

Baylor
College of
Medicine

Pedi Press

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



Vol. 10, Issue 3, Part II

Summer 2021



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Front Cover: Texas longhorn cooling in summer heat, courtesy of Sherri Geyman Hendrix; editing by George Wallace Beasley



DEPARTMENT NEWS FACULTY, FELLOWS, RESIDENTS & STAFF

Dr. Schutze and Dr. Versalovic Step Down from Interim Roles

On October 1, 2021, **Dr. Gordon Schutze** (above, left) and **Dr. Jim Versalovic** (above, right) stepped down from their interim roles as Interim Chairman of the Department of Pediatrics, BCM, and Interim Pediatrician-in-Chief of TCH, respectively. They had held these positions for 21 months, during one of the most challenging times ever experienced by either institution. Dr. Schutze is Professor of Pediatrics and has served as executive chair of the Department of Pediatrics and as executive Vice President for BIPAI. He is an active member of the American Academy of Pediatrics and the American Board of Pediatrics, where he has served as Chair of the Pediatric Infectious Disease Sub-Board. Dr. Versalovic is the Milton J. Finegold Professor and Vice Chair of Pathology and Immunology at BCM, and is Professor of Pediatrics, Molecular & Human Genetics, and Molecular Virology & Microbiology; He is co-director of the Texas Medical Center Digestive Diseases Center. Dr. Catherine Gordon has been welcomed as the new Chairman and Pediatrician-in-Chief (see part I, p. 3)

With the increasing responsibilities, the role at TCH has changed from Physician-in-Chief, first held by Dr. Russell J. Blattner and then Dr. Ralph D. Feigin, to Pediatrician-in-chief. During the Faculty Meeting, Dr. Versalovic outlined some of the highlights of their time working together: managing a seemingly never-ending pandemic, overseeing the formation of a mental health trifecta (psychiatry, psychology, and the Meyer Center), providing leadership for 27 Sections, recruiting new leaders and section chiefs, planning for expansion into Austin, and transitioning the Children's Sleep Center.

The faculty and staff of both institutions thank them for their enormous contributions to BCM and TCH and for their continued support and encouragement during these especially trying times.

A Fond Farewell to Dr. Mallory

"I have worked with some really fine surgeons, nurses, physical therapists, child life specialists, and social workers. It has been a huge privilege to forge teams and develop close working relationships always on behalf of our patients and their families."

-- Dr. Mallory, on the BCM website



At the Department Meeting held virtually on August 4, 2021, Dr. Gordon Schutze, Professor and Interim Chairman, paid tribute to Dr. George B. Mallory, who retired on July 1, 2021. The information contained herein is extracted from that tribute.

Dr. George B. Mallory, Professor, was born in Connecticut. He and his wife Debbie are the parents of two daughters and grandparents of four grandsons.

He graduated from Harvard College with a BA and matriculated Albert Einstein College of Medicine. He did a residency in pediatric pulmonology at Children's Hospital of Pittsburgh, where he was Chief Resident (1977-1978) and the first Pediatric Pulmonology Fellow (1981-1983). He is board certified in both Pediatrics and Pediatric Pulmonology.

In 1990, he was the founding medical director of the pediatric lung transplant program at St. Louise Children's Hospital. It became the leading program during his tenure. Subsequently, he came to Baylor College of Medicine / Texas Children's Hospital, where in 2002 he became the founding medical director for the lung transplant program, which supplanted the St. Louis program as the most active pediatric lung transplant program in the world. He is considered the world's expert in pediatric lung transplantation, and has been an invited speaker for national and international meetings on pediatric lung transplantation.

He holds memberships in the American Thoracic Society, the International Society for Heart and Lung Transplantation, the Pediatric Transplant Committee of United Network for Organ Sharing, and the Christian Medical and Dental Society. He also has served on the Cardiopulmonary Disease Committee of the American Academy of Chest Physicians as Chair, Vice Chair, and Steering Committee member, and as Secretary/Treasurer of the International Pediatric Lung Transplantation Consortium.

He has authored/co-authored 110 manuscripts and 9 book chapters and served on journal editorial boards for *Pediatric Pulmonary*, *Journal of Bronchology*, and *UpToDate*.



Some "fun facts" about Dr. Mallory are that he has lived in Texas longer than any other location in his life, but he does not own one pair of cowboy boots; he does, however, own 90 bow ties! He is an active cyclist and a devoted member of his church.

In his retirement, he says he hopes to "write a book about my experience in pediatric lung transplantation."

New Leaders Announced



Dr. Kris Reber was named the new Section Chief and Section Head of Neonatology effective July 1, 2021. She came from Columbus, Ohio where she served as Professor, Senior Vice-Chair, Associate Division Chief and Medical Director at Nationwide Children’s Hospital and The Ohio St University Wexner Medical Center. Dr. Reber earned her BS from Ohio University and her MD from The Ohio State University College of Medicine. She did her Internship, residency, and a fellowship at Columbus Children’s Hospital in Columbus, Ohio.



Dr. Arpit Agarwal, Asst. Professor, was named the Chief Medical Information Officer at ChofSA. He received his MD from King George’s Medical University, did his residency at Maimonides Infants and Children’s Hospital in Brooklyn, New York, and a fellowship in pediatric cardiology at University of Miami, Florida. . His primary interests are in 3D computed tomography and MRI reconstructions, 3D printing, and fetal echocardiography.

Dr. Hotez Recognized by the AMA and the AAMC



Dr. Peter Hotez, Professor and Dean of the National School of Medicine, was honored by the **American Medical Association** with its **2021 Scientific Achievement Award**. The AMA “gold medallion” award is presented to individuals on special occasions in recognition of outstanding work in scientific achievement. He also was the recipient of the **2021 Robert Wood Johnson David E. Rogers Award** from the **Association of American Medical Colleges**. The award recognizes his commitment to the healthcare needs of the nation.

Dr. Hotez is a pioneer in the investigation of the molecular science behind neglected tropical diseases and has been instrumental in the development of vaccines for numerous diseases, including human hookworm, schistosomiasis, chagas disease, and SARS. His team has developed a low-cost vaccine for COVID-19 that is in clinical trials in India. He is an avid vaccine advocate and promotes vaccine diplomacy efforts globally.

Congratulations!

CHofSA Faculty Teaching Awards

Faculty Excellence in Teaching

Oluwadamilola Ejike, MD (Nephro)

Mentor of the Year

Samiya Razzaq, MD (AGP)

Perla N. Soni, MD (AGP)

New Faculty of the Year

Beth A. Byrne, MD, MPH (PHM)

Kirstin G. Henley, MD (CCM)

Faculty Excellence in Clinical Care

Summer D. Donovan, DO (ID)

Richard S. Wayne, MD (AGP)

Dr. Osvaldo Requiera Humanism in Medicine

Rebecca L. Huston, MD, MPH (AFP)

CHofSA Honor Role for Teaching Faculty

Niveditha Balakumar, MD (CCM)

Beth A. Byrne, MD, MPH (PHM)

Anthony G. Gardea, MD, MPH (AGP)

Kirstin G. Henley, MD (CCM)

Cory L. Henson, MD (PHM)

Lauren A. Kjolhede, DO, (PHM)

Franca M. Iorember, MD, MPH (Nephro)

Melisa D. Svoboda, MD (Neuro)

Adam D. Wolfe, MD, PhD (Heme-Onc)

Resident Graduation Houston Teaching Awards

Outstanding Continuity Clinic Attending

Dr. Margaret Wood

Most Outstanding Teaching Attending

Dr. Rathi Asaithambi

Dr. Drutz Society Coach Award

Dr. Timothy J. Porea

Dr. Andrea Dean

Academic Promotions

Professor

Caraciolo J. Fernandes, MD, MBA (Neo)

Associate Professor

Sanjiv Harpavat, MD, PhD (GI)

Javier J. Lasa, MD (CCM)

Jennifer H. Foster, MD, MPH (Heme-Onc)

Carla N. Falco, MD (PHM)

Shailendra Das, DO (Pulm)

Ionela Iacobas, MD (Heme-Onc)

Sonia A. Monteiro, MD (Beh-Dev)

Ashley A. Joshi-Patel, DO (PHM)

Sowdhamini S. Wallace, DO, MS (PHM)

Nidhi Bansal, MBBS, MPH (Endo)

Aarti C. Bavare, MD, MPH (CCM)

Adam D. Wolfe, MD, PhD, MS (CHofSA-Heme-Onc)

Faculty College Graduates Announced

The second graduation of the Faculty College was held on June 8, 2021 (for more information on the Faculty College, see Part I, page 26)

Graduates

Via Anderson, MSN, CPNP

Lisa Bouchier-Hays, PhD

Jacqueline G. Broda, PA-C

Erin E. Doherty, MD

Clinton Fuller, MD

Megan N. Gentry, MHA, PA-C

Tracilyn R. Hall, MD

Holly K. Harris, MD

Honey H. H. Herce, MD

Peace Imani, MD, MPH

Priya Mahajan, MD

Fatema Malbari, MD

Jennifer A. Mauney, MSN, APRN

Asha Morrow, MD

Diane Nguyen, PharmD

Julie D. Ortiz, MD

Roshni Sambasivan, MD

Jonathan Santana, DO

Charu J. Shegal, DO

Shreya Sheth, MD

Welcome



NEW INTERNS: Houston



NEW INTERNS: San Antonio

Faculty Briefs

Dr. Hugo Bellen, Professor, is among the 64 life scientists elected to the European Molecular Biology Organization

Dr. Edward Buchanan, Assoc. Professor, is working with Sawbones to develop NeoEar, a novel ear molding device for pediatric patients that protects against skin breakdown due to the malleable nature of the ear mold. NeoEar can be conformed to an individual patient's ear without the need to shave the child's head for use.

Dr. Ashley Butler, Assoc. Professor, has been selected for the Eugene Washington PCORI Engagement Award funding for her project, "Building Capacity in Hispanic-Serving Institutions for Patient-Centered Outcomes: Research/Comparative Effectiveness Research focused on Mental Health Impacts of COVID-19." The project will help develop a skilled community of patients and other stakeholders from across the healthcare enterprise and involve them meaningfully in every aspect of PCORI's work.

Dr. Moreshwar S. Desai, Assoc. Professor, was invited to give a presentation on cardiovascular complications of acute and chronic liver failure to the ACLF Special Interest Group at the Liver Meeting in November.

Dr. Elaine Fielder, Assoc. Professor, was invited to participate in the think tank addressing the Pediatric Training Redesign for the country.

Dr. Douglas Fishman, Assoc. Professor, is conducting a pediatric clinical pilot study with the TubeClear system from Actuated Medical Inc., which clears sluggish and clogged feeding tubes at the bedside while the tube remains in place in pediatric patients.

Dr. Saul Flores, Asst. Professor, was accepted as Vice-Chair for Ultrasound Pediatric and Neonatal at the Congress 2022 of the Society of Critical Care Medicine.

Dr. Milenka Cuevas Guaman, Asst. Professor, was elected as the Secretary of the Executive Board for the BPD Collaborative and International Collaborative working to improve the care and outcomes of patients with established severe BPD.

Dr. Jimmy L. Holder, Asst. Professor, received from NIH a grant for 5 years for a total funding of \$2,625,171 for "Harnessing post-translational regulation of shank3 as a boosting strategy for Phelan-McDermid Syndrome."

Dr. Rebecca Huston, General Pediatrics Section Chief at CHofSA, was the recipient of the Sidney Kaliski Award of Merit, which recognizes a member of the Texas Pediatric Society who has served as an advocate for children and has made a substantial contribution to both the health and welfare of the children of Texas and to the Texas Pediatric Society.

Dr. Ionlea Iacobas, Asst. Professor, has been invited to join the Scientific Committee of the International Society for the Study of Vascular Anomalies (ISSVA). The Scientific Committee consists of 10 international experts in the field and drives the organizations initiatives and oversees the scientific program at the ISSVA World Congress of 2022.

Dr. Parag Jain, Asst. Professor, and Dr. Craig Rusin were awarded a \$1.5 million grant from the National Science Foundation. The objective is to develop a new Bluetooth-enabled vital sign monitoring sticker, called "e-tattoo." This technology will be integrated with a state-of-the-art virtual patient monitoring system called Sickbay, with the goal of diagnosing pneumonia in both inpatient and outpatient settings (home monitoring).

Dr. Keila Lopez, Assoc. Professor

-- was selected as a 2021 National Hispanic Medical Association Leadership Fellow

-- served on a national campaign sponsored by the CDC and Johnson & Johnson as an individual Vaccinate4all Champion .

Dr. Philip Lupo, Assoc. Professor, and Dr. Karen Rabin received a 3-year, more than \$1.1 million per year NIH P20 grant for their project, "Improving Outcome Disparities for Latino Children and Adolescents with Acute Lymphoblastic Leukemia." In addition to reducing disparities among Latino children by identifying biological factors that result in increased toxicities, the project will lay the groundwork for establishment of the first Specialized Programs of Research Excellence (SPORE) devoted to pediatric leukemia.

Dr. Sanghamitra Misra, Assoc. Professor, is the first BCM faculty member to complete the Robert Wood Johnson Foundation Clinical Scholars Fellowship. The 3-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 topics.

Dr. Elizabeth A. Onugha, Asst. Professor, was selected as a Junior Faculty Scholar for the Baylor College of Medicine Center for Excellence in Health Equity, Training and Research.

Dr. Elyse N. Portillo, Asst. Professor, was selected as a Junior Faculty Scholar for the Baylor College of Medicine Center for Excellence in Health Equity, Training and Research.

Dr. Karen Rabin, Assoc. Professor, and Dr. Philip Lupo received a 3-year, more than \$1.1 million per year NIH P20 grant for their project, "Improving Outcome Disparities for Latino Children and Adolescents with Acute Lymphoblastic Leukemia." In addition to reducing disparities among Latino children by identifying biological factors that result in increased toxicities, the project will lay the groundwork for establishment of the first Specialized Programs of Research Excellence (SPORE) devoted to pediatric leukemia.

Dr. Kim Raghubar, Asst. Professor, was awarded an \$2m from the NIH/NINR to evaluate the feasibility and preliminary effectiveness of systematic bright light exposure for reducing fatigue and improving cognitive efficiency in survivors of pediatric brain tumors. The goal of the research is to trial interventions that mitigate cognitive late effects to improve quality of life in these survivors. Findings will be used to refine the intervention and inform a larger randomized controlled trial

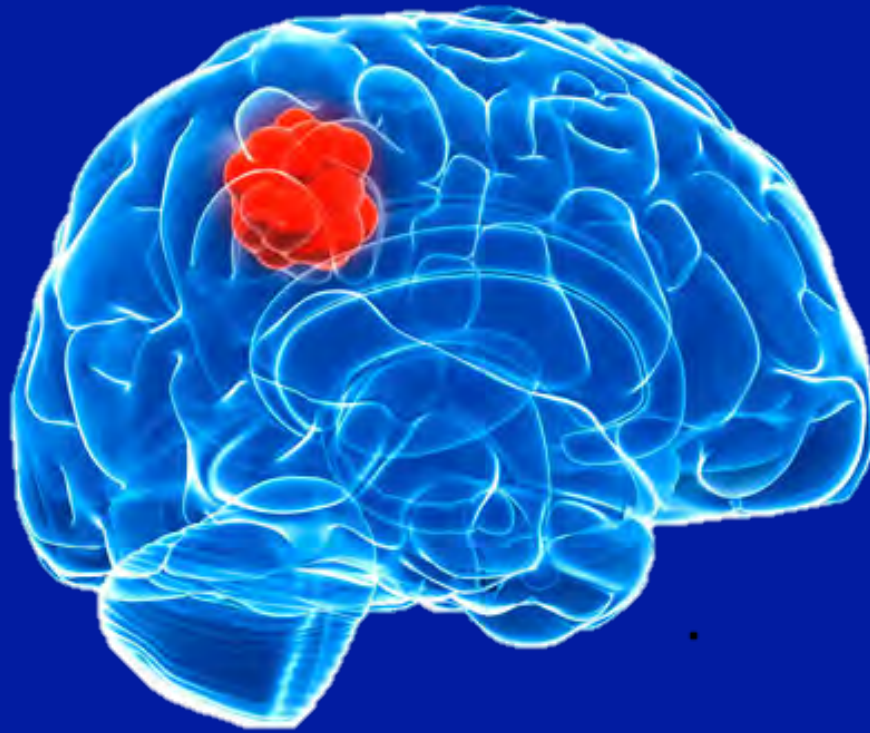
Dr. Rayne Rouse, Asst. Professor, has received the 2021 Outstanding Women in Science award from the Association for Women in Science – Gulf Coast Houston. She was recognized for her clinical work with pediatric leukemia and lymphoma patients and her research on T cell immunotherapy. Rouse also serves as associate dean of community engagement at Baylor and has been actively involved in diversity and inclusion initiatives. She was honored at a ceremony July 7.

Dr. Craig Rusin, Assoc. Professor, and Dr. Parag Jain were awarded a \$1.5 million grant from the National Science Foundation. The objective is to develop a new Bluetooth-enabled vital sign monitoring sticker, called "e-tattoo." This technology will be integrated with a state-of-the-art virtual patient monitoring system called Sickbay, with the goal of diagnosing pneumonia in both inpatient and outpatient settings (home monitoring).

Dr. Michael E. Schuerer, Professor, received a grant for survivorship and access to care for Latinos to understand and address disparities, for a 2-year total of \$2,045,980.

Dr. Roy Sillitoe, Assoc. Professor, received the Landis Award for Outstanding Mentorship from the National Institute of Neurological Disorders.

Dr. M. Hossein Tcharmtchi, Assoc. Professor, was appointed to the Credentials Committee of the American College of Critical Care Medicine. The Committee reviews and analyzes all applications for Fellowship into the ACCM and recommends a course of action for each applicant to the Board of Regents for approval or additional review.

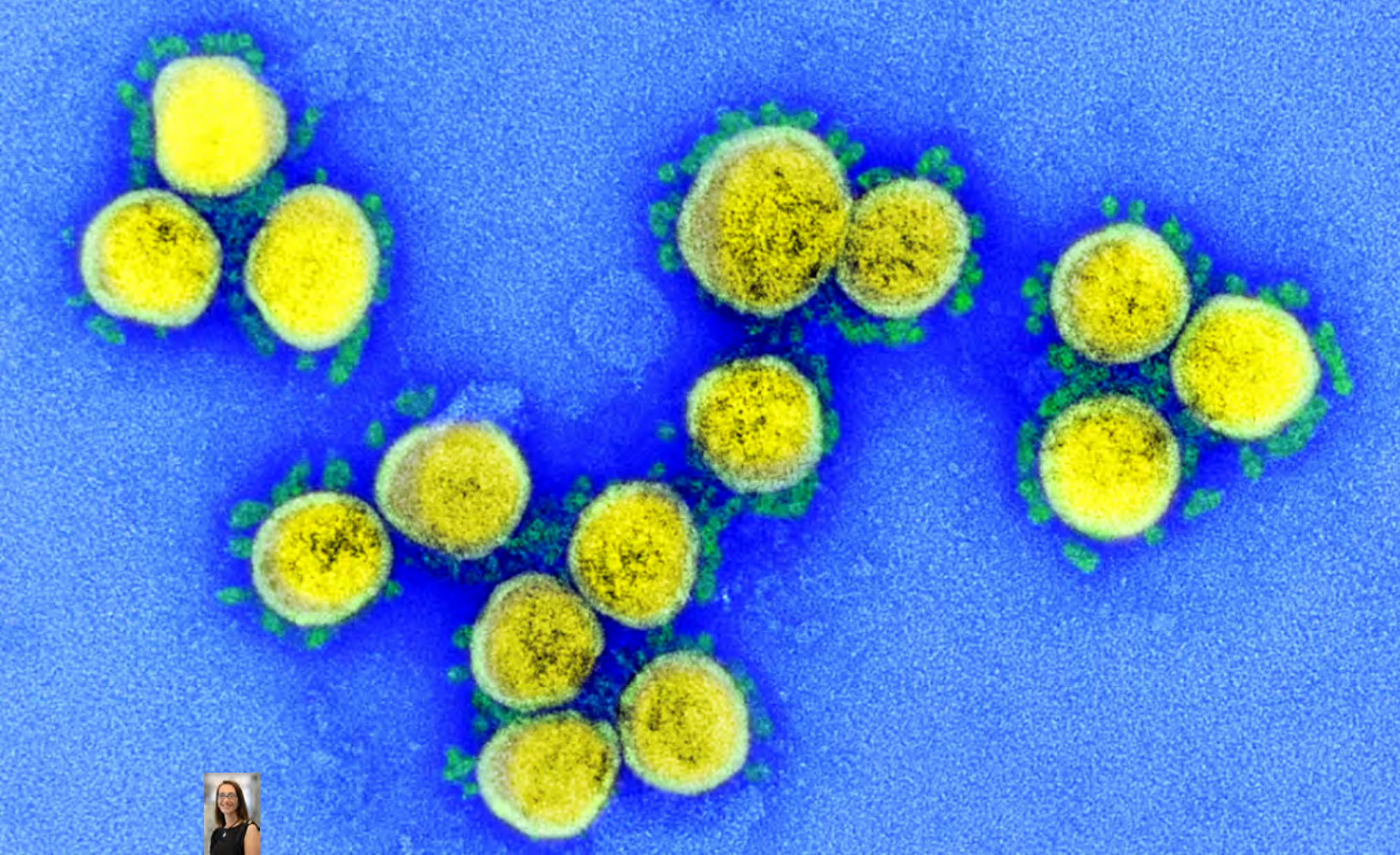


DEPARTMENT NEWS RESEARCH

Restoring the Molecular Clock Affects Neuroblastoma



Dr. Eveline Barbieri, Asst. Professor, and her team found that the molecular clock may be critical to treating neuroblastoma. They studied patients with high expressions of MYCN, a major oncogenic driver of neuroblastoma, and found that two main components of the molecular clock, BMAL1, which oscillates to drive the clock cycle, and RORa, which activates BMAL1, were repressed. The repression correlated with poor clinical outcomes. To determine if restoring these components of the molecular clock would stop growth in neuroblastoma cells, they tested two approaches: genetic overexpression of RORa in the lab and a pharmaceutical approach using a synthetic ligand that reactivates RORa. Both techniques successfully restored BMAL1 expression and oscillation and also blocked tumor growth, suggesting that repression of the molecular clock is, indeed, oncogenic. Dr. Barbieri explained that, "Our cells follow a molecular clock that controls cell metabolism, much like the body's circadian rhythm controls sleep cycles. We know that metabolic processes are really important in how tumors develop resistance to chemotherapy. In the future, if we can develop therapeutics that restore the molecular clock in a clinical setting, we may be able to use them in combination with standard chemotherapy to avoid treatment resistance." The results of the study were published in *Nature Communications*, with **Dr. Myrthala Moreno-Smith** and **Dr. Ling Tao**, both researchers in Dr. Barbieri's lab, as first and second authors, respectively.



*Color-enhanced transmission electron micrograph of SARS-CoV-2 particles, isolated from a patient with COVID-19
Courtesy, National Institute of Allergy and Infectious Diseases*

Researchers Publish Results of Study for Vaccine Candidate



Dr. Peter Hotez, Professor and Dean for the National School of Tropical Medicine (NSTM) (pictured left), and **Dr. Maria Bottazzi**, Professor and Section Head of Pediatric Tropical Medicine and Associate Dean of the NSTM (pictured right), were

part of a multidisciplinary team that was the first to demonstrate that combining yeast-expression technology with a novel adjuvant formulation produces a vaccine candidate that is effective against SARS-CoV-2. The researchers from BCM and colleagues at Yerkes National Primate Research Center (NPRC) at Emory University, Infectious Disease Research Institute, and 3M paired BCM's SARS-CoV-2 receptor binding domain (RBD) recombinant protein formulation vaccine candidate with IDRI's aluminum-based formula of 3M's

toll-like receptors 7 and 8 agonist 3M-052 to enhance immune response against SARS-CoV-2 and, thereby, increase the vaccine's effectiveness against COVID-19. The candidate will be easy to produce on a large scale and will be cost-effective, so it has important potential for vaccinating people worldwide, especially in low- and middle-income countries. The vaccine candidate also is beneficial in inducing a balanced antibody and CD8+T cell response not seen previously with other protein-based vaccine approaches. In addition, they demonstrated a substantial reduction in virus shedding from the upper airways, suggesting that the candidate may also slow or even halt virus transmission.



The research team is hopeful that the vaccine comprising a recombinant RBD protein with its novel 3M-052 adjuvant formulation will be strongly effective against the emerging variants because it has the capability to induce both neutralizing antibodies and CD8+ T cells, which can kill the virus if it enters the cells. This ability is critical for reducing the incidence of virus transmission and impact. Another

The widespread use and outstanding safety track record of yeast-expressed recombinant protein immunizations offer promise for using this approach to produce and deliver COVID-19 vaccines for global health.

-- Dr. Peter Hotez

critical advantage is that the vaccine potentially reduces the levels of SARS-CoV-2 and limits inflammation by blocking the expansion of pro-inflammatory monocytes.

The team also identified a combination of blood markers that predict the virus burden in the lungs, which could potentially help healthcare providers monitor disease and adjust treatments for optimal effectiveness.

Testing was performed on two groups of five rhesus monkeys each with RBD+alum (Group 2) or RVD+3M-052+Alum (Group 3). All animals in these

two groups received three immunizations over the course of 10 weeks. An additional five rhesus monkeys (Group 1) served as unvaccinated controls. All animals were challenged with SARS-CoV-2 via combined intranasal and intratracheal route one month after receiving the third vaccination. The Group 3 animals showed clear advantages in antibody response, neutralizing activity, and effectiveness over the Group 2 animals.

To the authors' knowledge, this study is the first to report the use of a recombinant RBD immunogen and the 3M-052/Alum adjuvant to

induce CD8+ T cell responses. They are confident that the T cell responses will be easily translatable from the rhesus monkey model into humans for protection against a broad range of pathogens, including the emerging SARS-CoV-2 variants.

The study results were published in *Science Immunology* 2021 Jul 15;6(61):eabh3634 doi:10.1126/sciimmunol.abh3634

Our results showed producing the RBD recombinant protein using the yeast expression platform would meet the demand for vaccinating communities around the world.

-- Dr. Maria Elena Bottazzi



Heat stress tolerant crops



Wild-Type (WT) plants

GRXS17 plants

Heat Tolerance of Genetically Modified Tomatoes. Control plants on the left and modified plants on the right were subjected to several days of high temperatures and then returned to normal growth conditions. Note that the modified plants retain their vigor. They will go on to produce fruit whereas the wild-type will not. (Image courtesy of the Kendal Hirschi lab)

Researchers Patent New Gene that Creates Heat-Resistant Plants

Recently, **Dr. Kendal Hirschi**, Professor, and **Dr. Ninghui Cheng**, Asst. Professor, discussed a patent awarded to the Kendal Hirschi Lab for a gene that makes plants more tolerant of hot weather.¹

This discovery has important implications for the environment and future plant crops. Abiotic stress adversely affects plants' growth and development and limits agricultural productivity, which can cause billions of dollars of loss annually. One example is wheat, which can be reduced in yield by 50% simply by a sustained increase in temperature of 2 degrees.

¹ <https://www.seedtoday.com/article/243839/new-gene-to-make-plants-heat-tolerant-in-rising-temperatures>

The new gene protects plants when the temperature rises, thereby allowing for better growth and increased yield. For wheat, the 2 degrees increase in temperature would have no effect, thereby doubling the yield from what would be the case without the gene.

As the environment continues to get warmer, developing means to overcome the effects on crops will be critical to the food supply. Traditional breeding approaches are effective but take years or even decades to produce tolerance to heat. The lab's invention is concerned with "plants having ectopic expression of an exogenous, abiotic-stress-tolerance

"We're speculating that high temperatures affect plants because they trigger an inflammatory response similar to what we see in our bodies. Inflammation is associated with reactive oxygen species, compounds made by cells to serve as signaling molecules for normal biologic processes. However, reactive oxygen species also can be detrimental to cells, ultimately disrupting biological processes. We think this gene reduces the reactive oxygen species that are generated during heat - it distresses the plant"

-- Dr. Kendal Hirschi



"In commercial agriculture, we want high yield and nutritious foods. In hot temperatures, the yield can be low, which is a problem. With this new gene, we're protecting plants when the temperatures rise so they can grow better."

-- Dr. Ninghui Cheng



gene, which thereby have increased tolerance or resistance to abiotic stresses relative to a control plant." It is concerned also with different methods of increasing a plant's tolerance or resistance to abiotic stresses by ectopic expression of an exogenous, abiotic-stress-tolerance gene in a plant. The invention is suitable for use with various plants, including both monocotyledons and dicotyledons, and can be used to produce plants with enhanced tolerance to various abiotic stresses such as extreme temperatures, availability of water, and salinity.

In one or more embodiments, the exogenous abiotic-stress-tolerance gene (i.e., that which originates from a source outside a particular plant species and is introduced into another plant species to create the transgenic plant) is heterologous. The ectopic expression or overexpression of this gene increases the tolerance or resistance of the transgenic plant to abiotic stress. The resulting plants can be crossed to prepare progeny and, preferably, homozygous progeny or seeds. Hence, the abiotic-stress-tolerant plants are capable of being produced indirectly by breeding parent plants having the stress tolerance with other abiotic-stress-tolerant plants, or even with other cultivars with additional desired characteristics. The resulting progeny can be screened to identify the ones that are abiotic-stress-tolerant.

The Hirschi Lab is part of the Children's Nutrition Research Center, which houses laboratories of varied disciplines, a vast array of state-of-the-art equipment, a greenhouse, observation labs and accommodations for research volunteers, a metabolic kitchen, and an elite group of scientists conducting groundbreaking research.

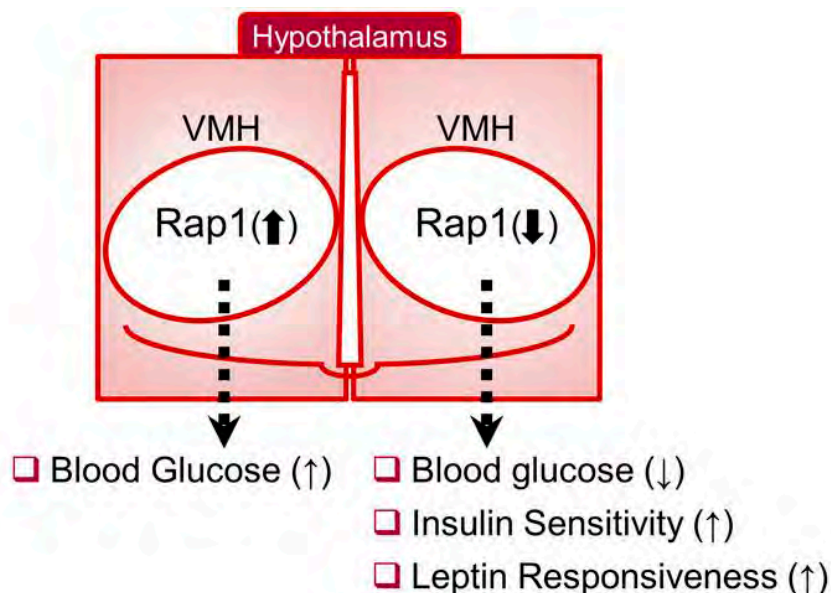
Information extracted from <https://patents.google.com/patent/US11066677B2/en>

Unlike many other transgenic plants that have similar improvements in tolerance to stressors, the plants created by the invention have a phenotype/morphology that is otherwise substantially similar to, or nearly identical to, wild type plants of the same species. However, when grown under stress, the transgenic plants grown according to various embodiments of the invention, have significantly improved morphologies compared to the control plants.

Another advantage of the invention is the enhancement of abiotic stress tolerance of plants by silencing the expression of an endogenous glutaredoxin gene that the plant normally expresses. As used by the authors, the term *silencing* refers to any suitable method of reducing or even completely suppressing the expression of the protein from a gene or a coding sequence. This method inhibits the expression, activity, or function of an endogenous glutaredoxin gene and, thereby, produces a modified plant that has enhanced resistance to abiotic stress and is especially resistant to drought. Plants with a silenced endogenous glutaredoxin gene have phenotypes/morphologies that are otherwise substantially similar to or nearly identical to the wild type plants of the same species.

Other collaborators include Dr. Sunghun Park, professor of crop functional genomics at Kansas State University.

Study Reveals Effects of Rap1 in the VMH on Glucose Homeostasis



"A growing body of evidence strongly suggests that the brain is a promising yet unrealized therapeutic target for type 2 diabetes, as it has been shown that it can regulate glucose metabolism. To further materialize this concept, it is of great interest to identify potentially druggable molecular targets mediating the brain's antidiabetic effects."

-- Dr. Makoto Fukuda



Research has shown that the brain can regulate glucose metabolism, rendering it a promising but unrealized therapeutic target for type 2 diabetes. Within the hypothalamic region of the brain is the ventromedial nucleus of the hypothalamus (VMH), a small area that contains glucose-sensing neurons. It also regulates glucose metabolism in peripheral tissues and is capable of correcting diabetes conditions independently of an effect on energy balance, but the signaling mechanism with VMH neurons that mediate whole-body sugar control are elusive.

Dr. Makoto Fukuda, Asst. Professor, and his team, worked with a diabetes model of high-fat, diet-induced (HFD-induced) obesity in mice and either activated or eliminated Rap1, an enzyme known to mediate overnutrition-associated disorders, specifically in VMH neurons, using genetic or pharmacological techniques. They reported that increasing Rap1 activity selectively in the medial hypothalamus elevated blood glucose without increasing the body weight of the HFD-fed mice. Contrariwise, decreasing the hypothalamic Rap1 activity protected mice from diet-induced

hyperglycemia but did not prevent weight gain. The remarkable glycemic effect of Rap1 was reproduced when Rap1 was specifically deleted in steroidogenic factor-1-positive neurons in the VMH known to regulate glucose metabolism.

Despite "having no effect on body weight, regardless of sex, diet, or age, *Rap1* deficiency in the VMH SF1 neurons markedly lowered blood glucose and insulin levels, improved glucose and insulin tolerance, and protected mice against HFD-induced neural leptin resistance and peripheral insulin resistance at the cellular and whole-body levels." In addition, acute pharmacological inhibition of the brain exchange protein directly activated by cAMP2 corrected the imbalance in glucose in obese mouse models.

The authors stated in their article published in *JCI Insight* that these findings uncover the primary role of VMH Rap1 in glycemic control and implicate Rap1 signaling as a potential target for therapeutic intervention in diabetes.

Kaneko K, Lin H-y, Fu Y, et al. Rap1 in the VMH regulates glucose homeostasis. *JCI insight* [10.1172/jci.insight.142545](https://doi.org/10.1172/jci.insight.142545)

Study Demonstrates How the Brain Handles Eating Behaviors

According to the Centers for Disease Control and Prevention, the prevalence of adult obesity in the United States was 42.4% in 2017-2018, an increase from 30.5% in 1999-2000. Obesity-related conditions include heart disease, stroke, type 2 diabetes, and certain cancers, and are among the leading causes of preventable, premature death. The annual medical costs of obesity are in the billions of U.S. dollars. The CDC prevalence in the pediatric population for 2017-2018 was 19.3%, affecting approximately 14.4 million children and adolescents. The CDC defines obesity as “a body mass index (BMI) at or above the 95th percentile of the CDC sex-specific BMI-for-age growth charts, which can be accessed at https://www.cdc.gov/growthcharts/clinical_charts.htm.

Often, people eat for reasons other than hunger, such as social pressures, the presentation of foods, the sense of comfort derived from food, or just because they “want one more bite.” Such overeating usually leads to obesity and the accompanying inherent physical, mental, and psychological problems.



Dr. Yong Xu, Professor, together with an international team of researchers, investigated an animal model to determine how the brain regulates feeding triggered by hunger or other

factors. They identified two distinct brain circuits formed by serotonin-producing neurons in the mouse midbrain: one extends into the hypothalamus and the other into another region of the midbrain. These circuits play distinctively different roles. The circuit that extends to the hypothalamus primarily regulates hunger-driven feeding, whereas the other circuit regulates primarily the nonhunger-driven feeding but not feeding triggered by hunger.

These findings have specific relevance for identifying potential molecular targets associated with the circuits that can be used to treat overeating and, thereby, obesity. One potential target, as noted by Dr. Xu, is “serotonin receptors, which are molecules that mediate the functions of the neurotransmitter serotonin produced by the neurons.” He explained that the team found that two receptors, serotonin 2C receptor and serotonin 1B receptor, are involved in both types of feeding behaviors. Their data indicate that combining compounds directed at both receptors might result in a synergistic benefit by suppressing eating.

The researchers also identified two ion channels associated with the circuits that could offer an opportunity to regulate feeding behaviors. One, the GABA A receptor, is a chloride channel that was found to be important in regulating serotonin circuits during hunger-driven feeding but not during nonhunger-driven feeding. The other, a potassium channel, influences feeding triggered by hunger-independent cues but not hunger-driven feeding.

These findings have encouraged the researchers to conduct studies to identify more molecules that could modulate the activity of the ion channels to produce anti-overeating effects in animal models. They also plan to explore how external factors related to nutrition might affect ion channel functions at the molecular level.

Their work was reported in the journal *Molecular Psychiatry*.

The following authors also contributed to this work: Yanlin He, Xing Cai, Hailan Liu, Kristine M. Conde, Pingwen Xu, Yongxiang Li, Chunmei Wang, Meng Yu, Yang He, Hesong Liu, Chen Liang, Tingting Yang, Yongjie Yang, Kaifan Yu, Julia Wang, Rong Zheng, Feng Liu, Zheng Sun, Lora Heisler, Qi Wu, Qingchun Tong, Canjun Zhu and Gang Shu.

2021-2022 Faculty Awards

Upcoming Deadlines of Peer reviewed Awards
Administered through the Office of Faculty Affairs and
Faculty Development



BARBARA AND CORBIN J. ROBERTSON, JR. PRESIDENTIAL AWARD FOR EXCELLENCE IN EDUCATION

Nominations open Nov. 1, 2021

Deadline Dec. 10, 2021

CLARK FACULTY SERVICE AWARD

Nominations open Nov. 1, 2021

Deadline Dec. 13, 2021

BEN AND MARGARET LOVE FOUNDATION BOBBY ALFORD AWARD FOR ACADEMIC CLINICAL PROFESSIONALISM

Nominations open Jan. 3, 2022

Deadline Feb. 21, 2022

FACULTY AWARDS FOR EXCELLENCE IN PATIENT CARE

Early Career - Portfolio submission deadline Nov. 15, 2021

Star - Portfolio submission deadline Jan. 10, 2022

Master Clinician - Nominations due Feb. 14, 2022

FOR ADDITIONAL INFORMATION:

Contact Debbie Fernandez,

dfaced@bcm.edu

NORTON ROSE FULBRIGHT FACULTY EXCELLENCE AWARD

“End with good stuff”

-- Dr. Gordon Schutze



ASTROS FANS!

**Top: Omri, AKC CGC, AKC 2020 Trick Dog Elite Performer, Licensed Pet Therapy Dog
(owned by Karen Cadenhead)**

**Bottom: Borden's Lady Brit of the Liffey (Brittany), AKC CGC, Licensed Pet Therapy Dog
(owned by Lee Ligon-Borden & Gordon Borden)**