resuscitation in austere settings, these projects are promoting collaborative relationships with UW Department of Surgery and UW Medicine Regional Burn Center with HIPRC, long-time and new international research partners, Ghana Health Service, and Walter Reed/

AFRIMS Research Unit in Nepal (WARUN). These projects also support resident and fellow research and development of future surgeon researchers at UW and within Ghanaian and Nepalese training programs.



Drs. Barclay Stewart and research resident Kajal Mehta in Ghana meeting with collaborators Dr. Adam Gyedu (surgeon and injury control researcher at Kwame Nkrumah University of Science and Technology) and Commander Kwesi Nsful (surgeon and burn director at 37 Military Hospital) to discuss logistics of U.S. Department of Defense-funded, 'Far-Forward, Fluid First,' enteral resuscitation (4F EnteroResus) for major burn injuries in Ghana: a hybrid type II effectiveness-implementation cluster randomized trial.

INTERESTED IN LEARNING MORE ABOUT RESEARCH IN THE DEPARTMENT OF SURGERY?

PLEASE JOIN US FRIDAY, MARCH 25TH, 2022
FOR THE 27TH ANNUAL
SCHILLING RESEARCH SYMPOSIUM

"ACHIEVING HEALTH EQUITY IN SURGERY"



Guest Lecturer: Dr. Kathie-Ann Joseph

Professor, NYU Langone/NYU Grossman School of Medicine
Professor, Population Health
Vice Chair for Diversity and Health Equity
Department of Surgery and Transplant Institute

Where – UW Tower Auditorium and Zoom
(email dosadmin@uw.edu for Zoom invite)

RESEARCH STAFF HIGHLIGHTS

Erin Carney Fannon

Director, Program Operations
Surgical Outcomes Research Center (SORCE)



Erin and family

How did you get into this line of research?

I've been lucky enough to be involved in clinical research for the last 15+ years. I began as an Emergency Room Tech and Research Coordinator and have had the pleasure of working at several academic institutions around the country (and Switzerland) and on many different types of studies. I have been fortunate to work for passionate faculty members who direct their energy in improving healthcare and patient outcomes!

What does your typical workday look like/ what do you do?

My workday is a combination of project and grant meetings, as well as lots of coordination! I oversee all the Research Operations for our SORCE faculty members, which means every day and week is a little different depending on our priorities.

What has been your most significant accomplishment/finding?

We recently completed our [CODA Study](#) and have had our [results](#) published in several journals. This study is what brought me to the Pacific Northwest and SORCE, and I love the team we built here at UW and across the country. It has been instrumental to see the hard work your team has done put into practice, and even more exciting to hear how it impacts patients daily.

ASSOCIATION OF HSD3B1 (1245C) GENOTYPE WITH RECURRENCE AMONG POST-MENOPAUSAL WOMEN WITH ESTROGEN RECEPTOR-POSITIVE, HER2-NEGATIVE BREAST CANCER

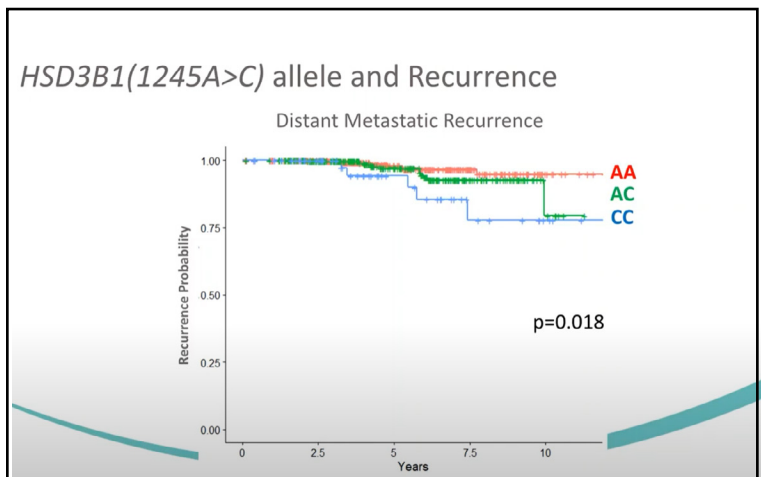
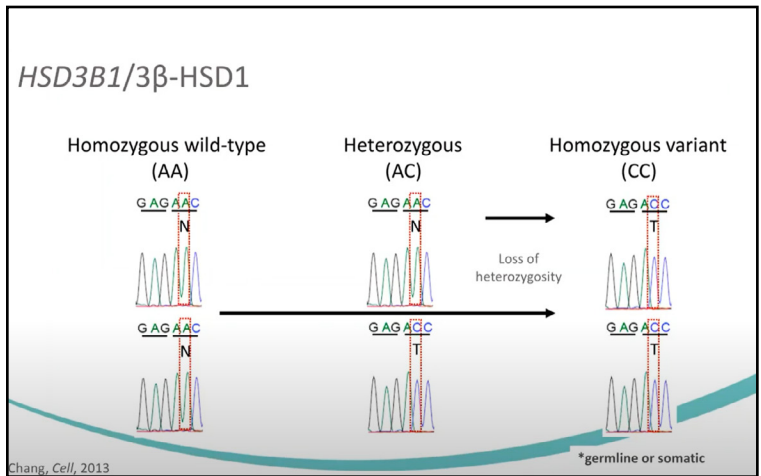


By: Meghan Flanagan, MD, MPH
Assistant Professor

Dr. **Meghan Flanagan**, Assistant Professor, Division of General Surgery, is a breast surgical oncologist who joined the UW Department of Surgery faculty in 2018. Furthering relationships she had established during her surgical residency at UW, she formed a cross-institutional, multidisciplinary team of researchers and physicians with basic science, clinical, translational and population health experience to investigate whether breast cancer outcomes are worse for the 25% – 30% women with postmenopausal estrogen receptor positive (ER+) breast cancer who harbor a genetic variation that changes the way they metabolize hormones. Inheritance of a single nucleotide polymorphism (1245A>C) in the gene hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1 (*HSD3B1*) results in gain-of-function in a key enzyme (3 β HSD1) involved in the conversion of adrenal androgens to estrogen. Her research team hypothesized that inheritance of the *HSD3B1* (1245C) allele would negatively impact breast cancer outcomes.

For this project, the gene was sequenced in 635 postmenopausal women with stage I-III, ER+, HER2/neu negative (HER2-) breast cancer who had been enrolled in a population-based study in Western Washington. Using extensively collected clinical and pathologic data about patient demographics, tumor and treatment data and recurrence rates, the team was able to show that women with two mutations in the *HSD3B1* gene had higher rates of distant metastatic recurrence compared to those women who did not have this mutation. Future studies will be forthcoming to determine how this

mutation may decrease the effectiveness of anti-estrogen medications that are used universally in post-menopausal ER+ breast cancer. This mutation is found in up to 15% of ER+ post-menopausal breast cancer patients, and if shown to decrease the effectiveness of anti-estrogen medications, there would be potential indications for alternative treatment strategies in these patients.



COMPARING OUTCOMES OF ANTIBIOTIC DRUGS AND APPENDECTOMY (CODA)



By: **David R. Flum**,
MD, MPH, FACS
Professor, General Surgery
Adjunct Professor, Pharmacy
and Health Services
Associate Chair for Research



By: **Giana H. Davidson**,
MD, MPH, FACS
Associate Professor,
General Surgery
Director, CODA Trial Clinical
Coordinating Center

What makes the CODA trial unique?

The CODA trial is the largest study of treatments for appendicitis to date and the first ever large-scale trial of treatments for appendicitis in the United States. CODA was designed as a pragmatic trial and launched at 25 different health systems across the US to represent a broad range of patients and healthcare systems. It was conducted in 14 US states as a collaboration of emergency medicine physicians, surgeons, health services researchers, and patient partners. By limiting study exclusions, we recruited a broad group of study participants to try to capture the wide range of appendicitis in the US population. Our randomized cohort included:

- The average age of participants is 38 years, and 24% of participants are over 50;
- 47% of participants identify as Hispanic;
- 37% of participants are women, and 34% speak Spanish as their primary language;
- 40% of participants have commercial insurance, and 18% of participants have Medicaid

Additionally, the CODA trial includes participants with a broad range of appendicitis severity. Prior studies have excluded most patients with the type of appendicitis typically seen in the United States. CODA included nearly all degrees of appendicitis severity, as well as patients who have an appendicolith, which

is a calcified deposit or stone in the appendix that is diagnosed by a CT scan. Appendicoliths are seen in ~27% of patients and are suspected of being related to more complicated cases of appendicitis. Since people with an appendicolith have usually been excluded from clinical trials of treatments for appendicitis, the CODA trial is the first to produce data to support this assumption regarding severity.

What are the main findings of CODA so far?

On October 25, 2021, the CODA trial team published its longer-term outcomes in the New England Journal of Medicine. These results report on CODA participants at 4 years following their initial treatment (i.e., antibiotics or surgery). Read the full report of results [here](#).

Deciding Between Antibiotics & Surgery for Appendicitis: Findings from the CODA Trial

Results of the CODA Trial tell us that both antibiotics and surgery may be good options for treating appendicitis. Each treatment has pros and cons. If you have appendicitis, you can talk with your doctor about what is most important to you when deciding on your treatment.

What is Important to Me	Antibiotics	vs	Surgery
Good Health	After 1 month, participants rated their general health about the same in both groups.		After 1 month, participants rated their general health about the same in both groups.
Initial Time in ER & Hospital	During the first visit, time spent in the ER or hospital was about the same in both groups.		During the first visit, time spent in the ER or hospital was about the same in both groups.
Symptoms Go Away	After 1 month, symptoms like pain or fever were about the same in both groups.		After 1 month, symptoms like pain or fever were about the same in both groups.
No Surgery	✓ About 7 in 10 (71%) did not have surgery within 3 months. Nearly 50% have surgery by 2 years.		✗ An appendectomy is surgery.
No Initial Hospital Stay	✓ About half (47%) did not have to be admitted to the hospital for their antibiotics treatment.		✗ Almost all (95%) participants were admitted to the hospital for their surgery.
Less Work Missed	✓ Participants missed an average of 5.3 days of work.		✗ Participants missed an average of 8.7 days of school or work.
Fewer Healthcare Visits	✗ 9 in 100 (9%) participants needed to visit an emergency room or urgent care clinic within 3 months.		✓ 4 in 100 (4%) participants needed to visit an emergency room or urgent care clinic within 3 months.
Appendicitis Does Not Return	✗ Appendicitis can come back if the appendix is not removed. This occurred in about 1 in 3 patients.		✓ The appendix is fully removed when surgery is successful.
One Time Treatment	✗ About 3 in 10 (29%) overall had surgery within 3 months. About 4 in 10 (41%) who had an appendix stone (appendicolith) had surgery within 3 months.		✓ Most likely to be completed in one hospital visit.
Complications (Unexpected Problems)	For every 100 participants, there were about 8 complications in the antibiotics group. There were about 4 complications for every 100 participants in the surgery group. The higher number of complications in the antibiotics group was related to participants who had a small stone in their appendix, called an appendicolith.		

The CODA Collaborative. A Randomized Trial Comparing Antibiotics with Appendectomy for Appendicitis. Published online October 5, 2020 at NEJM.org.
The CODA Collaborative.
Long-term Outcomes Paper still being published

For more information:
[CODAStudy.org](https://codastudy.org)

In the CODA trial, we found that antibiotics were not worse than surgery (called an appendectomy), based on a measure of general health and symptom resolution at 30 days. Approximately 3 in 10 of the participants who took antibiotics had to have an appendectomy by 90 days after starting antibiotics. At 1 year, the rate of appendectomy among those assigned to antibiotics was 40% and about 50% by 3 and 4 years.

We found that participants with a calcified deposit or stone in their appendix, called an appendicolith, were at higher risk for complications than those without an appendicolith. Increased risk of appendectomy in participants with appendicolith was observed mainly in the first 48 hours after randomization, and the association was largely reduced thereafter. Appendectomy was more common among those with appendicolith compared

with those without appendicolith at 1 year (52% vs 36%) and at 2 years (54% vs 43%).

Participants in the antibiotics group spent more time in healthcare settings (emergency department, hospital, urgent care clinics, etc.) but reported fewer missed days of work than those in the surgery group.

A BIT OF OUR HISTORY...

How A Surgical Research Powerhouse Is Built-One Chair At A Time



HIGH IMPACT COLLABORATIONS BETWEEN SURGERY AND ENGINEERING

In 1947 **Henry N. Harkins** becomes the first Chair of Surgery at the University of Washington. He was a founding member of the International Surgical Club and editor-in-chief of the journal, *Review of Surgery*.

- He recruited **K. Alvin Merendino** in 1949, who later performed the first open heart procedure on the West Coast in 1956. In 1950, Dr. Merendino becomes director of the Experimental Surgical Laboratory, and initiates a decades-long collaboration with bioengineers developing numerous surgical techniques and medical devices. He later becomes Department Chair in 1964.
- In 1960, **Eugene Strandness** joins the Department. At the rank of Associate Professor in 1966, he first described the clinical applications for the Doppler in diagnosis of peripheral arterial and vascular disease. In collaboration with UW engineers, he creates the duplex scanner in 1979, changing the science and practice of vascular medicine.



ADVANCES IN CARDIOVASCULAR RESEARCH

From 1983–1990, **C. James Carrico** is Chair and makes major faculty recruitments in cardiothoracic surgery and general surgery.

- In 1989 Ed Verrier is recruited and builds our strength in NIH-funded cardiovascular translational research.



STRATEGIC RESEARCH INVESTMENT AND CREATION OF A NEW DIVISION

In 2017 **Douglas Wood** becomes the Chair and adds to the Department's research mission, creating the Division of Healthcare Simulation Science, the Center for Surgical Ethics, as well as expanding the Department's research portfolio by recruiting 10+ surgeon scientists with research interests spanning Global Surgery, Oncology, Heart Failure, Trauma, Reconstruction and Pediatrics.



KEY RECRUITS ESTABLISH HARBORVIEW AS AN INTERNATIONAL LEADER IN TRAUMA, BURN AND CRITICAL CARE RESEARCH, AND GROUNDBREAKING VASCULAR RESEARCH BEGINS

In 1975 **John A. Schilling** begins as Chair and adds more than 40 new faculty members.

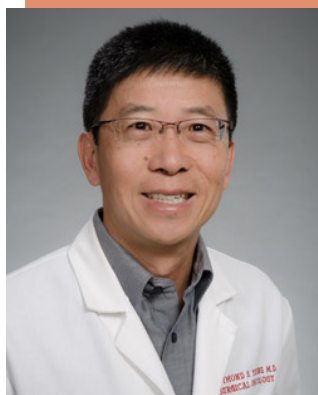
- **Loren Engrav, David Heimbach, C. James Carrico, and Ronald Maier** establish Harborview as an international leader in trauma, burn and critical care research. Our faculty lead major NIH-funded research initiatives including the GLUE grant led by Dr. Maier and several faculty, and in the arena of burns and inflammation, led by **Nicole Gibran**, with next phase work led by many current faculty.
- In 1980 **Alec Clowes** was recruited. He led a powerhouse vascular biology lab with continuous NIH-funding for over 30 years, and his vascular biology research continues today. Dr. Clowes also served as an interim chair preceding Dr. Pellegrini.



EXPANDING THE BREADTH OF CLINICAL AND TRANSLATIONAL RESEARCH

In 1993 **Carlos Pellegrini** is appointed as Chair and over the next 20 years grows the Department to more than 100 clinical or research faculty and over 50 APP faculty. Many faculty go on to develop robust clinical and translational research programs in Videoendoscopic Surgery, Simulation Science, Hepatobiliary Research, Global Health and Education. He also supports the establishment the multi-disciplinary Surgical Outcomes Research Center (SORCE) with its focus on improving the quality of surgical care, as well as the Center for Research in Education and Simulation Technologies (CREST), a program devoted to advancing the current state of medical train and patient education.

HPB RESEARCH



By: **Raymond Yeung**,
MD, FRCS (C), FACS
Professor
Division of General Surgery

The Hepatopancreatobiliary (HPB) Section maintains an active translational research program that focuses on key clinical questions directly related to the management of cancers arising from the liver, bile duct and pancreas. Examples of the current research portfolio are illustrated in the figures, which have received generous funding from extramural sources (e.g., National Institutes of Health, Department of Defense), along with industry, institutional, and philanthropic support. A common thread that runs through all of the

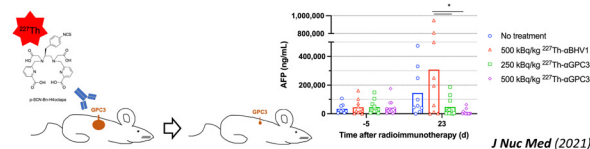
projects is the spirit of collaboration with scientists across many disciplines to apply the latest technologies in solving clinical problems. The highly acclaimed research environment at the University of Washington and **Fred Hutchinson Cancer Research Center** has provided fertile grounds for the HPB surgeons to work hand-in-hand with world-class experts in engineering, pharmacology, immunology, systems biology and data science to advance the highlighted areas of focus. We also partner with other colleagues in surgery, medicine, radiology, and pathology to generate ideas and to shape the optics of our research enterprise.

With the support of the Seattle Translational Tumor Research (STTR) Program, the HPB surgery team utilizes their ready access to clinical specimens to create a biorepository for multiple collaborations throughout the Puget Sound region. In recent years, the team led by Heidi Kenerson, Research Scientist in the Surgical Oncology Lab, has created and optimized a platform to study intact human cancers with the preserved tumor microenvironment. Operating through an IRB-approved biorepository, the organotypic models we generate have been adopted by many investigators to explore the behavior of tumors in response to drugs and other perturbagens using the new technology to define dynamic 3D tumor biology.

Another component of the HPB research program embraces the conduct of clinical trials to address critical gaps in patient care, such as the role of Lanreotide in suppressing fistula following pancreatectomy, the effectiveness of thermal (i.e., microwave) and non-thermal (i.e., electroporation) ablation in hepatic and pancreatic neoplasms, and the efficacy of hepatic arterial infusion chemotherapy in primary and secondary liver cancers. As these current and future studies play out, there is an increasing need to build a sustainable research infrastructure within the Department to protect and expand our basic and clinical research mission.



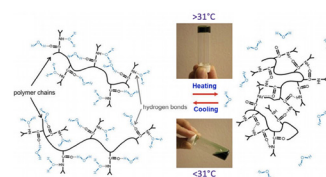
Improving liver cancer detection & therapy: α -GPC3 theranostics



James Park, MD, FACS
Professor
Division of General Surgery



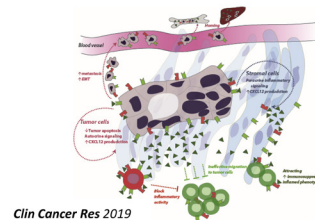
Reducing pancreatic fistula: thermo-responsive polymer



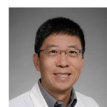
Jonathan Sham, MD, MBEE
Assistant Professor
Division of General Surgery



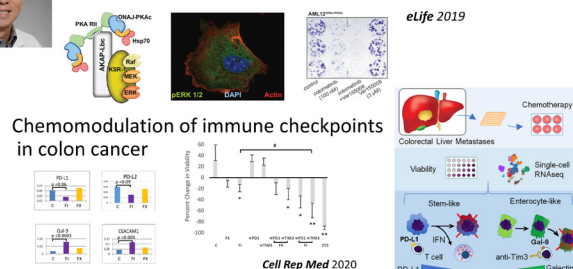
Overcoming immune escape in pancreatic and colorectal cancer



Venu Pillarisetty, MD, FACS
Professor
Division of General Surgery



Discovering new drugs for fibrolamellar liver cancer



Raymond Yeung, MD, FRCS (C), FACS
Professor
Division of General Surgery

SURGICAL EDUCATION RESEARCH GROUP



By: **Karen Horvath**,
MD, FACS

Professor, General Surgery
Associate Chair for Education
Chief, Division of Education

"I'm extremely proud to provide this introduction to the DOS Surgical Education Research Group (est. 2019). One goal of the new DOS Division of Education (est. 2017) is to come together as a community and bring expertise in all-things-education under one umbrella. Our Division's foundational early work has been to first focus on administrative infrastructure by convening our incredible education staff across the department. We added the DOS Residency Program Council and then Education Division meetings to find new ways to work together. The parallel introduction of a research arm with the DOS Surgical Education Research Group is an inspired and substantial contribution.

So if you're interested in education research, "Come one, come all!" Our hope is to have people from all corners of the department represented and benefiting in a symbiotic way. On behalf of the Division of Education and our department community: "Thank you Drs. Tatum and Langdale for your visionary leadership"



By: **Lorrie Langdale**, MD, FACS

Professor & Chief,
Section of General Surgery
VA Puget Sound Health Care System

The University of Washington Department of Surgery (DOS) has been a leader in surgical research for decades. Projects have ranged from analyses of the inner workings of macrophages and cancer cells to the evolution of atherosclerotic plaque, refinement of anti-reflux procedures and outcomes related to clinical decisions in surgical practice. Despite these successes, securing protected time and funding to push back the walls of science has proven increasingly difficult, and faculty have found their interests veering toward the third mission of academia: education.



Dr. Roger
Tatum

Two years ago, Dr. **Roger Tatum**, Professor & Chief, Division of VA Health Care, and I inaugurated the Surgical Education Research Group. The group is open to any faculty with a passion for education. All that is required is commitment, ideas, and enthusiasm. We meet monthly to propose projects, develop aims and methodology, discuss results and to resolve any barriers to project completion. Basically, this is the Education Lab meeting! Faculty may assume a variety of roles: project leader/primary author; team member with responsibility for specific sections of a project; editing and manuscript review. Their reward is authorship commensurate with their

contributions. The goal is to raise all boats, enhancing education of medical students, residents, and faculty while also supporting junior faculty promotion. I admit my role is primarily that of taskmaster, setting goals for completion, offering editorial advice, and getting the project across the finish line!

We have already seen some significant successes. Here are a few examples:

Drs. **Sarah Atkinson**, Assistant Professor, Division of General Surgery, **Nicole Zern**, Assistant Professor, Division of General Surgery, **Deborah Marquardt**, Division of VA Health Care, and Roger Tatum, designed a project to assess the impact of remote learning during the pandemic on medical student career choices. This project was presented as an abstract for the Association of Surgical Education meeting for 2021 and the paper is under review.

Dr. Zern is surveying surgical program directors about their expectations of new interns, day one versus month three. Given the many changes in medical school curricula as well as AAMC/ACGME requirements over the last 20+ years since I asked a similar question (not to mention the impact of remote learning), it will be interesting to gauge current impressions of appropriate surgical residency preparation.



Dr. Sarah
Atkinson



Dr. Deborah
Marquardt



Dr. Nicole
Zern

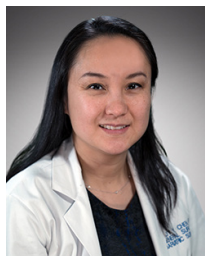


Dr. Kathleen
Berfield

Dr. **Kathleen Berfield**, Assistant Professor, Division of Cardiothoracic Surgery, corralled a **WWAMI** student to build a valid abdominal wall model that can be assembled at home and used to teach skin and fascial closure by Zoom during the Transition to Residency sessions. Dr. Marquardt is the overall surgical lead for the surgical section of this School of Medicine requirement. Together, she and Dr.

Berfield have designed and refined didactic and practical learning modules that work well, even in a remote format and their stellar evaluations reflect the appreciation of several graduating classes!

Dr. **Judy Chen**, Assistant Professor, Division of General Surgery, is working with David Hananel, Director, Center for Research in Education and Simulation Technologies, to develop a bowel anastomosis simulation model in conjunction with the Healthcare Simulation Sciences Division. This one is very challenging, requiring a detailed description of nearly every conscious (and unconscious) movement and decision that goes into an anastomosis, and an analysis of the quality of materials integral to the engineers' understanding of how to build a true to life simulated but reusable bowel.



Dr. Judy
Chen

Dr. **Kristine Calhoun**, Professor, Division of General Surgery, who has been very successful independent of our group in a variety of education projects, has joined with Dr. **Sara Kim**, Research Professor, Division of General Surgery, to develop a study exploring medical student expectations of their surgical clerkship experience.



Dr. Kristine
Calhoun

With DoS chair Dr. Douglas Wood's support, Deborah Marquardt, Sara Kim, **Jeff Friedrich**, Professor, Division of Plastic Surgery, and I completed a paper triangulating respect scores from medical students, residents and patients assessing surgical faculty. The data potentially allow identification of mentors and coaches to improve fellow faculty behavioral interactions with students, residents and even patients. This paper is in press in the high-profile journal, *Surgery*.



Dr. Jeffrey
Friedrich

This is an exciting time in the Department of Surgery if you have a passion for education. You'd be welcome to bring your ideas, the time, and commitment to the DOS Surgical Education Research Group.

FANTA-SIM FOOTBALL

The 7th Department of Surgery Resident Robotic Simulation Tournament, FANTA-SIM FOOTBALL, is in full swing! The theme for this edition is based on fantasy football and will have six teams of six highly skilled residents from all levels battle it out on the virtual gridiron to see who gets to hoist the trophy at the end of the season. The grueling 16-week season is comprised of eight games, each consisting of two to three simulation training modules of varying degree of difficulty. The competitors have two weeks to perfect their composite scores on the modules for each game. FANTA-SIM FOOTBALL kicked off on October 8th, and will end February 11, 2022 two days prior to the 56th Superbowl Sunday. With a lot on the line for the competitors – trophy, prize money, academic recognition, and most importantly, bragging rights—we anticipate that the competition will be just as fierce as those of previous years. A special recognition to our colleagues at the WWAMI Institute for Simulation in Healthcare, for providing us a COVID safe environment for 24/7 scrimmages and heated competition.



SURFING THE RESEARCH WAVE



By: Billanna (Billie) Hwang, DHsc
Research Scientist



Dr. Michael Mulligan

A little over eight years ago, Dr. [Michael Mulligan](#), Professor & Chief, Division of Cardiothoracic Surgery, and Billanna (Billie) Hwang, DHsc, Research Scientist, embarked on a journey focused on investigating the complex host immune responses and development of therapeutics in the field of lung transplantation—an area that has been underserved in the research arena. Both wanted to focus on the importance of translational research, merging preclinical benchwork with clinical outcomes. With their leadership, [Drs.](#)

[Mulligan and Hwang's work](#) has impacted the field of lung transplant by redefining the “classical” understanding of transplant immunology through identification of a novel class of immune mediators called exosomes. Characterization of exosomes to create profiles and correlating to adverse clinical outcomes posttransplant has started to provide new understanding in many areas including donor selection, primary graft dysfunction (PGD), and acute and chronic rejection processes. Along with these studies, the lab has also been able to lead the way in other novel projects investigating the role of exosomes in a variety of diseases including cystic fibrosis and idiopathic pulmonary fibrosis (IPF), and in other solid organ transplants. In addition to their own research, Drs. Mulligan and Hwang created a network of clinicians looking to collaborate on translational research projects. These studies included work with Dr. [Farhood Farjah](#), Endowed Chair in Lung Cancer Research, Division of Cardiothoracic Surgery, in identifying novel biomarkers in non-small cell lung cancer, Dr. [David Mathes](#), Professor and Chief of the Division of Plastic and Reconstructive Surgery, University of Colorado Anschutz Medical Campus, in investigating the role of exosomes in a vascularized composite allotransplantation model, and Dr. [Aaron Cheng](#), Associate Professor, Division of Cardiothoracic Surgery, and in acute kidney injury after lung transplantation.



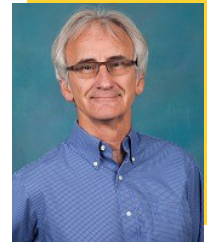
Dr. Farhood Farjah



Dr. David Mathes



Dr. Aaron Cheng

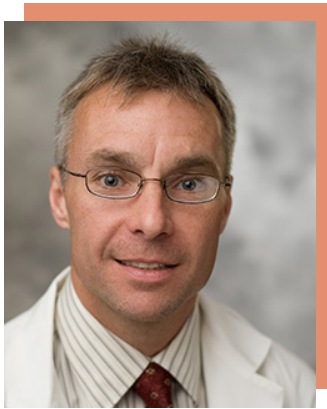


Dr. James Bryers

Another novel collaboration that Drs. Mulligan and Hwang started five years ago was the development of a “satellite” lab with Dr. [James Bryers](#), Professor, Department of BioEngineering. This collaboration is focused on addressing the need to develop therapeutic technologies that could be used in transplant to understand the host response to these biomaterials. Currently, studies have focused on the use of porous templated scaffolds (PTS) and the ability to change the host response towards an anti-inflammatory/regenerative process at the cellular and exosome levels.

In addition to being the pioneers in exosome immunology, Drs. Mulligan and Hwang identified a lack of access to clinical biospecimens for research in lung transplantation and plans to develop an infrastructure were started in 2018. In 2019, the University of Washington Lung Transplant Biorepository (LTB) centralized repository was started and housing biospecimens from patients including serum, cells, exosomes, and explants at various time points throughout a transplant. The overall success of this endeavor was achieved through strong leadership in coordinating a network of collaborating teams within the UW DOS including the pulmonary department, donor procurement, nurses, and research groups. Because of the continued success, the UW LTB was recently used as a template for the development of a future national lung transplant biorepository, which both Drs. Mulligan and Hwang will possibly be leading in 2022. Drs. Mulligan and Hwang could not have done these studies without the amazing support of their research staff and clinical teams, and are extremely excited about the impact these studies will have in their respective fields.

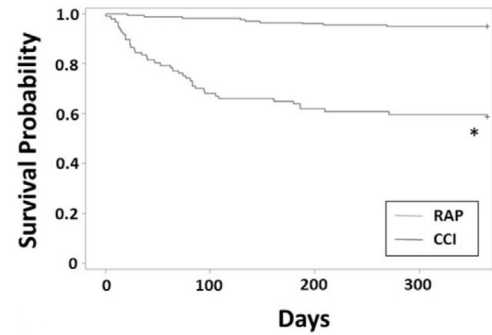
TRANSLATIONAL RESEARCH AIMED TO UNDERSTAND THE SYSTEMIC METABOLIC RESPONSE AND TO IMPROVE TREATMENT AND OUTCOMES IN SEVERELY INJURED PATIENTS



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

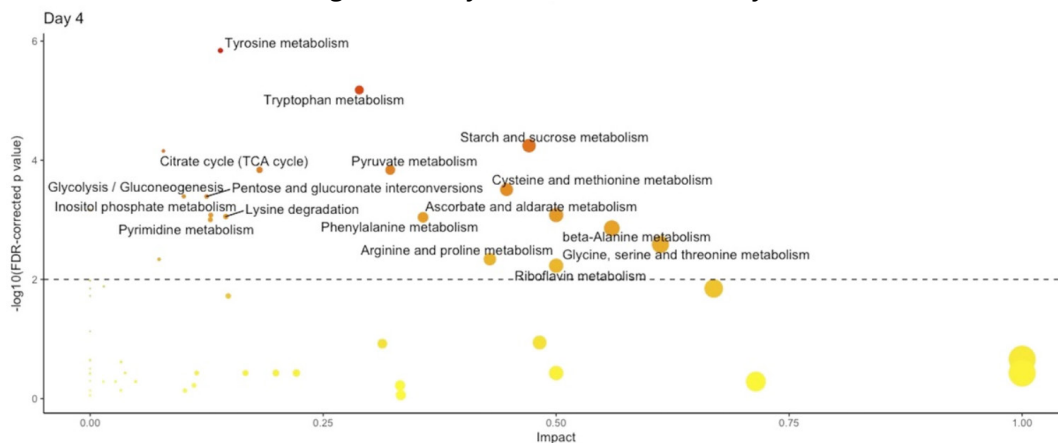


in the days to weeks after trauma and critical illness in ways that will improve longer term outcomes. The overarching aims of our research program are threefold:

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

Surgery News

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