Pedi Press

A Quarterly Publication of the Department of Pediatrics
Baylor College of Medicine

Vol. 10, Issue 2, Part II

Spring 2021

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Center Expresses Appreciation for Dr. Mott's Contributions

Dr. Anthony "Tony" Mott, Assoc. Professor, was honored with a reception in May, for his "time with us, before he goes on some extended leave." Since 2013, Dr. Mott has been one the great pillars of the Heart Center, the Department, and the Hospital, serving as attending and medical director of the inpatient cardiology services. Dr. Mott is the epitome of a good pediatrician and beyond that, he is a central figure in the community here at Texas Children's Hospital and Baylor College of Medicine. Co-workers attested that they have all learned so much from him, not just about pediatric cardiology, but most especially about how to treat each other. In order to give people an opportunity to bid him farewell, to thank him for everything that he has done, and to congratulate him for everything he has achieved, an 'open-house' was held in the reception area in front of the Taussig Lecture Hall on the 16th floor of Legacy Tower on Friday May 14, between 2 and 4 pm. Due to social distancing requirements, they were not able to have the traditional mass celebration, but rather they invited people to drop in /out during that period.

Dr. Jan Drutz Honored at Department Meeting as He Retires

Dr. Jan Drutz was honored for his long career at Baylor College of Medicine and his "Monumental Achievements" by **Dr. Raphael**, during the Department of Pediatrics faculty meeting on April 1, 2021.

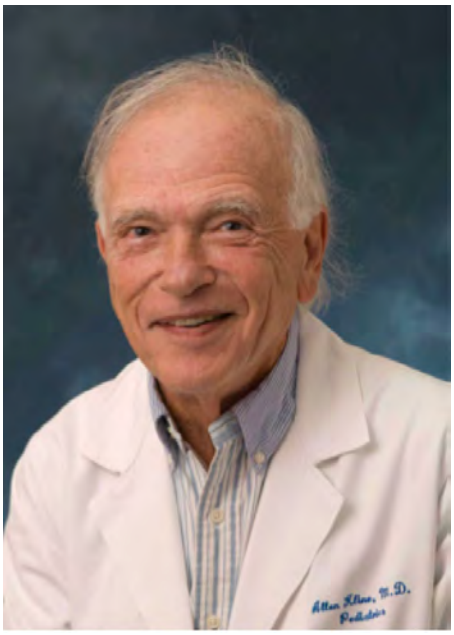
Beginning with his Pediatric Residency at BCM from 1968-1971, followed by his chief residency in 1971, Dr. Drutz held important positions and made lasting changes as Pediatrician, Town and Country Pediatrics from 1973-1987 and then as Director of Pediatric Continuity Clinics at BCM and Inpatient Teaching Attending from 1987 until his retirement in 2021. Dr. Raphael listed his monumental achievements, found in the box accompanying this article.

Dr. Drutz received his B.A. from University of Louisville and his M.D. from University of Louisville School of Medicine. In addition to his residency at BCM, he had advanced training from BCM Affiliate Hospitals in 1969 and 1971.

MONUMENTAL ACHIEVEMENTS

- Service in the Military
- President, Houston Pediatric Society
- President, Medical Staff
- Program Director, Annual Pediatric Postgraduate Symposium
- Program Director, Annual Primary Care Pediatric Course
- Elected Chairman, Academy of Distinguished Educators
- Chairman, Kirkland Society for Pediatric Residents
- Recipient of four Fulbright and Jaworsky Faculty Excellence Awards
- Recipient of the Arnold J. Rudolph Baylor Pediatric Award for Lifetime Excellence in Teaching
- Recipient of the Barbara and Corbin J. Robertson, Jr., Baylor College of Medicine, Presidential Award for Excellence in Education
- Founding Chairman, Continuity Clinic Special Interest Group, Academic Pediatric Association
- Section Editor, *UpToDate*
- Faculty Facilitator at the Harvard Macy Program for Educators in Health Professions

In Memoriam



Dr. Allen Kline
May 2, 1931 – June 29, 2021

Dr. Allen Kline, Houston long-time pediatrician with Baylor College of Medicine/Texas Children's Hospital and in private practice, died on June 29, 2021, at the age of 90. He was born in Houston, Texas, on May 2, 1931, and attended Houston public schools, where he was a member of the National Honor Society and the National Athletic Honor Society, in addition to being an Eagle Scout. He lettered in four sports and was Houston Boys' tennis champion in 1946.

He matriculated The University of Texas, Austin, as a zoology major, where he was a member of Alpha Phi Omega Service fraternity, Rush Literary Society, and Silver Spurs. He played varsity baseball and was a member of the 1950 College World Series Champions.

In 1951, Allen entered Baylor College of Medicine, where he became a member of the Osler Society. He completed his pediatric residency at Johns Hopkins Hospital before serving two years at the U. S. Naval Hospital, Jacksonville, Florida. After completing his military service, he returned to Houston and became Chief Resident at Texas Children's Hospital. He entered private practice in addition to being on the administrative faculty in the Department of Pediatrics at BCM.

Dr. Kline met "the love of his life," Maude Rose Brown, on a blind date Christmas Eve, 1952, and they were married a week later, on New Years' Eve. Their first child, Allen Jr., was born a year later, followed by Glen, two and a half years later. They were active in the boys' schooling, sports, and scouting, with both boys achieving Eagle Scout.

Dr. Kline was board certified in pediatrics, a member of the American Academy of Pediatrics, Ambulatory Pediatric Associates, Texas Pediatric Society, Texas Medical Association, and the Harris County Medical Society. He is survived by his wife of 68 years, his two sons and their wives, four grandchildren, and one great-granddaughter, as well as one sister and one brother. He was predeceased by his parents, Adrienne and Harry Kline.

Section Head Named for Tropical Medicine

On June 3, 2021, Drs. Gordon Schutze and Peter Hotez announced that **Dr. Maria Elena Bottazzi**, Professor, will assume the position of **Section Head of Pediatric Tropical Medicine**, effective July 1, 2021. She has been serving as Co-Section Head alongside Dr. Hotez since 2018 and also serves as Co-Director of Texas Children's Hospital Center for Vaccine Development and as Associate Dean of the National School of Tropical Medicine. She serves as Co-Chair of the Vaccines and Therapeutics Taskforce of the *Lancet* Commission on COVID-19 and is a member of the NASEM Committee on Vaccine Research and Development Recommendations for Advancing Pandemic and Seasonal Influenza Preparedness and Response.

Dr. Bottazzi joined Baylor College of Medicine in 2011 as Professor of Pediatrics and Molecular Virology and Microbiology, where she leads a team of scientists and programs to accelerate the development of new vaccines for neglected tropical and emerging infectious diseases (including coronavirus).

Dr. Bottazzi is an internationally recognized tropical and emerging infectious disease vaccinologist and advocate with two decades pioneering and leading the advancement of a vaccine portfolio from discovery to clinical trials for diseases such as coronavirus, hookworm, schistosomiasis, and Chagas, all neglected diseases that affect disproportionally the world's poorest populations. She also has established innovative partnerships in Latin America, Middle East, and South East Asia, making significant contributions to innovative educational/research programs, catalyze policies, and disseminate science information to reach a diverse set of audiences.

She is also a Fellow of the American Society of Tropical Medicine and Hygiene, the Executive Leadership in Academic Medicine, the Leshner Leadership Institute for Public Engagement, and Sr. Fellow of the American Leadership Forum. She is a member of the National Academy of Science of Honduras and Emerging Leader in Health and Medicine of the National Academy of Medicine in the United States. In August 2020, Forbes LATAM selected Dr. Bottazzi as one of 100 Most Powerful Women in Central America.

New Medical Director Announced for Children's Sleep Center

Dr. Binal Kancherla, Assoc. Professor, has been named as the next **Medical Director** of the **Children's Sleep Center** at TCH**, effective July 1, 2021**. Dr. Kancherla completed her fellowship training in Pediatric Pulmonology and Sleep Medicine in 2010 and joined our faculty as Assistant Professor of Pediatrics that same year. She was promoted to Associate Professor of Pediatrics in 2020. Dr. Kancherla has served as Associate Medical Director of the Children's Sleep Center since January 2019 (based at the West Campus) and has steered the community service line of our Sleep Center during a period of dramatic growth in patient care. She will assume the reins from **Dr. Daniel Glaze,** who has served as the physician leader of sleep medicine in Baylor Pediatrics and founding Medical Director of the Center since the program's inception in July 1982. For nearly 4 decades, Dr. Glaze has been a national and international leader in pediatric sleep medicine and child neurology. We owe so much to Dr. Glaze for his commitment and dedication to this patient population.

The Children's Sleep Center will be moving its administrative hub to the West Campus and its subspecialty administrative home from Pediatric Neurology to Pediatric Pulmonary Medicine in July 2021. The Center has a strong interdisciplinary collaboration with several subspecialty services including ENT (Surgery), Neurology, Psychiatry, Psychology, and Pulmonary Medicine, contributing significantly to its success and mission. Robust interdisciplinary collaboration will sustain this Center as a leading sleep medicine program for children and adolescents for many years to come.

Dr. Peter Hotez Recognized for His Many Accomplishments

Dr. Peter Hotez, Professor and Dean of the National School of Tropical Medicine, was honored by his alma mater, **Weill Cornell Medical College**, with its **Alumni Association Award of Distinction**. The award was established in 1949 and is presented annually to an alumnus who has "demonstrated outstanding achievement in research, education or patient care, and has brought acclaim to the institution." The award was presented May 20, 2021, at Weill Cornell Medicine's virtual commencement ceremony.

After he graduated from Yale University, he earned a doctorate in biochemistry from the Rockefeller University and his medical degree from Weill Cornell Medical College as part of the Tri-Institutional M.D.-PhD. Program.

Dr. Hotez commented, "It feels wonderful to be recognized by a medical college where I spent so many important years of my life. I have such fond memories of the institution, my professors and my peers."

Dr. Hotez also was the recipient of an **Honorary Degree D.Sc.** ***Honoris Causa*** from the **Elmezzi Graduate School of Molecular Medicine** at Northwell Health on Long Island, NY.

The 2021 Commencement Exercises were held on May 27, 2021. Dr. Hotez also was one of the distinguished speakers for the Feinstein Academy of Scholars Symposium, held at the Graduate School.

Dr. Annette Lee, Dean of the Elmezzi Graduate School of Molecular Medicine, who presented the degree, noted "You've greatly impacted the medical research community and are an inspiration to all physician scientists." Prof. Kevin J. Tracey, MD, added, "As physician-scientists, be prepared to speak to the world because the world needs your voice" as he congratulated all the graduates and, especially, Dr. Hotez and Dr. Olopade (the other recipient) on their honorary degrees.

Multidisciplinary Pediatric Team Volunteers at Vaccine Clinic

Immediately after receiving FDA authorization for COVID vaccines for patients 12-16 years old, Xavier Educational Academy offered a vaccine clinic for teens on May 13 and again on June 3.

Several BCM/TCH physicians volunteered to administer vaccines. **Drs. Andrea Cruz**, Assoc. Professor, Emergency Medicine; **Laura Loftis**, Assoc. Professor, Critical Care; **Mona McPherson**, Medical Director, TCH Mission Control; **David Paul**, Assoc. Professor, Diabetes and Endocrinology; and **Hossein Tcharmtchi**, Assoc. Professor, Critical Care vaccinated almost 300 adolescents with the Pfizer vaccine in conjunction with Texas RX Solutions and Compounding pharmacy. These physicians talents were especially useful as the clinic had several adolescents with neuro-sensory issues and special needs.

(Photos by Brandon Bell)

Congratulations!

Academic Promotions

Distinguished Emeritus Professor

Jan E. Drutz, MD (AGP)

Professor

Andrea T. Cruz, MD, MPH (PEM)
Javier Chinen, MD, PhD (IAR)
Mohan Pammi, MD (Neo)
Jack F. Price, MD (Cards)
M. Hossein Tcharmtchi, MD (CCM)

Associate Professor

Patricia A. Baxter, MD, MS, MBA (Heme-Onc)
Melissa M. Carbajal, MD (Neo)
Anki Dutta, MD, MPH (ID)
Jill A. Jarrell, MD, MPH (Pal Care)
Joshua A. Kailin, MD (Cards)
Ruchi Kaushik, MD, MPH (ChofSA-AGP)
Wilson W. Lam, MD (Cards)
Yuezhen "Linda" Lin, MD, MS (Endo)
Keila N. Lopez, MD, MPH (Cards)
Sarah K. Lyons, MD (Endo)
Joseph Lubega, MD, MS (Heme-Onc)
Tracy E. McCallin, MD (ChofSA-PEM)
J. Chase McNeil, MD, MS (ID)
Lakshmi "Sara" Nandiwada, PhD, MSc (IAR)
Muralidhar H. Premkumar, MD, MS (Neo)
Nino C. Rainusso, MD (Heme-Onc)
Amee Revena, DO (Pulm)
Kevin M. Roy, MD (CCM)
Jeremy S. Slone, MD, MPH (Heme-Onc)
Kristen S. Tejtel, MD, PhD, MPH (Cards)

Department of Pediatrics Outstanding Clinicians 2020

Amy Arrington (CC)
Shaeequa Dasnadi (Neo)
Sue Denfield (Card)
Rosa Diaz (Hem-Onc)
Michael Gleason (Hem-Onc)
Mary Suell (Hem-Onc)
Betul Yilmaz Furtun (Card)

Master Clinician Award for Excellence in Patient Care

Carolyn A. Altman, MD (Cards)
Eileen D. Brewer, MD (Renal)
William J. Dreyer, MD (Cards)
Caraciolo J. Fernandes, MD, MBA (Neo)
Charleta Guillory, MD, MPH (Neo)

Star Awards for Excellence in Patient Care - BCM

Gladstone Airewele (Heme-Onc)
Kathryn Ban (Endo
Shaeequa Dasnadi (Neo)
Jenny Despotovic (Heme-Onc)
Rosa Diaz (Heme-Onc)
Teena Hadvani (PHM)
Galit Holzmann-Pazgal (ID)
Pablo Lohmann (Neo)
Priya Mahajan (Heme-Onc)
Mini Michael (PHM)
Heather Moore (AGP)
Alice Obuobi (Neo-Cl)
Tim Porea (Heme-Onc)
Ghadir Sasa (Heme-Onc)
Deborah Shardy (Heme-Onc)
Alexandra Stevens (Heme-Onc)
Mary Suell (Heme-Onc)
Rajkumar Venkatramani (Heme-Onc)
Seema Walsch (GI)
Scott Wenderfer (Renal

BCM Women of Excellence 2021

Milenka Cuevas Guaman, MD (Neo)
Rachel L. Marek, MD (PHM)
Shweta Parmekar, MD (Neo)

BCM Molecular & Human Genetics Annual Awards

RESEARCH MENTOR AND CLINICAL TEACHING AWARD
Alison A. Bertuch, MD, PhD.

2021 BCM Clark Award

Susan L. Gillespie, MD, PhD.

Center for Research, Innovation and Scholarship in Education (CRIS) 2021 Fellow Excellence in Medical Education Award

Kristen DeRay, MD (ID)
Kristen Fisher, DO (Neuro)
Claire Gahm, MD (EM)
Adam Stevens, MD (Cards)

Academic Pediatric Association

TEACHING AWARD FOR FACULTY 2021
Adam D. Wolfe, MD, PhD.

Chief Residents for 2022 – 2023 Announced

Faculty Briefs

Dr. Ashley Butler, Assoc. Professor
-- received the 2021 Diversity Service Award from the Society of Pediatric Psychology in recognition of her leadership, service, and mentorship in the areas of diversity, equity, and inclusion in pediatric psychology.
-- received a 3-year, $900,000 grant from the Health Research & Services Administration's FIRST program to create and test a home telehealth behavioral self-management intervention for youth with type 2 diabetes and their families; she will partner with the Diabetes Care Center and the University of Houston Bounce Program on this work.

Dr. Corrie E. Chumpitazi, Assoc. Professor, was appointed to the new Women in Pediatrics Emergency Medicine Subcommittee of the AAP Section on Emergency Medicine

Dr. ZoAnn Dreyer, Professor and Clinical Director of the TCH Cancer Center Long-Term Survivor Program, was recognized by Northwest Mutual as a female hero in the fight against childhood cancer.

Dr. Maria Monica Gramatges, Assoc. Professor, and colleagues received a highly competitive cohort-building grant from the National Cancer Institute to study disparities in childhood cancer survivorship. They will receive approximately $2.1 million over the next 2 years to understand and address factors related to disparities in adverse outcomes and access to survivorship care, specifically among Latinos.

Dr. Christopher Greeley, Professor and Head of the Section of Public Health and Child Abuse Pediatrics at TCH, was elected to the Executive Committee of the Council on Community Pediatrics of the American Academy of Pediatrics for a 3-year term. The council seeks to promote health equity and address social determinants of health by supporting community pediatricians in clinical care, advocacy, education, and collaboration with families.

Dr. Heather Haq, Asst. Professor and Chief Medical Officer for the Baylor International Pediatric AIDS Initiative at Texas Children's Hospital, was re-elected to serve as education chair on the Executive Committee of the American Academy of Pediatrics Section on Global Health, 2021-2024.

Dr. Deborah Hsu, Professor, was appointed to the new Women in Pediatrics Emergency Medicine Subcommittee of the AAP Section on Emergency Medicine; she also serves as the Chair-Elect of the AAP Section on Emergency Medicine Executive Committee.

Dr. Peter Hotez, Professor, and Dean of the National School of Tropical Medicine
-- was the recipient of the 2021 Award of Distinction from Weill Cornell Medical College
-- received an honorary degree D.Sc. *Honoris Causa* from the Elmezzi Graduate School of Molecular Medicine at Northwell Health on Long Island, NY (see Part II, p. 7)

Dr. Ionela Iacobas, Asst. Professor and Medical Director of the TCH Vascular Anomalies Center, was invited to join the Scientific Committee of the International Society for the Study of Vascular Anomalies. The committee, which consists of 10 international experts in the field, drives the organization's scientific initiatives and oversees the scientific program at ISSVA's World Congress.

Jennifer Cervantes, Instructor, was selected as the Latino/x Social Worker of the Year by Latino/x Social Workers of Greater Houston.

Dr. Lisa Kahalley, Assoc. Professor and Assoc. Chair of Research, and colleagues received a highly competitive cohort-building grant from the National Cancer Institute to study disparities in childhood cancer survivorship. They will receive approximately $2.1 million over the next 2 years to understand and address factors related to disparities in adverse outcomes and access to survivorship care, specifically among Latinos.

Dr. Ruchi Kaushik, Asst. Professor, was recognized by the Collaborative of Texas Educators in Advocacy and Community Health for her advocacy education to improve trainee education in this area.

Dr. Rachael Keefe, Asst. Professor, was elected to the Executive of the Council on Foster Care, Adoption, and Kinship Care for the American Academy of Pediatrics. This important national committee sets policy and protocols for pediatricians around the country.

Dr. Youngna Lee Kim, Assoc. Professor, was elected to the Association of Pediatric Program Directors Executive Committee.

Dr. Christina Y. Miyake, Assoc. Professor, received the Dr. Mark L. Entman Award for Excellence in Cardiovascular Education from the Cardiovascular Research Institute.

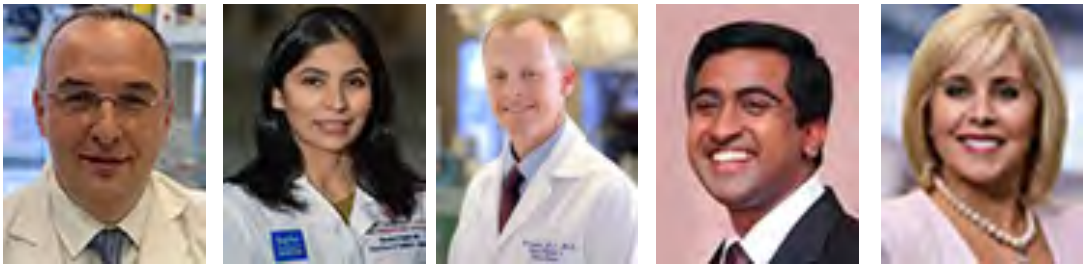
Dr. Tim Porea, Assoc. Professor, received the inaugural Dr. Drutz Society Coach Award, named after Dr. Jan Drutz, Professor of Pediatrics. Dr. Porea received this award to highlight the significant impact he has made in training pediatric residents as an advisor for one of the BCM pediatric residency's societies. In this role, he helps to mentor a group of 25 residents, offering guidance in both clinical and career areas.

Dr. Michael Scheurer, Professor, and colleagues received a highly competitive cohort-building grant from the National Cancer Institute to study disparities in childhood cancer survivorship. They will receive approximately $2.1 million over the next 2 years to understand and address factors related to disparities in adverse outcomes and access to survivorship care, specifically among Latinos.

Dr. Binoy Shivanna, Assoc. Professor, was appointed Co-Chair of the Mid-Career Neonatologists Leadership Committee of the AAP Section on Neonatal Perinatal Medicine.

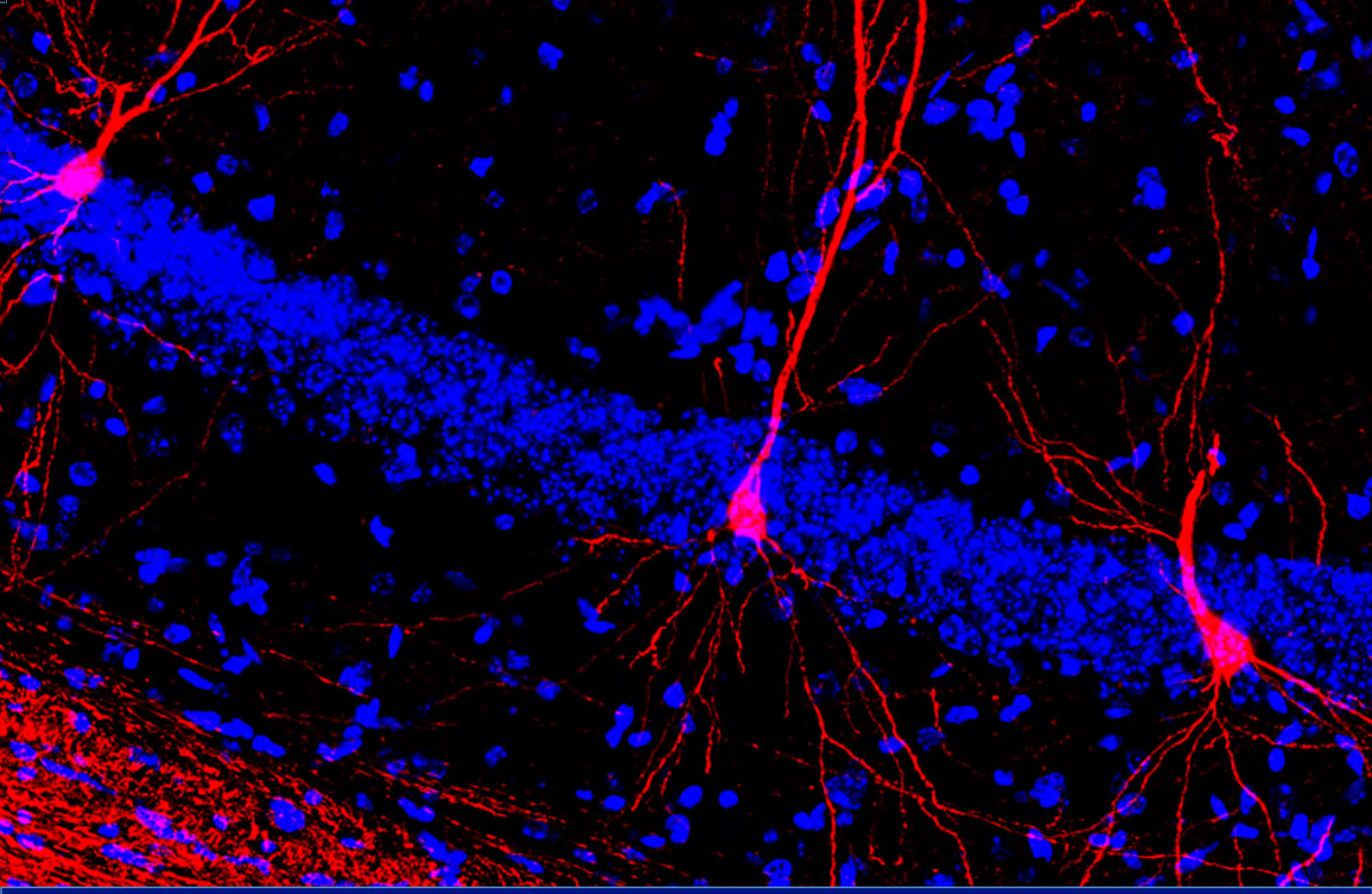
Dr. Jeffrey R. Starke, Professor, received the Lifetime Achievement Award from the Union-North America Region, which recognizes the valuable contributions of colleagues working in the field of tuberculosis control and prevention.

Dr. Fernando Stein, Professor, was awarded the Americanism Medal from the National Society of Daughters of the American Revolution, one of the two highest honors from the society. **(**see Part I, page 20)



The **St. Baldrick's Foundation-Stand Up 2 Cancer Pediatric Cancer Dream Team** has been selected as this year's recipient of the AACR Team Science Award. **Dr. Nabil Ahmed**, **Dr. D. William Parsons**, **Dr. Meenakshi Hegde**, **Dr. Sujith Joseph**, and **Bambi Grilley** of Baylor are among those recognized. The award recognizes an outstanding interdisciplinary team of researchers for their innovative cancer research. Bambi Grilley and Melanie Frost Moll also were recognized for their contributions to the team as advocates of childhood cancer research. (see Part I, p. 24)

Three faculty members were invited to participate on **National Cancer Institute Childhood Cancer Data Initiative Working Groups**. Pictured left to right, **Dr. Donald W. "Will" Parsons** is on the Molecular Characterization Protocol Working Group, **Dr. Monica Gramatges** is on the Childhood Cancer Cohort Working Group, and **Dr. Philip Lupo** is on the Engagement Committee. The goal of the CCDI is to build a community of pediatric cancer researchers, advocates, families, hospitals, and networks committed to sharing data to improved treatments, quality of life, and survivorship of every child with cancer.



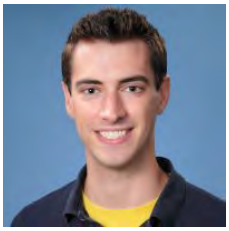
DEPARTMENT NEWS

RESEARCH

Study Reveals Advantages of Physical Training of Rett Mice

"We show in Rett mice that there is a critical window in early life when intensive behavioral training significantly improves behavioral deficits."

--Nathan P. Achilly



In a study published in *Nature*, **Nathan P. Achilly**, student in BCM's M.D./Ph.D. program (Developmental Biology working in **Dr. Huda Zoghbi's** lab) and first author, early physical training of Rett mice (e.g., swimming in a water maze) resulted in the development of more dendritic arbors or cellular projects in a task-specific group of neurons in the hippocampus (indicated in red in photo above). Their experiments revealed that task-specific neurons that are activated repeatedly during early training enable dendritic arbors or cellular projections to form and maintain neuronal circuits that enhance their functionality. Dr. Zoghbi noted that, "Our findings lead us to propose that newborn genetic testing for Rett syndrome, followed by prompt intensive training in the tasks that will be affected, could help the girls retain specific milestones and delay the onset of symptoms."

(Photo courtesy of Nathan P. Achillly/Zoghbi lab)

Biological E. Limited to Begin Phase III Clinical Trials with BCM/S TCH Vaccine

By Molly Chiu*

Biological E. Limited (BE), an Indian vaccine and pharmaceutical company, announced that it has completed the Phase I/II clinical trial of its COVID-19 subunit vaccine candidate in India and received the approval to start the Phase III clinical trial from the Central Drugs Standard Control Organization - Subject Expert Committee (SEC). The candidate includes an antigen developed by the Texas Children's Hospital Center for Vaccine Development at Baylor College of Medicine and in-licensed to BE by BCM Ventures.

"Having our Texas Children's and Baylor vaccine construct advance into phase III clinical studies in India and globally, highlights the importance of advancing traditional protein-based vaccine platforms, which now brings added hope for a people's vaccine to be scaled and deployed in low- and middle-income settings," said **Dr. Maria Elena Bottazzi**, Associate Dean of the National School of Tropical Medicine at BCM and co-director of the Texas Children's Hospital Center for Vaccine Development.

"India is now in the midst of a dire public health crisis as COVID-19 tears through the country. Our hope is that our Baylor/Bio E. vaccine will progress through phase 3 so it can be released through emergency authorization in India soon," said **Dr. Peter Hotez**, Professor and Dean of the National School of Tropical Medicine at BCM and co-director of the Texas Children's Hospital Center for Vaccine Development.

The vaccine also includes Dynavax Technologies Corporation's advanced adjuvant CpG 1018TM. The Coalition for Epidemic Preparedness Innovations (CEPI) and the Biotechnology Industry Research Assistance Council (BIRAC) have provided support for the Phase I/II clinical trials and the upcoming Phase III trial.

BE's Phase I/II clinical trial evaluated the safety and immunogenicity of the vaccine candidate. About 360 healthy subjects in the age range of 18 to 65 years took part. The vaccination schedule consisted of two doses for each study participant, administered via intramuscular injection 28 days apart. The vaccine was found to be safe, well-tolerated, and immunogenic.

The Phase III clinical study will be conducted in 15 sites across India. It will evaluate the immunogenicity and safety of the vaccine for protection against COVID-19 disease in about 1268 healthy subjects in the age range of 18 to 80 years. It is intended to be part of a larger global Phase III study.

"We are delighted with the success of the Phase I/II clinical trials of our COVID-19 vaccine candidate. The results of these clinical trials are very positive and promising. We believe that our vaccine candidate will become another effective global COVID-19 vaccine as we move forward into Phase III clinical trials," said Mahima Datla, managing director of Biological E. Limited.

*published in Baylor College of Medicine News and reprinted with permission

Regulation of Brain Circuit Signals Affects Food Consumption

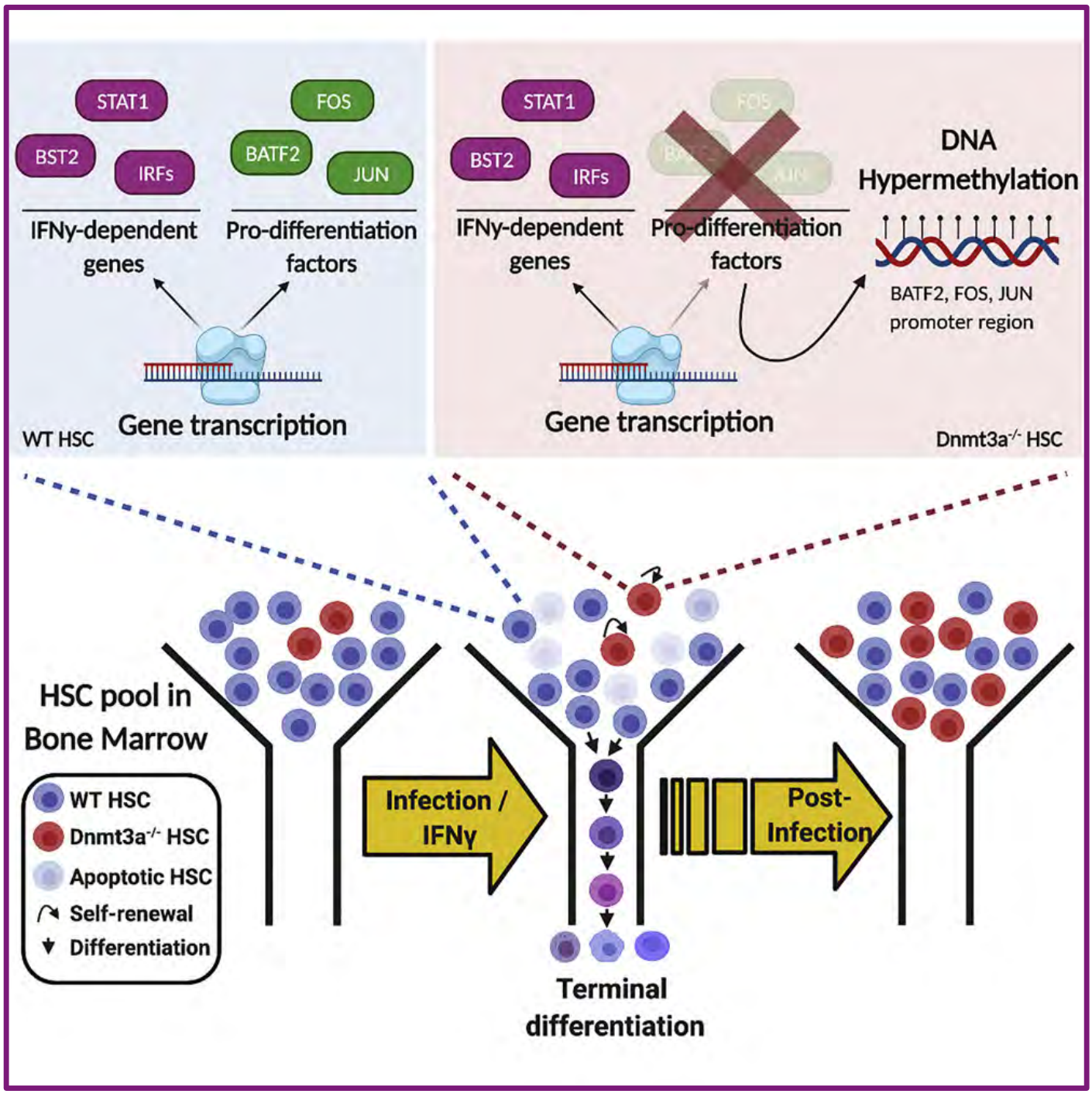
Dr. Qi Wu, Asst. Professor (pictured, top), **Dr. Yong Han**, Postdoctoral Associate (pictured, bottom), and their colleagues have uncovered new aspects of little-known neural circuits and neurotransmitters involved in ending food consumption. The study, with Dr. Han as first author and Dr. Wu as corresponding author, appears in the journal *Science Advances*. The study addresses concerns related to a search for a way to address the alarming increase in obesity among youth.

The research team used several advanced techniques, including cell-specific circuitry mapping, optogenetics, and real-time recordings of brain activity, to study neural function. They discovered a novel circuit that connects a subset of dopamine-producing neurons (DA-VTA) with downstream target neurons in the hindbrand (DRD1-LPBN) and potently suppresses food intake by triggering satiation, in a mouse model. In examining two sets of neurons while the mice were eating, they observed that the activity of the DA-VTA neurons increased immediately before the animals stopped eating. When the team genetically inhibited these neurons, the mice prolonged their feeding, with drastically increased weight gain. Contrariwise, when they enhanced the activity of the DRD1-LPBN neurons, which receive the signals from the DA-VTA neurons, they generated a robust meal termination.

Although other brain circuits have been proposed to regulate feeding, Dr. Han noted that, "the one we discovered is the first to be fully described to regulate portion size via dopamine signaling [and] . . . shows that a circuit connecting neurons that produce dopamine, a chemical messenger previously known for the regulation of motivation and pleasure, has a new role in the control of feeding through dynamically regulating the satiety response."

The team also found that methylphenidate (MPH), a drug approved for mitigating attention-deficit-hyperactivity discord, mediates a noticeable weight-loss effect by activating this particular circuit, thereby rendering the possibility that by regulating this circuit, people could control weight gain. Dr. Wu noted that the finding that MPH suppresses feeding and reduces body weight in laboratory mice suggests a potential off-label application of a class of MPH and derivatives in tackling obesity, as well as "has implications for the future development of circuitry-based precision medicine that can deliver weight-reducing results with higher safety and effectiveness."

Han Y, Xia G, He Y, He Y, Farias M, Xu Y, Wu Q. A hindbrain dopaminergic neural circuit prevents weight gain by reinforcing food satiation. Sciences Advances 7(22); eabf8719, 2021. DOI:10.1126/sciadv.abf8719.



Study Demonstrates Effects of Long-Term Infection and Inflammation on HSCs

In a recent study published in *Cell Stem Cell*, **Dr. Katherine King**, Assoc. Professor, and colleagues demonstrated that chronic infection significantly impairs the ability of wild-type hematopoietic stem cells (HSCs) to remain in a quiescent stem cell state. Exposure to a body-wide bacterial infection over a prolonged period of time promoted extensive differentiation of HSCs. The finding is significant because HSCs, which collectively ensure lifelong production of blood and immune cells, can either reproduce to generate more stem cells or differentiate into distinct immune cell lineages to fulfill specific functions.

"We are excited by the findings of this study which opens several areas of future investigations. We have shown for the first time how chronic inflammation due to long-term infections or autoimmune conditions such as rheumatoid arthritis, ulcerative colitis or Crohn's disease dampen the body's immune response as we age. Moreover, it sheds light on the critically important role of DNMT3a in modulating immune responses during chronic infection or stress and also explains how aging and inflammation are linked to blood cancers."

--Dr. Katherine King

The direction in which the cells go is important for ensuring that the body achieves the fine balance between having sufficient immune cells to fight infection and retaining enough HSCs to maintain future production of blood. They found that long-term infection caused specific expansion of Dnmt3a-loss-of-function HSCs, as well as a concomitant reduction in their ability to differentiate into immune cells, a behavior contrary to that exhibited by normal HSCs.

These HSCs also were more resistant to exhaustion and less sensitive to stress-induced apoptosis during chronic infection than were normal HSCs. Further, these cells exhibited an entirely opposite set of cellular responses and global changes in gene expression patterns in response to IFNy, compared to wild-type HSCs. The changes tended toward preserving or even increasing the number of stem cells at the expense of mounting an effective response against imminent invaders or stress.

As we age, HSCs form mutations lead to a phenomenon known as *clonal hematopoiesis* (CH), which is associated with significantly higher risk of developing blood cancers, cardiovascular disease, stroke, and all-cause mortality. Dr. King's research has been focused for some time on CH.

The current study demonstrates for the first time that long-term infection and prolonged inflammation drive CH mediated by the loss of Dnmt3a function, offers key insights into the mechanism by which chronic inflammation leads to CH, and demonstrates the critical role that DNMT3a plays in regulating normal HSC responses to infections.

In this study, the researchers predicted that defective differentiation and increased duplication of Dnmt3a HSCs allowed them to overtake and outcompete normal HSCs when fighting chronic infections or facing long-term inflammatory conditions.

To test that hypothesis, they used a combination of experimental and mathematical modeling experiments. Mosaic mice they generated by transplanting a mixture of whole bone marrow from Dnmt3a-mutant mice and normal mice into irradiated mice were used for experimental validation.

Hence, the current study demonstrates for the first time that long-term infection and prolonged inflammation drive CH mediated by the loss of Dnmt3a function, offers key insights into the mechanism by which chronic inflammation leads to CH, and demonstrates the critical role that DNMT3a plays in regulating normal HSC responses to infections.

Photo courtesy of Dr. King

Hormaechea-Agulla D, Matatall KA, Le DT, Kain B, Long X, Kus P, Jaksik R, Challen GA, Kimmel M, King KY. Chronic infection drives Dnmt3a-loss-of-function clonal hematopoiesis via IFNy signaling. Cell Stem Cell 2021.

https://www.sciencedirect.com/science/article/abs/pii/S1934590921001089?via%3Dihub

dio: 10.1016/jstem.2021.03.002

Newly Discovered Biomarker Will Help to Better Understand Neurogenesis

A team of researchers led by **Dr. Mirjana Maletć-Savatić**, Assoc. Professor, and Dr. Louis Manganas of Stony Brook University sought a unique way to study the fundamental biological process related to identifying the core molecular mechanism responsible for preserving neural stem cells in the human brain, despite the lack of specific neural stem cell markers amenable for advanced imaging and *in vivo* analyses. This identification is fundamentally important if neurogenesis is to be used to halt or reverse hippocampal age-related pathology.

The team's goals are to maintain neurogenesis throughout life at the same level as found in young brains, to prevent the decline in cognitive capabilities, and to reduce the tendency toward mood disorders associated with aging.

Although antibodies are typically made against known antigens, the team decided to generate antibodies for unknown target proteins, even though that process was more challenging.

They used an age-old method of generating the antibodies by injecting mice with whole-cell or membrane preparations, which resulted in 1648 clones, of which 39 reacted with NSCs. Close evaluation revealed one potential candidate that most strongly labels NSCs.

Using mass spectrometric analysis of the human hippocampal tissue, they identified the target protein as the brain-abundant signal protein (BASP-1), which previously had been shown to be present in the neurons of the mouse brain but not in NSCs. The antibody that recognizes BASP-1 in NSCs does not label neurons or any other cells, apart from NSCs, indicating its possible use as a means to visualize these cells in the live mammalian brain.

"Using our new antibody, we found that BASP-1 is restricted to NSCs in neurogenic niches in the mammalian brains, including humans, during development in utero and after birth. Thus, our work identified membrane-bound BASP-1 protein as a possible biomarker of NSCs that would allow us to examine the mechanisms of adult human neurogenesis as well as to explore its role in the process."

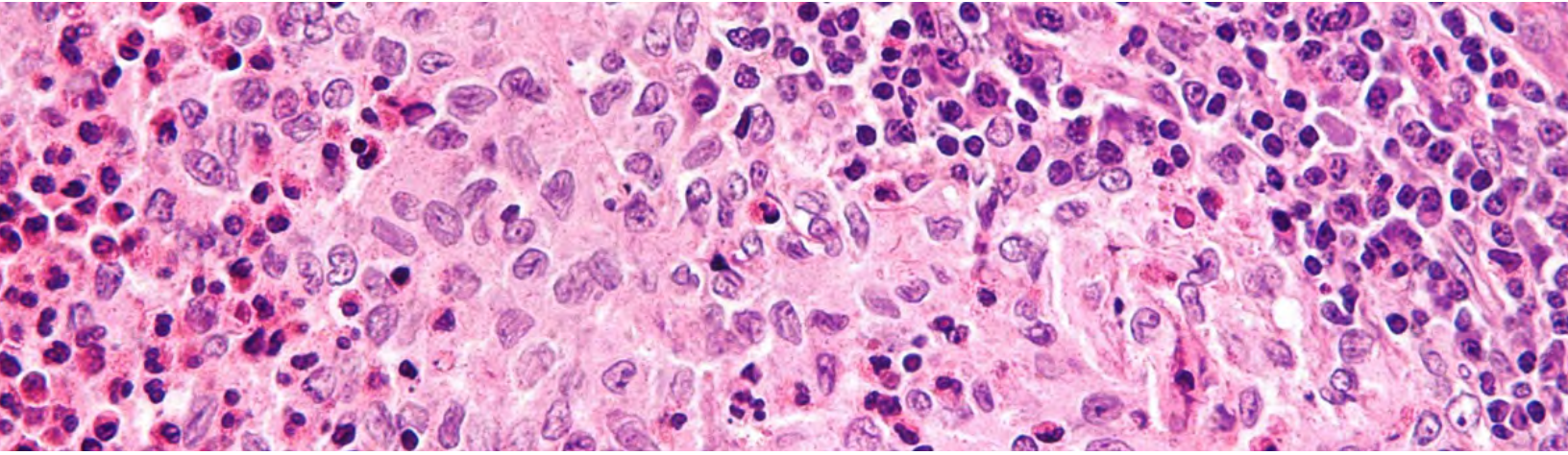
-- Dr. Maletić-Savatić

To reach those goals, they knew that they had to understand elusive but fundamental process in human brains. So far, the tools to do so are not available, with analyses all coming from postmortem brains. Further, Dr. Maletić-Savatić noted that, "And we cannot develop tools to detect this process in people because existing NSC markers are present within cells and unreachable for in vivo visualization."

Reasoning that if they could find proteins on the surface of NSCs, then they could eventually make agents to "see" NSCs in the human brain, the team sought to find surface markers and then develop tools such as ligands for positron emission tomography to visualize them using advanced real-time, *in vivo* brain imaging.

This newly discovered biomarker will allow scientists to better understand the relevance and intricate mechanisms of neurogenesis, which in turn may lead to new therapeutic approaches to treat and manage neurological and neuropsychiatric disorders associated with diminished neurogenesis.

Other authors involved in the study include Louis N. Manganas, Irene Durá, Sivan Osenberg, Fatih Semerci, Mehmet Tosun, Rachana Mishra, Luke Parkitny and Juan M. Encinas.



Synergistic Therapy Offers Hope for Patients with LCH

Dr. Rikhia Chakraborty, Asst. Professor, and her research team have been focusing on identifying the causes of Langerhans cell histiocytosis (LHC) in order to develop better therapies for patients with this rare cancer. LCH (microscopic image of LCH cells above) is an inflammatory myeloid neoplasia, characterized by granulomatous lesions containing pathological CD207+dendritic cells with persistent MAPK pathway activation. Dendritic cells are a type of white blood cells that usually help defend against infections. Chemotherapy, which is the current standard of care, cures fewer than half the patients, and optimal strategies for relapsed and refractory disease are not defined. Although most cells in LCH lesions are not abnormal dendritic cells, other invading immune cells (e.g., T cells) are recruited to sites of disease. Dr. Chakraborty and her colleagues characterized the types and activities of immune cells in LCH lesions in order to "understand the composition of the immune microenvironment in LCH and why the accessory immune cells are present," according to Dr. Chakraborty.

The results of their study were published in *Blood*. They found that both cytotoxic and regulatory T cells are present in increased numbers in LCH lesions, but the cytotoxic T cells are paralyzed, or "exhausted," and ineffective in preventing the formation of an LCH lesion. Such exhausted T cells usually are associated with viral infections. In this current study, Dr. Chakraborty and her team describe a new therapeutic option for LCH that is directed at the inflammatory immune compartment. The approach uses immunotherapy to target the PD-1 receptors that incapacitate T cells, in combination with inhibition of the MAPK to target the dendritic cells that cause the disease.

Their hypothesis was that this therapeutic combination would be synergistic. They used murine models of LCH developed in collaboration with Dr. Miriam Merad and her team at Icahn School of Medicine at Mount Sinai to measure the response to MAPK inhibitor treatment alone, anti-PD-1 treatment alone, and the two treatments combined. In the first model (MAPK inhibitor alone), they found a reduction in the number of diseased LCH cells but not the infiltrating T cells. The models with anti-PD-1 treatment had an opposite result: reduction in the number of infiltrating T cells but not the diseased LCH cells. However, the combine therapy proved to be synergistic, with a significant decrease in numbers of both diseased LCH cells and infiltrating T cells. These findings could offer hope to patients with relapsed disease, and the therapy could help reduce the toxicity that occurs with the current standard of care. The journal article noted that, "These results are consistent with a model that MAPK hyperactivation in myeloid LCH cells drives recruitment of functionally exhausted T cells within the LCH microenvironment, and they highlight combined MAPK and checkpoint inhibition as a potential therapeutic strategy.

Sengal A, Valazquez J, Hahne M, Burke TM, Abhyankar H, Reyes R, Olea W, Scull B, Eckstein OS, Bigenwald C, Bollard CM, Yu W, Miriam M, McClain KL, Allen CE, Chakraborty R. Overcoming T-cell exhaustion in LCH: PD-1 blockade and target MAPK inhibition are synergistic in a mouse model of LCH. Blood 137(13):1777-1791, 2021 doi:10.1182/blood.2020005867.

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