Pedi Press

A Quarterly Publication of the Department of Pediatrics

Baylor College of Medicine

Vol. 10, Issue 4, Part II

Fall 2021



TABLE OF CONTENTS PART II

DEPARTMENT NEWS: FACULTY, FELLOWS, RESIDENTS & STAFF	
Dr. Heslop Elected to National Academy of Medicine	3
Chair Announces Vice Chair Appointments	4
Faculty Recognized for Outstanding Contributions to their Fields	6
Endowed Chairs and Professor Announced	7
Tropical Medicine Researchers Featured in "Herminthology"	8
Faculty briefs	10
DEPARTMENT NEWS: RESEARCH	
Patent-Free Vaccine in India Comes All the Way from Texas	13
Vaccine Candidate Receives Approval in India	14
Study Provides Rationale for Pediatric Trial of Treatment for pAML	16
Genetic Studies Demonstrate Value of Using Set of Criteria for Evaluating	
Multilocus Pathogenic Variations	17
Researchers Study Role of Endothelial Cells in Blood Clotting	18
UPCOMING EVENTS	19
"END WITH GOOD STUFF"	
Therapy for Medical Staff Comes with Four Paws	21



DEPARTMENT NEWS FACULTY, FELLOWS, RESIDENTS & STAFF

Dr. Heslop Elected to National Academy of Medicine



Dr. Helen Heslop, Professor and Dan L. Duncan Chair at BCM, was elected to the **National Academy of Medicine** in October 2021. She is among 90 regular members and 10 international members who were announced at this year's annual meeting. A physician-scientist, she is engaged in translational research that focuses on adoptive immunotherapy with gene-modified effector cells to improve hemopoietic stem cell transplantation and cancer therapy. Her extensive experience includes developing and

conducting transplant studies and cell and gene therapy studies. She currently holds more than 20 investigational new drug applications. She has played major roles nationally in societies that focus on the intellectual and clinical development of cellular therapies and accreditation of facilities delivering cell therapies. Election to the National Academy of Medicine is one of the highest honors one can achieve in the fields of health and medicine. It recognizes individuals who have demonstrated outstanding professional achievement, including major contributions to the advancement of the medical sciences, health care, and public health, and commitment to service; new members are elected by current members.

Chair Announces Vice Chair Appointments



In October and November, **Dr. Catherine Gordon**, Professor and Chair of the Department of Pediatrics, announced the following leadership appointments:



Dr. Lara Shekerdemian, Professor and Division Chief, Critical Care, was appointed to the position of **Executive Vice Chair**, with a focus on clinical operations. Dr. Gordon noted that, "Lara has done a spectacular job leading our critical care teams through the pandemic, including surges of both RSV and

COVID-19. She will be our fourth Executive Vice Chair (with Drs. Kang, Shook and Schutze)." Dr. Shekerdemian came to BCM/TCH in September 2010 from The Royal Children's Hospital in Melbourne, Australia, to assume the positions of Chief of Critical Care at TCH and Chief of the Division of Critical Care at BCM.

A native of London, England, she trained at The Royal Brompton Hospital and The Great Ormand Street Hospital in London and at The Hospital for Sick Children in Toronto, Canada. She is an internationally recognized leader in pediatric intensive care.

Before joining BCM, she served as Director of Intensive Care at The Royal Children's Hospital in Melbourne, Australia, and as an associate professor of Pediatrics at the University of Melbourne. At Royal Children's, she established a groundbreaking program that transported patients receiving extracorporeal membrane oxygenation (ECMO) treatment hundreds of miles to the hospital. Despite medical challenges of providing critical care in a mobile setting, this service achieved survival rates that rival ECMO programs at some the world's top children's hospitals.



Dr. Jean Raphael, Assoc. Professor and Division Chief, Academic General, was appointed to the position of Clinical Vice Chair (Dr. Shekerdemian's previous role). Dr. Gordon noted that, "In his new role, he will continue to work closely with Dr.

Chris Greeley as together, they consider opportunities for community engagement."

He received his B.A. from Williams College, MD from Harvard Medical School, and MPH from the Harvard School of Public Health. He also completed the Commonwealth Fund Harvard University Fellowship in Minority Health Policy.

Dr. Raphael is founding Director of the Center for Child Health Policy and Advocacy at TCH and serves as Chair of the Public Policy and Advocacy Committee of the Academic Pediatric Association. He is a past appointee of the Lieutenant Governor to the Texas Health Disparities Task Force. He is a nationally recognized health services researcher with a focus on improving systems of care for underserved and minority children with chronic conditions.

Dr. Raphael's awards have included the Research Mentorship Award from the Department of Pediatrics at BCM, Health Advocacy Award from Doctors for Change, and Meritorious Service Award from the Texas Health and Human Services Commission.



Dr. Jeff Joongmyung Kim, Professor, was appointed to the position of Vice Chair for Faculty Development. Dr. Kim received his MD from University of Illinois, Chicago Circle. He did his internship and residency in pediatrics at University of Illinois.

In 2006, he completed fellowships in pediatric cardiology and pediatric electrophysiology at Baylor College of Medicine.

Dr. Kim is the Director of the Arrhythmia and Pacing (Electrophysiology) Service at Texas Children's Hospital. He is also a member of the Heart Failure / Cardiomyopathy Service. He is involved in collaborative translational research in molecular cardiology and is on faculty with the Translational Biology and Molecular Medicine Department, as well as the Cardiovascular Research Institute.

His specific clinical interests include cardiac ablation techniques in children and the management of genetic arrhythmia syndromes. He also has a special interest in molecular mechanisms of sudden death and arrhythmias in heart failure.

His research interests include the clinical characterization of arrhythmias and cardiomyopathies, as well as the delineation of their molecular and genetic bases. He has a particular interest in the role of pharmacogenetics in the management of arrhythmias and cardiomyopathy.



Dr. Susan Lanelle Gillespie, Assoc. Professor, was appointed to the position of Vice Chair for Diversity, Equity and Inclusion (DEI). She received her MD and PhD from Case Western Reserve University, Cleveland, Ohio, and did her internship at Washington

University, St. Louis, Missouri.

She has served as an Associate Program Director for the Pediatric Residency Program, as the Director for Senior Electives for the Department of Pediatrics, and as mentor to pediatric residents. As a part of BIPAI, Dr. Gillespie has worked in Zambia, Kyrgyzstan, and Kenya and most recently served as the Director of Medical Services in Tanzania, where two BIPAI clinical centers of excellence are located. She spent two years working to establish the BCM Centers of Excellence in Mbeya and Mwanza, Tanzania. She is an invited member of the American Academy of Pediatrics Committee on Pediatric AIDS.

Dr. Gillespie's clinical activities reflect a strong interest in international health and in providing care to underserved populations. She has cared for children and adolescents exposed to or infected with HIV both in the U.S. and in several countries in Sub-Saharan Africa. In addition, she provides care for children adopted from other countries, care and advice for children who travel outside the country, and primary care to children at the San Jose Clinic, a facility dedicated to the care of families who are uninsured in the Houston area.

Dr. Gillespie also has an interest in program development and would like to conduct quality improvement projects in various facilities to optimize patient care and safety and maximize use of limited resources.

Dr. Gordon invited all of the candidates for the position of DEI Vice Chair to join the Department's Executive Steering Committee in the Department of Pediatrics, established by **Dr. Gordon Schutze**, Professor, during his tenure as Interim Chair.



Faculty Recognized for Outstanding Contributions to their Fields



Dr. Morven S. Edwards, Professor, an expert on bacterial infections in newborns, is the recipient of a 2021 Distinguished Physician Award from the Pediatric **Infectious Diseases Society** (PIDS). The annual award recognizes a pediatrician who

has an extensive and distinguished career in pediatric infectious diseases marked by significant accomplishments and contributions in infectious diseases, including those as a clinician, educator, and/or investigator.

The honor was presented this year following the virtual IDWeek (September 29 - October 3, 2021), the premier scientific meeting for infectious diseases professionals.

Dr. Edwards is recognized worldwide as an expert on neonatal infections, most notably those caused by Group B *Streptococcus* bacteria. Her innovative work has defined the epidemiology, clinical characteristics, pathogenesis, and outcomes of these serious infections, which still affect far too many infants with tragic consequences. She has also detailed how this pathogen affects vulnerable adults and has advanced our understanding of the body's immune response to this bacteria, thereby leading towards the development of vaccines.

A skilled clinician and educator, Dr. Edwards has also been an inspiring role model for medical students and other trainees throughout her time at BCM, where she has supervised or co-supervised the research of 36 postdoctoral fellows and pediatric residents. She has published more than 160 original publications and 70 book chapters and reviews, from epidemiologic and clinical studies of pediatric bacterial meningitis, pneumonia, bone and joint infections, and fungal infections to basic science and translational research about the pathogenesis of disease.

Dr. Edwards earned her medical degree and completed her residency at BCM. She completed her fellowship training in pediatrics and pediatric infectious diseases at Baylor and Harvard Medical School in Boston.

Dr. Huda Zoghbi, Professor and Director of the Jan and Dan Duncan Neurological Research Institute, accepted the Lundbeck Foundation Brain Prize, the largest prize for neuroscience in the world, at a recent awards



ceremony in Copenhagen. Her co-recipient was Sir Adrian Bird of the University of Edinburgh, Scotland,

The award recognized her role in discovering a gene mutation that causes Rett syndrome and in establishing the importance of epigenetic regulation in both brain development and the maintenance of normal adult brain function. These discoveries also point to novel opportunities for treatment of this syndrome and other neurodevelopmental disorders.

The annual award, formerly known as the Grete Lundbeck European Brain Research Prize, recognizes highly original and influential advances in any area of brain research. The prize, worth more than \$1.5 million, is awarded to one or more scientists who have distinguished themselves through outstanding contributions in their field. Winners are decided by a panel of the world's top neurological researchers after nomination by peers.

Dr. Zoghbi began studying Rett syndrome in 1983, and in 1999, she identified the gene mutation that causes the disorder. Her research revealed that Rett syndrome is caused by mutations in the MECP2 gene that encodes a protein with the same name, MECP2, which Sir Adrian Bird identified in 1992. Her monumental discovery created a path to developing a diagnostic genetic test, allowing early and accurate diagnosis of Rett syndrome.

Dr. Zoghbi commented, "I am deeply honored and humbled to receive the Brain Prize. I share this with all my trainees, past and present, who have worked so hard to advance research on Rett syndrome. I am grateful to the Lundbeck Foundation for this prize and what it means for our ability to continue pushing the boundaries of discovery to help people with Rett syndrome and MECP2 duplication 6 disorder."

Endowed Chairs and Professor Announced

Dr. Susan M. Blaney, Chair of the Division of Hematology-Oncology, announced the following new endowed chairs and professorship:



Dr. Carl E. Allen Milton and Allene Nirken Chair in Pediatric Oncology

Dr. Allen is director of the Basic and Translational Research Strategy for the Texas Children's Cancer and Hematology Center.

He also serves as co-director of the Histiocytosis and Lymphoma Programs, where he leads a team of over 30 clinicians and scientists dedicated to improving the outcomes of children and adults with histiocytic disorders, lymphoma and lymphoproliferative disorders.



Dr. ZoAnn E. Dreyer Sidney L. and Donald F. Faust Professor in Pediatric Cancer Survivorship

Dr. Dreyer has been the clinical director of the Long-Term Survivor Program since its

inception in 1988 and is nationally recognized for her work in survivorship. Under Dr. Dreyer's leadership, the Texas Children's Cancer Center Survivorship Program was the recipient of the Inaugural Survivorship Champion's Prize from the Children's Cancer Cause, in recognition of the Program's innovate work to provide comprehensive, integrated care for childhood cancer survivors.



Dr. Philip J. Lupo Endowed Chair in Molecular Epidemiology

Dr. Lupo is a leading molecular epidemiologist whose research is focused on the origins of childhood cancer and other

pediatric conditions. He is the Director of the Epidemiology and Population Sciences Program at the Center, Chair of the Epidemiology Committee in the COG, and is involved in leadership positions for several national and international organizations, including the Society for Birth Defects Research and Prevention.



Dr. Leonid S. Metelitsa Endowed Chair in Cancer Immunotherapy

Dr. Metelitsa is director of the Center for Advanced Innate Cell Therapy, co-director of the Neuroblastoma Program, and

an Associate Director of the Texas Children's Cancer and Hematology Center. Dr. Metelitsa's research focuses on a subset of immune cells known as natural killer T (NKT) cells and their role in fighting cancer.



Dr. Donald Williams "Will" Parsons Sidney L and Donald F. Faust Chair of Pediatric Cancer Precision Medicine

Dr. Parsons is a board-certified pediatric oncologist and the D

Deputy Director of Texas Children's Cancer and Hematology Center. Research discoveries from his team have provided key insights into cancer genetics and impacted the diagnosis and treatment of both childhood and adult cancer patients.



Dr. Michael Scheurer Sidney L. and Donald F. Faust Chair of Pediatric Cancer Epidemiology

Dr. Scheurer is a molecular epidemiologist at Texas Children's Cancer and

Hematology Center and serves as co-leader of the Cancer Prevention and Population Sciences Program in the Dan L. Duncan Comprehensive Cancer Center at Baylor College of Medicine. Dr. Scheurer's research focuses on understanding the environmental and genetic risk factors (especially viruses and immune function) for cancer development, and characterizing the factors that contribute to poor outcomes for children and adolescents treated for cancer.

Tropical Medicine Researchers Featured in "Herminthology"**

"My fascination for parasitology, especially soiltransmitted helminths, started during my training by joining field projects to establish the prevalence of intestinal worms in remote Honduran communities."

Dr. Maria Elena Bottazzi Associate Dean National School of Tropical Medicine Baylor College of Medicine, Texas







"I love what I do because my job allows me to care for patients with tropical diseases, perform research with the goal of preventing future patients from acquiring tropical diseases, and teach the next generation of tropical medicine and HIV specialists!"

Dr. Eva Clark Assistant Professor National School of Tropical Medicine Baylor College of Medicine, Texas



"Since my veterinary training I have been fascinated by zoonotic disease, in particular how parasites can move between mammalian hosts and humans, the environment, and sometimes insect vectors."

> Dr. Kathryn Marie Jones Research Veterinarian National School of Tropical Medicine Baylor College of Medicine, Texas



BALBc mice 26 days post infection with *Trypanosma cruzi* Dr. Kathryn Marie Jones

*extracted from Instagram



"As a Hispanic, it feels great to make a difference with all our research findings in countries like Honduras and create to awareness of and develop better solutions for global health issues."

> Maria Jose Villar Mondragon Master of Science candidate National School of Tropical Medicine Baylor College of Medicine, Texas



"Trypanosoma cruzi – the cause of Chagas disease – is not only pretty, but also a challenging and smart parasite that avoids the host immune response trying to eliminate it."

> Dr. Cristina Poveda C. Research Associate Baylor College of Medicine, Texas and Center of Vaccine Development, Texas Children's Hospital





Immunofluorescent microscopy DC2.4 cells 24 hours post transfection with *Trypanosoma cruzi* Antigen 1 + Antigen 2 mRNA Dr. Cristina Poveda

"My career goal is to become a leader in helminthology in order to positively impact our global community through performing high-quality translational research in tropical medicine and investing in the education of future generations of tropical medicine academic trainees."

Dr. Jill Weatherhead Physician-scientist National School of Tropical Medicine Baylor College of Medicine, Texas





Ascaris larvae Dr. Jill Weatherhead

Faculty briefs ...

Dr. Samiya Fatima Ahmad, Asst. Professor, received the A. B. Baker Teacher Recognition Award from the American Academy of Neurology. The award recognizes "respect and appreciation for neurologic teaching," with acknowledgement that "excellent teachers deserve recognition for their contributions to improving neurology now and in the future."

Dr. Saleh Bhar, Asst. Professor, received the BCM Early Career Faculty Award for Excellence in Patient Care in December 2021.

Dr. Maria Elena Bottazzi, Professor and Associate Dean of the National School of Tropical Medicine, was recognized as an 'Outstanding Woman' by the Commission for Women, Children, Youth and Family of the Central American Parliament within the framework of the Forum of Women of Political Parties of Honduras. Organized by the Honduran Parliament Bench, Dr. Bottazzi was recognized for her work in vaccine research and development, especially her contributions to advance a COVID-19 vaccine.

Dr. Dave Brennen, Asst. Professor, received a Red Pin TCH Ambulatory Practitioner Award for Excellence in Patient Experience. The award recognizes providers with mean score of 99% or above on the provider section of Press Ganey Survey.

Dr. Daniel Calame, Postdoctoral Fellow, was one of 11 researchers across the country awarded a Development Grant from the Muscular Dystrophy Association. These grants are awarded to investigators at the beginning of their careers with the goal of supporting the next generation of researchers. Dr. Calame's project is titled "Uncovering the Genomic Architecture of Undiagnosed Neuromuscular Disease."

Dr. Judith Campbell, Professor, was elected President of the Texas Children's Hospital medical staff for 2022.

Dr. Hsiao-Tuan Chao, Asst. Professor, spoke on November 19 on a virtual panel about her part in "STAT Wunderkinds: 5 Years of Progress." The STAT Wunderkinds program is for early career researchers in health and medicine. Chao is a McNair scholar for the McNair Medical Institute at the Robert and Janice McNair Foundation and investigator in the Jan and Dan Duncan Neurological Research Institute at Texas Children's Hospital.

Dr. Corrie Chumpitazi, Assoc. Professor, was

-- nominated as one of the Pediatric Emergency Medicine Representatives to the FLEXpeds group of the American Academy of Pediatrics

-- appointed as the AWAEM (American Women in Academic Emergency Medicine) Vice President of Corporate Development for 2022 – 2023

-- appointed to the Board of the Society of Pediatric Sedation

Dr. Teresa Davis, Professor, was recognized as an American Society for Nutrition Fellow at the annual meeting. The Fellow Award is the highest honor that ASN bestows and recognizes scientists who have had distinguished careers in the field of nutrition. She is editor-in-chief of *The Journal of Nutrition* and a past-president of ASN.

Dr. Ricky Flores, Asst. Professor and Clinical Director of the Cancer and Hematology Center, TCH in The Woodlands, was

-- recognized with the 2021 Outstanding Community Caretaker Award by The Morgan Frazier Cancer Foundation, which included a special recognition from Mayor Sylvester Turner.

-- honored by the University of Houston with a Philanthropy Award in recognition of his outstanding community service and generosity.

Dr. Saul Flores, Assoc. Professor, was elected to membership in the Society for Pediatric Research (SPR).

Dr. Lisa Forbes, Asst. Professor, was elected to membership in the Society for Pediatric Research (SPR).

Dr. Susan Gillespie, Assoc. Professor, was selected as the Vice Chair for Diversity, Equity, and Inclusion for the Department.

Dr. Maria Monica Gramatges, Assoc. Professor, was elected to the American Society of Clinical Investigation.

Dr. Heather Haq, Asst. Professor,

-- graduated from the Young Physician Leadership Alliance (YPLA) program, a 2.5-year longitudinal leadership development program through the American Academy of Pediatrics Section on Early Career Physicians in October 2021. This program is designed to accelerate leadership skills of promising young physician leaders, through seminars, workshops, coaching, and a longitudinal leadership project.

-- presented leadership reflections on "Developing a Multi-Level COVID-19 Preparedness and Response Support System for the Baylor College of Medicine International Pediatric AIDS Initiative (BIPAI) Network" at the YPLA summit in October 2021.

Dr. Helen Heslop, Professor, was named in the Clarivate Highly Cited Researchers List for 2021.

Dr. Peter Hotez, Professor and Dean of the National School of Tropical Medicine, was awarded the 2021 Robert Wood Johnson Foundation David E. Rogers Award at the virtual ceremony recently held by the AAMC. The award honors a medical school faculty member who has made major contributions to improving public health and healthcare.

Dr. Sara Iman, Resident, received a PEAR (Professional Educator Appreciation and Recognition) award, an award recently founded by BCM students that requires submission of nomination by a student of any year attesting to the physician's personal influence or inspiration.

Dr. Shaniqua (Shani) Johnson, Fellow, received the 2021 Jeanne Marie Lusher Diversity Fellowship Award from the National Hemophilia Foundation for her research entitled, Determining Clinical Severity and Molecular Profiles of Acute Chest Syndrome in Sickle Cell Disease. The award includes \$52,000/year for up to three years.

Dr. Jaime Jump, Asst. Professor, received the BCM Early Career Faculty Award for Excellence in Patient Care in December 2021.

Dr. Jeffrey Kim, Professor, was appointed Vice Chair of Faculty Development at TCH.

Dr. Katherine King, Assoc. Professor, was

-- elected to the American Society of Clinical Investigation.

-- named member of the American Pediatric Society. Its members are "recognized child health leaders of extraordinary achievement who work together to shape the future of academic pediatrics. New members are nominated by current members through a process that recognizes individuals who have distinguished themselves as child health leaders, teachers, scholars, policymakers and/or clinicians."

Dr. Emy Kuriakose, Asst. Professor, received a Bronze Pin TCH Ambulatory Practitioner Award for Excellence in Patient Experience. The award recognizes providers with mean score of 99% or above on the provider section of Press Ganey Survey.

Dr. Philip Lupo, Assoc. Professor, was recently elected to the Children's Oncology Group (COG) Nominating Committee as one of the four members representing the Non-Hematology/Oncology disciplines. COG is a National Cancer Institute supported clinical trials group and is the world's largest organization devoted exclusively to childhood and adolescent cancer research.

Dr. Rachel Marek, Asst. Professor, was elected in November to serve as Chair-elect of the Section on Pediatric Hospital Medicine (SOHM) of the American Academy of Pediatrics. Dr. Marek will replace Dr. Geeta Singhal.

Dr. Sonal Malhotra, Asst. Professor, was interviewed on Fox26 News, "Too much or too little sleep can cause cognitive decline," on October 28, 2021.

Dr. Sanghamitra Misra, Assoc. Professor, completed the prestigious Robert Wood Johnson Foundation Clinical Scholars Fellowship. The three-year leadership program for clinical researchers focuses on equity, diversity, inclusion, racism, bias, communication, media management, difficult conversations, cultural competency, adaptive leadership, conflict resolution, advocacy, op-ed writing and other relevant leadership topics.

Dr. Flor Munoz, Assoc. Professor, who was the PI for vaccine studies at TCH, was one of the authors on an article published in the *NEJM* "Evaluation of the BNT162b2 Covid-19 Vaccine in Children 5 to 11 Years of Age," showing the regimen of two 10-mg doses to be safe, immunogenic, and efficacious; the study was funded by BioNTech and Pfizer.

Dr. Venessa Lynn Pinto, Asst. Professor, received the BCM Early Career Faculty Award for Excellence in Patient Care in December 2021.

Dr. Ricardo Quinonez, Assoc. Professor and Chief of the Division of Pediatric Hospital Medicine, was invited to and presented Grand Rounds at U Mass Memorial Children's Medical Center on December 5, 2021, detailing his work on the Choosing Wisely campaign. This work was recently published in the journal *Hospital Pediatrics*

Dr. Rayne Rouce, Asst. Professor, was

-- invited to join the Board of Directors of Be The Match, a global leader in bone marrow transplantation for patients with life-threatening blood cancers.

-- recently selected as Digital Commissioning Editor for the journal *Blood Advances*, a peer-reviewed, open-access medical journal published by the American Society of Hematology.

Dr. Hasti Sanandajifar, Asst. Professor, received a Red Pin TCH Ambulatory Practitioner Award for Excellence in Patient Experience. The award recognizes providers with mean score of 99% or above on the provider section of Press Ganey Survey.

Dr. Lanlan Shen, Asst. Professor, will serve on the Faculty Research Fellowship Support Committee in a process oversight role, a result of the BCM Institutional Committee At-Large Faculty Summer Elections.

Dr. Geeta Singhal, Professor began a 2-year term as Chair of the Section on Pediatric Hospital Medicine (SOHM) of the American Academy of Pediatrics.

Dr. Nidhy P. Varghese, Professor, was

-- accepted to the Scientific Sessions Planning Committee for Pulmonary Hypertension Association Conference 2022.

-- recipient of the TCH Provider Excellence Award: Red Pin.



Fall 2021 Norton Rose Fulbright Faculty Excellence Awards Recipients

Dr. Meghna Raphael – Teaching and Evaluation Dr. Nicholas Ettinger – Teaching and Evaluation Dr. Aderonke Ojo – Educational Materials Dr. Tim Porea – Teaching and Evaluation Dr. Sarah Sartain – Teaching and Evaluation Dr. Stephanie Deal – Teaching and Evaluation

2021 Research Mentor Awardees

2021 Young Investigator Awardees

Hyun Kyoung Lee, MS, PhD	Assistant Professor	Eveline Barbieri, MD, PhD	Assistant Professor
Stephanie Sisley, MD	Assistant Professor	Austin Brown, PhD	Assistant Professor
Bethanie Van Horne, MPH, DrPH	Assistant Professor	Hyun Kyoung Lee, MS, PhD	Assistant Professor
Marisa Hilliard, PhD, MA	Associate Professor	Jane Montealegre, PhD	Assistant Professor
Maria Kim, MD, MSc	Associate Professor	Nancy Moran, PhD	Assistant Professor
Philip Lupo PhD	Associate Professor	Jacquelyn Powers, MD, MS	Assistant Professor
Benjamin Shneider, MD	Professor	Rayne Rouce, MD	Assistant Professor
		Stephanie Sisley, MD	Assistant Professor



DEPARTMENT NEWS RESEARCH

Patent-Free Vaccine in India Comes All the Way from Texas

Very soon, millions of doses of a new, inexpensive vaccine will be available in India, coming all the way from a lab in Texas. The researchers who developed the vaccine, **Dr. Peter Hotez** and **Dr. Maria Elena Bottazzi** of Baylor College of Medicine/Texas Children's Hospital, do not hold any intellectual property, rendering the vaccine an ideal vaccine for bridging the global equity gaps. Countries such as India remain without access to the mRNA vaccines produced by Pfizer-BioNTech and Moderna, which have been purchased and distributed largely by wealthy nations.

Because this vaccine, named CORBEVAX, is relatively inexpensive to produce and easy to store, it can be created anywhere hepatitis B vaccines are manufactured, can be produced by any country because no property rights will be violated, and will fulfill these researchers dedication to producing vaccines for underserved countries.

More information follows in the article on the next page.

Above, a patient in India receives the CORBEVAX vaccine.



Vaccine Candidate Receives Approval in India

A vaccine created by **Drs. Peter Hotez**, Professor and Dean for the National School of Tropical Medicine, and **Maria Elena Bottazzi**, Professor and Assoc. Dean of the National School of Tropical Medicine, was finally authorized in December 2021 for use in India to combat COVID-19. Both researchers are leading experts in the fields of vaccine development. The vaccine, CORBEVAX, uses old but proven vaccine technology and can be manufactured more easily than most other candidates being used today. The vaccine will be particularly beneficial to low-income countries, which can now produce these vaccines and distribute them in a way that will be affordable, effective, and safe.

The vaccine is not new; in fact, the researchers began working on this candidate some two decades ago when they were researchers at George Washington University, Washington, DC. When, in 2003, a strain of coronavirus known as SARS broke out, they began their work, which they brought with them when they came to Houston to affiliate with BCM and TCH's Center for Vaccine Development. They created the vaccine candidate using protein subunit technology, which involves using proteins from a virus or bacterium that can induce an immune response without causing the disease itself.

The SARS vaccine candidate looked promising, but as the SARS outbreak diminished, the need for a vaccine also diminished. However, they kept the work in refrigeration for years, and when a new strain of coronavirus hit pandemic proportions, they retrieved their old technology and modified it for use against the COVID-19 virus, which was quite similar to SARS. "This announcement is an important first step in vaccinating the world and halting the pandemic. Our vaccine technology offers a path to address an unfolding humanitarian crisis, namely the vulnerability the low- and middle-income countries face against the delta variant."

-Dr. Peter Hotez

"Our decade-long studies advancing coronavirus vaccine prototypes has led to the creation of this vaccine, which will fill the access gap created by the more expensive, newer vaccine technologies and that today are still not able to be quickly scaled for global production."

-- Dr. Maria Elena Bottazzi

All efforts to engage government officials were fruitless, and the emphasis on innovation technologies overrode the practical approach to developing a low-cost, durable, easy vaccine that could be used quickly worldwide at minimal expense. Nonetheless, Drs. Hotez and Bottazzi persevered and finally were able to obtain funding from private philanthropies, including the JPB Foundation in New York, the Fleberg Foundation, the John S. Dunn Foundation, Tito's Vodka, and the MD Anderson Foundation.

Unlike the mRNA vaccines from Pfizer and Moderna ad the viral vector vaccine from Johnson & Johnson, CORBEVAX is in a class that has a track record. Hence, the researchers were confident that it would safe and effective ... and, it could be produces for less than \$2 a dose.

Clinical trials proved their predictions to be accurate. An unpublished study of 3000 volunteers performed in India revealed the vaccine to be 90% effective in preventing disease caused by the original COVID-19 strain and 80% effective against the delta variant. CORBEVAX[™] after completing two Phase III clinical trials involving more than 3000 subjects was found to be safe, well tolerated, and immunogenic:*

- CORBEVAX[™] demonstrated superior immune response in comparison with COVISHIELDTM vaccine when assessed for Neutralizing Antibody (nAb) Geometric Mean Titers (GMT) against the Ancestral-Wuhan strain and the globally dominant Delta variant. CORBEVAX[™] vaccination also generated significant Th1 skewed cellular immune response.
- CORBEVAX[™] nAb GMT against Ancestral-Wuhan strain is indicative of vaccine effectiveness of >90% for prevention of symptomatic infections based on the Correlates of Protection assessment performed during Moderna and Astra-Zeneca vaccine Phase III studies.
- CORBEVAX[™] nAb GMT against the Delta strain indicates a vaccine effectiveness of >80 percent for the prevention of symptomatic infections based on published studies.
- While none of the subjects who took CORBEVAX[™] or COVISHIELD[™] had serious adverse events, CORBEVAX[™] had 50 percent fewer adverse events than COVISHIELDT[™].
- In the continuous monitoring of phase II studies, CORBEVAX[™] showed high persistence of immune response as indicated by <30% drop in nAb GMT till 6 months second dose as compared to >80% drop observed with majority of the vaccine

*source: TCH website, https://www.texaschildrens.org/texas-children's-hospitaland-baylor-college-medicine-covid-19-vaccine-technologysecures-emergency

In contrast to the Pfizer and Moderna candidates, for which the technology is not shared by the manufacturers, the intellectual property of the CORBEVAX vaccine will be available to everyone so that it can be manufactured in numerous other countries. The mission of these researchers has always been to enable technologies for low- and middle-income countries.

The only seeming drawback is that modification cannot be done as quickly as with mRNA vaccines to adjust to new variants. Nonetheless, the availability of the technology and that it is extremely less expensive to manufacture should prove the vaccine candidate to be an ideal alternative to the other candidates.

Study Provides Rationale for Pediatric Trial of Treatment for pAML



Dr. Joanna Yi, Asst. Professor, and colleagues performed the first enhancer mapping of pediatric acute myeloid leukemia (pAML) in 22 patient samples, focusing specifically on super-enhancers, in a study published in *Blood Advances*. In

the article for which Dr. Yi is senior author, "Defining the Transcriptional Control of Pediatric pAML Highlights RARA as a Super-Enhancer Regulated Druggable Dependency," they noted that "somatic mutations are rare in ... pMLA, indicating alternate strategies are needed to identify targetable dependencies." marked overexpression of super-enhancer-regulated genes, which "enforce cell identity and drive oncogene expression in a growing number of cancers, including adult AML."

In the current study, Dr. Yi and her colleagues identified super enhancers associated with many known leukemia regulators and found that the retinoic acid receptor alpha (RARA) gene was differentially regulated in their cohort. They also detected a RARA-associated super enhancer in 64% of the cohort, across all cyto/molecular subtypes tested. The RARA super-enhancer-positive pAML cell lines and samples had high RARA mRNA levels and were specifically sensitive to the synthetic RARA

Currently, children with AML achieve approximately 65% overall survival, but that survival rate is completely dependent on extremely toxic chemotherapy and stem cell transplant, both of which the authors note cause significant



agonist tamibarotene in vitro.

The drug tamibarotene slowed proliferation, apoptosis induction, differentiation, and upregulate retinoid target gene expression, as compared to the RARA superenhancer-

negative samples.

It also prolonged

Microscopic view of acute myeloid leukemia, courtesy Cancer Institute

short- and long-term toxicities including potential heart failure, secondary malignancies, and graftversus-host disease. They also noted that genome sequencing studies reveal that pAML has fewer mutations than does adult AML, but structural alterations are more common.

They explain that they seek to define the transcriptional control of human diseases by identifying and validating super-enhancers, a subset that is highly and disproportionately bound by much of the cell's transcriptional machinery. The result is survival and suppressed the leukemia burden of a RARA super-enhancer-positive pAML patientderived zenograft (PDX) mouse model, compared to a RARA super-enhancer-negative PDX. The researchers concluded that the study provides rationale for a pediatric trial of tamibarotene in children with RARA-high AML.

Other authors on the study were Perez MW, Sias-Garcia O, Daramola A, Wei H, Terrell M, Rashid R, Park WD, Duong K, Horton TM, Li F, Cherayil N, VrabicKoren J, Gant VU, Junco JJ, Curry CV, Stevens AM, and Lin CY, all from BCM and/or TCH.

Genetic Studies Demonstrate Value of Using Set of Criteria for Evaluating Multilocus Pathogenic Variations

Dr. Tadahiro Mitani, Postdoctoral Associate currently at Jichi Medical University in Tokyo, Japan, is first author of a work involving a team of 50 investigators from around the world who worked to



identify genetic causes of rare neurodevelopmental disorders in 234 subjects and 20 previously unidentified causes of cases in the Turkish population. The work was published in October in the *American Journal of Human*

Genetics. Dr. Mitano, and other investigators in **Dr. James Lupski**'s, Professor and long-term attending physician at TCH (pictured above), including cocorresponding author **Dr. Davut Pehlivan**, Asst.



Professor (pictured left), integrated improved genomewide screening technologies to improve their ability to identify the genetic underpinnings of rare neurodevelopmental conditions. The technologies included exome

sequencing and whole-genome sequencing, as well as newly developed computational tools and bioinformatic analyses.

Genetic causes of rare neurodevelopmental disorders can be quite difficult to identify. This research project began in 2011; during the ensuing years, close collaborations developed among physicians and patients worldwide, as well as among researchers in the fields of genetics, genomics, and bioinformatics. Using GeneMatcher, a web-based 'matchmaking service,' the team was able to make connections among clinicians and researchers worldwide who share interests in the same genes.

The team identified new genes and confirmed genes previously associated with neurodevelopment disorders. They also made molecular diagnoses in 181 of 254 (71%) of the individuals in the study and in approximately 80% of neurodevelopmental disorders overall. They further found an explanation for the diagnostic challenge that occurs with conditions that have characteristics that do not match what has been reported in the medical literature. They determined that the accumulation of certain



combinations of rare disease-causing gene mutations of different genes, called *multilocus pathogenic variation*, results in complex characteristics unique to each individual, according to Dr. Mitani.

The prevailing concept that a single disorder is caused by a mutation in a single gene simply does not account for complex neurodevelopmental disorders; with multilocus pathogenic variation, one patient may have several mutated genes. Dr. Pehlivan explained that one gene mutation may result in muscle disease and a different gene mutation may lead to brain disease, where in another patient one mutation may affect the kidneys and another the brain. Hence, patients may present with neurodevelopmental disorders that share similarities but have important differences that need to be considered when making decisions about treatments and when evaluating risk factors for other family members.

Dr. Pehlivan explained that, "In this study, for the first time we strictly applied a set of criteria to evaluate multilocus pathogenic variation in our patients and found that it was present in 28.9% of the cases in which we established a genetic diagnosis. Our findings confirm the value of routinely applying these criteria to assess the contribution of multilocus pathogenic variation to rare neurodevelopmental disorders and again revealed why genomic studies are superior to single gene testing."

Researchers Study Role of Endothelial Cells in Blood Clotting

". . . our findings demonstrate that cell types that comprise the human vascular wall, ECs and fibroblasts, both form active prothrombinase complexes on their surfaces using distinct processes. Prothrombinase complexes on EC surfaces (FX-FV-FII) include membrane-attached FV and are further stabilized through interactions with phospholipids on EC membranes by calcium-dependent GLA-domains of FX and FII. On fibroblast surfaces, the prothrombinase complexes consist of membrane-attached FV and transient interactions with γ -carboxy-glutamate-deficient forms of FX and FII. This study contributes additional evidence that ECs and fibroblasts of the vascular wall have an active role in hemostasis. "



Dr. Clay Cohen, Asst. Professor, has been studying blood vessel walls to determine the roles they play in injuries, when coagulation proteins are critical to thrombosis and hemostasis. He has noted that

"most experts believe the proteins that contribute to the development of a blood clot come exclusively from the liver." His lab, in collaboration with researchers at Rice University, has been studying other sources, including whether endothelial cells, which form the lining of the blood vessel walls, also can produce coagulation proteins.

In a recent article published in *Scientific Reports*, they describe experiments that detail the expression and production of endothelial cells (ECs) and fibroblasts of the clotting proteins necessary for formation of active prothrombinase complexes to produce thrombin on endothelial cells and fibroblast surfaces. In an earlier study, they reported that human ECs express and produce their own coagulation factors that can activate cell surface FX without the addition of external proteins or phospholipids. In the current study, they identified EC and fibroblast thrombin generation by measuring thrombin activity, thrombin-antithrombin complexes, and the prothrombin fragment 1.2.

Their research revealed that human endothelial cells (HUVECs, GMVECs, and LSECs) and fibroblasts in culture produce coagulation proteins that are required for formation of the prothombinase complex. They also found that prothrombin (FII) is activated on ECs and fibroblast surfaces without the requirement of external coagulation proteins. These experiments indicate that thrombin is generated by cell types that compose human vascular walls. Some of the specific findings, taken from the article include:

• Prothrombin fragment 1.2 was detected only in the lysate/cell membrane fractions of ECs and primarily (~ 90%) in the supernatant of fibroblasts. Fibroblast expression levels of *GGCX* (the carboxylase) were between two and fivefold lower than HUVEC, LSEC, and GMVEC levels, whereas *VKORC1* (the reductase) expression levels were elevated in GMVECs compared to other cell types, although similar between fibroblasts and HUVECs and LSECs.

• Thrombin was generated and could be measured in EC and fibroblast lysate/cell membrane fractions. The measured thrombin activities were similar in all cell types. Thrombin was also generated and measured under more physiological conditions using live HUVECs and fibroblasts. In the more physiological experiments using live, intact cells, HUVECs produced almost twofold more thrombin than fibroblasts.

• FII/thrombin were co-detected with thrombomodulin on the surfaces of HUVECs and GMVECs. Surface thrombomodulin on ECs greatly exceeded FII/thrombin in immunofluorescence experiments. Fluorescent images demonstrate the copious amounts of thrombomodulin on the surfaces of HUVECs, LSECs, and GMVECs. Thrombomodulin was undetectable on fibroblast surfaces. Expression levels of *THBD* were ~ 30-fold higher in ECs than in fibroblasts.

• Each cell type expressed *SERPINC1* and these mRNA levels in fibroblasts were ~ 20-fold higher than EC levels. Antithrombin protein levels were similar in the supernatants of ECs and fibroblasts but were not detected in either of the cell lysate/cell membrane fractions.

The full study can be read here:

Cohen CT, Turner NA, Moake JL. Human endothelial cells and fibroblasts express and produce the coagulation proteins necessary for throbin generation. Scientif reports https://doi.org/10.1038/s41598-021-01360-w

Upcoming Events







SAVE THE DATE

Join the Coalition for Pediatric Medical Research and the Burroughs Wellcome Fund for a virtual convening: "Developing the Next Generation of Diverse Pediatric Researchers" Wednesday, February 9, 2022 11:00 AM – 3:00 PM EST



Keynote address by Dr. Maria Bernard, NIH Chief Officer for Scientific Workforce Diversity

Panel presentations on the following topics: Current Policy Initiatives: What Works? Institutional Initiatives: What Works and What is Needed? UIM and Women Investigators: What is Needed? Participate in small groups to review the current status and contribute to future policy initiatives

TO REGISTER:

<u>https://us06web.zoom.us/meeting/register/tZEtduGrpz8pH9HReoZvy-C2sy7ri8eI5fby</u> (Agenda forthcoming; This virtual meeting is open broadly so please pass this invitation along to others at your institution that may be interested in joining.)

In-Person Convening to be held on Thursday May 5th, 2022 in Washington, DC.

Questions? Contact Nicole Rottmueller-Jones, Program Coordinator, Cincinnati Children's Hospital, at <u>Nicole.Rottmueller-Jones@cchmc.org</u> or (513) 636-8918.



Ben and Margaret Foundation Bobby Alford Award Academic Clinical Professionalism Nominations Open January 3, 2022 Deadline February 21, 2022

Faculty Awards for Excellence in Patient Care Master Clinician – Nominations due February 14, 2022

Norton Rose Fulbright Faculty Excellence Award (Teaching and Evaluation, Educational Leadership, Educational Materials, Educational Research) Deadline to submit a portfolio – Spring 2022 Cycle March 21, 2022 by 5 p.m.

Pedi Press Department of Pediatrics News Magazine Winter 2022 Issue April 5, 2022

"End with Good Stuff."

-- Dr. Gordon Schutze

Therapy for Medical Staff comes with Four Paws



J&S Borden's Lady Abigail Prancin' by the Liffey, CKC, TDN Owned and Handled by Dr. Lee Ligon-Borden and Gordon Borden, MEd, MAR

9