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Cover:

Houston, Texas, experienced an unprecedented freeze and snow in February 2021, requiring a shut-down of much of the Medical Center for several days.

Dr. Gordon Schutze, Interim Editor-in-Chief
Dr. B. Lee Ligon, Managing Editor/Graphics Design
Julie O'Brien Anderson, Copy and Content Editor
Next Deadline
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DEPARTMENT NEWS

FACULTY, FELLOWS, RESIDENTS, & STAFF

Department Welcomes New Section Leader

Dr. Gordon Schutze, Professor and Interim Chairman, announced at the February faculty meeting a new leader for the Section of Neonatology. **Dr. Kristina “Kris” Reber** is Professor in the Department of Pediatrics at The Ohio State University College of Medicine, as well as Senior Vice-Chair of the Department of Pediatrics at The Ohio State University Wexner Medical Center.

She is the medical director for the Newborn Service/Neonatal Intensive Care Unit at The Ohio State University Wexner Medical Center and Associate Division Chief of the Division of Neonatology, Nationwide Children’s Hospital. In addition, she is an attending neonatologist at Nationwide Children’s Hospital and The Ohio State University Wexner Medical Center.

She is scheduled to start at Baylor College of Medicine/Texas Children’s Hospital in July.



Kristina Reber, M.D.

BIPAI Leader Retires

"Sebastian's life-long commitment and dedication to HIV/AIDS has been nothing short of extraordinary. He is one of the most intelligent and compassionate individuals I have ever had the honor and privilege to know and work with."

--Michael B. Mizwa, CEO, BIPAI



On February 20, 2021, **Michael Mizwa**, Chief Executive Officer of Baylor College of Medicine International Pediatric AIDS Initiative (BIPAI), announced that **Dr. Sebastian Wanless** (left), Assoc. Professor, is retiring from BIPAI, where he has served since 2007. He received his medical degree in Edinburgh, Scotland, before joining the Bristol-Myers Pharmaceutical Company, and later transferred to the Bristol-Myers Squibb Foundation. He was Senior Medical Director of the Bristol-Myers Squibb funded "Secure the Future" program based in Johannesburg, South Africa, from 2003-2007. After a 30-year successful career in numerous global research leadership positions at Bristol-Myers, Dr. Wanless joined BIPAI as Vice President of Research and Program Evaluation. Under his supervision and guidance, the BIPAI network embraced monitoring and evaluation by establishing a network-wide "Balanced Score Card." He oversaw 61 operational and clinical research studies through the network. Although he is officially retiring, he will continue to provide ongoing advice.

Clinician Wears Several Hats

"Music has always played a very special role in my life. I've always joked to those around me that they are very fortunate that I don't have a great singing voice, because I would never shut up. I started writing raps and freestyling years and years ago. It started as something my cousins and I would do just for fun, but I realized over the last few years, that I find it extremely cathartic."

-- Dr. Rayne Rouce

Dr. Rayne Rouce, Asst. Professor, was featured recently in an article about her musical interests in addition to her commitment to patients with leukemia and lymphoma. One instance is her Saturday Morning Science program, which she leads at BCM for young people to teach them science and medicine in a "fun and memorable" way. She is also known for "'splitting some bars as Rizzo,' a rapper who performs original music." Dr. Rouce's compositions of approximately 200 songs range from educational tracks to raps about social justice issues to scientific achievements. All are intended to uplift and inspire the listener.

As a pediatric oncologist and physician scientist, she has a full schedule of days that often require her to assume different roles. She juggles her time taking care of patients in the clinic and hospital with clinical trials and conducting clinical, translational, and laboratory research.

Because her patients come first, she remains flexible and often must change her schedule if a clinical issue arises. She also is passionate about community outreach, education, and health disparities. Her rap often opens doors for



communicating with people in the community, and her involvement with the Office of Institutional Diversity, Inclusion and Equity at BCM provides venues in which to lead community outreach efforts that enhance scientific awareness. Even during the COVID pandemic, she has been able to remain active by doing virtual seminars for schools, community centers, and nursing homes.

Baylor College of Medicine Professorship Announced



Dr. Sharon Plon, Professor, was honored for her years of service, contributions, and scientific excellence with a Dan L Duncan Comprehensive Cancer Center Professorship by vote of the Baylor College of Medicine Academic Council on December 14, 2020. Dr. Plon received her MD from Harvard Medical School and her PhD from Harvard University. She completed Fellowships at National Cancer Institute, University of Washington Affiliate Hospitals, and Fred Hutchinson Cancer Research Center. In addition to her position as Professor of Pediatrics, she holds the positions of Professor in Molecular and Human Genetics at BCM, Director of Cancer Genetics Clinical and Research Programs at TCH, and Co-Leader of the Pediatric Cancer Program at Dan L Duncan Comprehensive Cancer Center.

Chairman Announces New Academic Promotions

Dr. Gordon Schutze, Professor and Interim Chairman, announced the following Baylor College of Medicine Academic Promotions, at the Department Meeting held virtually on February 4, 2021:



Professor
Dr. Julie A. Boom (AGP)
Dr. Deborah L. Callanan (PEM-ChofSA)



Associate Professor
Dr. Andras A. Heczey (Heme-Onc)
Dr. Karen D. Evankovich (Psychology)



Faculty Appointed to Houston Advisory Board



Dr. Keila Lopez, Assoc. Professor, was named to Houston Mayor Sylvester Turner's Hispanic Advisory Board. The committee is composed of leaders from various professions, including business or law, and has been in existence for some time. Dr. Lopez is the first physician to be added to the board, which is especially important at this time, as the COVID-19 pandemic has disproportionately affected the health of the Latino community. Her passion for public health and working with minority and underrepresented groups, which began during her years in medical school training, has been seen in her participation in other endeavors. She is the only Latin physician chosen to work on the Mayor's Health Equity Response Task Force, which was designed to help address health disparities experienced among minority communities during the pandemic.

She was recognized earlier in the year when named the 2021 Paul V. Miles Fellow by the American Board of Pediatrics, an honor bestowed for her work to overcome health inequities in pediatric patients with congenital heart disease and to improve efforts to transition pediatric patients to adult care.

The full report is available here: <https://bcmfamily.bcm.edu/2021/03/03/a-passion-for-public-health/>

Chief Residents Announced

On February 23, 2021, **Dr. Elaine Fielder**, Assoc. Professor and Director of the Pediatric Residency Program, announced **the 2022-2023 Pediatric Chief Residents** and the **2021-2022 Global Health Chief Resident**.



Dr. Neelima Agrawal
2021-2022 Global Health Chief Resident



Dr. Doha Aboul-Foutouh



Dr. Mark McShane



Dr. Jasmine Pendergrass



Dr. Rachel Quinn

Congratulations

Project Managers Announced
From Mike Mizwa, Chief Executive Officer,
BIPAI and Director, Global Health:

Adam Gibson and Taylor Napier-Earle, in their individual roles as Project Managers, have continued to be instrumental in [our] endeavor, resulting in the exponential growth of our global footprint. As a result of their continued commitment to excellence and expanded roles and leadership responsibilities, Adam and Taylor have been promoted to Managers, Global Health, Texas Children's Hospital. These promotions are well deserved and testaments of their value to our global health network.

Please join me in congratulating Adam and Taylor!

All the best,

Mike



faculty briefs . . .

Dr. Maria Elena Bottazzi, Professor and Associate Dean of the National School of Tropical Medicine, has been appointed to a National Academies of Sciences, Engineering and Medicine committee aimed at developing recommendations to optimize vaccine research and development for future seasonal and pandemic influenza events. The committee is sponsored by the Department of Health and Human Services.

Dr. Corrie Chumpitazi, Assoc. Professor, was appointed to the new Women in Pediatric Emergency Medicine subcommittee of the American Academy of Pediatrics Section on Emergency Medicine. She is involved in career development activities on the subcommittee.

Dr. Peter Hotez, Professor and Dean of BCM's National School of Tropical Medicine, is the recipient of the Weill Cornell Medical College's 2021 Award of Distinction, the institution's most prestigious alumni award. Hotez is a world-renowned expert in neglected tropical diseases and vaccine development and advocacy who has served as a critical voice during the COVID-19 pandemic by sharing reliable, evidence-based information. He will be recognized at a virtual ceremony in May.

Dr. Deborah Hsu, Assoc. Professor, was appointed to the new Women in Pediatric Emergency Medicine subcommittee of the American Academy of Pediatrics Section on Emergency Medicine. She is also involved in career development activities on the subcommittee and serves as chair-elect of the AAP Section on Emergency Medicine Executive Committee.

Dr. Lisa Kahalley, Assoc. Professor, was awarded a \$6.7 million grant from the National Cancer Institute for a multinational, multidisciplinary study comparing symptom burden/toxicity, neurocognitive change and functional outcomes in pediatric brain tumor patients treated with proton vs. photon radiotherapy.

Dr. Susan Kirk, Asst. Professor, was recognized as a Distinguished Fellow by the American Academy of Pediatrics for her outstanding dedication to her profession.

Dr. Keila Lopez, Asst. Professor

-- was named by the American Board of Pediatrics as the 2021 Paul V. Miles Fellow. The award recognizes her outstanding work to overcome health inequities in pediatric congenital heart disease patients and help transition pediatric patients into adult care. As part of the fellowship, Lopez will give grand rounds at the University of North Carolina at Chapel Hill and Duke University medical schools and will speak to ABP staff about her work.

-- was named to Houston Mayor Sylvester Turner's Hispanic Advisory Board. As the only medical professional on the board, she will contribute her perspective and experience to assist in the care of Latino populations in Houston.

Dr. Rojelio Mejia, Asst. Professor, has received a donation of 10,000 albendazole pills from the Mark Cuban Cost Plus Drug Co. Mejia and his team are studying the prevalence of hookworm infection in children 2 to 18 years of age living in rural Alabama. They will be able to treat participants with the antiparasitic pills, valued at about \$2 million. (see also *Pedi Press*, Part I, page 22)

Dr. Ana Monterrey, Asst. Professor, contributed to a toolkit on food insecurity for clinicians from the American Academy of Pediatrics. Her input in the 'Words of Wisdom from the Field' section discusses implementation of food insecurity screening in the clinic, which included working in partnership with the Houston Food Bank to train doctors and staff.

Dr. Diane Nguyen, Asst. Professor and Director of Programs at BIPAI, has received a co-primary appointment to the BCM Department of Education, Innovation, and Technology (EIT).

Dr. Jacquelyn Powers, Asst. Professor, was appointed to a four-year term as a member of the American Society of Hematology Committee on Quality. The ASH COQ is charged to promote the highest quality care of patients with hematologic diseases and is responsible for overseeing and implementing the ASH quality initiative.

Dr. Jason Yustein, Assoc. Professor, has been appointed to the St. Baldrick's Foundation board of directors. The foundation is the largest nongovernment funder of childhood cancer research grants. Yustein also serves on the foundation's Scientific Advisory Committee and Advocacy Committee.

Dr. Huda Zoghbi, Professor, Director of the Jan and Dan Duncan Neurological Research Institute and Howard Hughes Medical Institute investigator, is one of five leaders in medicine to be elected to the National Academy of Medicine Governing Council for a three-year term.

The **Cancer and Hematology Centers** honored six team members with **Bravo Awards** for going above and beyond to ensure patients and families received the best care. They are:

Mackenzie Frederick, RD, LD, Main Campus

Kelly Miranda, RN, Main Campus

Rhoda Phillis, RN, Main Campus

Regina Salas, MA, Main Campus

Lisa Sowers, RN, Main Campus

Shelly Wilke, RN, The Woodlands Campus

Three pediatrics faculty members were invited to participate on **National Cancer Institute's Childhood Cancer Data Initiative Working Groups**:

Dr. Donald W. "Will" Parsons

is on the Molecular Characterization Protocol Working Group,

Dr. Monica Gramatges

is on the Childhood Cancer Cohort Working Group

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 improve treatments, quality of life and survivorship of every child with cancer.

Erratum

Dr. Maria Jose Redondo, Professor, was incorrectly identified as Associate Professor in the last issue of *Pedi Press*. *Pedi Press* apologizes for the oversight, and her designation also has been corrected on the BCM website to correctly recognize her rank.



DEPARTMENT NEWS

RESEARCH

Collaborative Seeks to Identify Environmental Causes of Pediatric Cancer



A landmark new study, under the direction of **Dr. Michael Scheurer**, Professor and Director of the Childhood Cancer Epidemiology and Prevention Program at TCH, aims to determine environmental causes of childhood cancer. The study, a joint project between TCH and The Oliver Foundation, is called The ReasonsWhy.U.s, which is also the title of the website where individuals can sign-up to participate.

The Oliver Foundation was founded by Simon and Vilma Strong, parents of a 12-year-old boy named Oliver, who died 36 hours after being diagnosed with acute myeloid leukemia, only a week after the onset of headaches. Oliver's death in 2015 left his distraught parents with numerous questions about what they might have done differently and/or what might have been an environmental causative agent. They had used Roundup herbicide, known to be linked to leukemia, in the yard and garden to kill weeds, and Oliver also had played as a goalkeeper on athletic fields of crumb rubber artificial turf, made with toxic petrochemicals. (continued on page 37)

They also note on their website that the surge in pediatric cancer since the 1970s, as well as that of other health conditions and diseases, aligns with the increased daily use of thousands of chemical-based, untested items.

Currently, data are insufficient for the most part to determine possible environmental causes of cancers, especially specific types. The study seeks to identify various environmental causes and “to build the evidence needed to identify and to protect us from the toxicants associated with child/teen cancer.” For this reason, The Oliver Foundation teamed with BCM for the pioneering research study. The patient-driven, online, and global study is based on scientific expertise and experience of leading epidemiologists and toxicologists in the United States and builds on the in-person pediatric cancer epidemiological study that has been conducted at TCH for years under Dr. Scheurer’s leadership.

The study includes a comprehensive online questionnaire of family history that includes diet, neonatal practices, medications, infections, sports, leisure, and other personal activities. It also collects clinical samples of saliva and baby teeth, if available. Dr. Scheurer has noted the need to “widen society’s focus on detection, diagnosis and treatment to assertively embrace prevention. Identifying and

trying to limit exposure to the environmental factors that can lead to cancer or malfunction of the immune, endocrine and other body systems in children, who are more vulnerable to these effects, may allow us to finally identify the causes for the 90-95% of childhood cancers for which we still don’t know the causes” (thereasonswhy.us). The BCM IBR gave final approvals in May 2020, after which the Strongs proceeded initiating the transfer to BCM of the contact data they had of the first 400 families. The following month, BCM began reaching out to those families. The role of TheReasonsWhy.Us is to enroll participants who have been affected by pediatric cancer and then to transfer their data to BCM, where the information is evaluated and from which the patients and families are contacted.

BCM hosts the data according to security and privacy protocols under the Health Insurance Portability and Accountability Act. Once all the data are collected, BCM will consolidate the information into a database that will be called Universal Study of Pediatric Cancer – TheReasonsWhyUs. Using the database, researchers at BCM will be able to assess exposures to key environmental toxicants and combine numerous datasets of air and water studies, pollution sites, and analysis of baby teeth for the presence of chemical exposure early in life.



Study Demonstrates How Maternal Diet Alters Human Milk Oligosaccharide



Drs. Morey Haymond, Professor, **James Versalovic**, Professor, and **Mahmoud Mohammad**, Instructor, along with other authors* published in *Nature Scientific Reports* their findings on the effects of maternal diet on milk

oligosaccharide composition. Research has confirmed traditional concepts that human milk is the optimal nutrition source for neonates and infants, and



this latest study uncovered a mechanism by which nutrition plays a factor in modulating the beneficial composition of mother's

milk. Although early studies provided evidence that a



mother's milk was modulated by what she ate, the underlying mechanisms of how the modulating occurs had not been elucidated.

The team of researchers previously reported that a lactating mother's diet affects the child's lifelong metabolic health. In the present study, they investigated the effects of the diet on the composition of human milk oligosaccharides (HMOs). Although HMOs are known to be inert substances to a mother or her baby, they exert health benefits by acting as fodder to microbes, both bacteria and some viruses. In a controlled setting at the USDA Children's Nutrition Research Center (CNRC), the team provided breastfeeding mothers with all their meals. The mothers were on a special diet for 30 to 70 hours and then after a 2-week washout period ate a different diet also provided by the researchers. Milk samples collected from each subject at different time

points, including the diet 'switches,' allowed each woman to serve as her own control in a "cross-over" trial design.

The design provided the opportunity for the researchers to control how individual women may vary in the amount of HMOs they make, as well as the possibility of confusing microbes in the milk with environmental contaminants. Analysis of the HMOs and microbiome composition of the milk yielded insights into the effect of the mothers' diets.

The study showed that distinct maternal carbohydrate and energy sources in the provided meals altered the milk concentrations of HMOs, leading to changes in



the metabolic capacity of the milk microbiome. Instead of directly affecting the microbes, the maternal diet affects the microbes' food (HMOs), thereby affecting the functional capacity of the microbes in the milk that the baby consumes. These changes occurred in a matter of 2 to 3 days after the mothers changed their diets.

These findings could have implications for both the baby and the mother, and they may have effects on a baby's health and development, including potential for promoting gut health at the mucosal surface. Senior author Dr. Kjersti Aagaard noted that the study suggests that HMOs seem to "preferentially affect the growth potential of microbes that may also impart health risk or benefit for the mother . . . by shaping the community of microbes in the milk in ways that may favor the growth of certain beneficial microbes via the simultaneous exclusion of those that cause mastitis during breastfeeding." Other ways that HMOs may prompt healthy microbiome is by acting as a decoy to attract and sequester potentially dangerous microbes, thereby breaking down and producing nutrients that may benefit other microbes.

* Drs. Maxim D. Seferovic, Rayan M. Pace, Melinda Engevik, Lars Bode, and Kjersti M. Aagaard.

Review Aims to Raise Awareness of 2020 Standards of Care for Diabetes

Dr. Maria J. Redondo, Professor, was lead author on an article published recently in Diabetes Care, publication of the American Diabetes Association (Diabetes Care 2021; 44:301-312). She kindly provided an invited summary of the article, entitled, "The Evolution of Hemoglobin A1c Targets for Youth With Type 1 Diabetes: Rationale and Supporting Evidence." Other authors on the article are Igrid Libman, David M. Maahs, Sarah K. Lyons, Mindy Saraco, Jane Reusch, Henry Rodriguez, and Linda A. DiMeglio.

By Dr. Maria J. Redondo



The American Diabetes Association (ADA)'s Professional Practice Committee updates its Standards of Medical Care in Diabetes annually in order to "ensure that clinicians, health plans, and policy makers can continue to rely on it as the most authoritative source for current guidelines for diabetes care."

In its 2020 Standards of Medical Care, the ADA recommends adopting an A1C goal of <7% (53 mmol/ml) for many children with T1D, with an emphasis on individualized targets based on the individual risk-benefit ratio

(Recommendation 13.21, Evidence Grade B). This recommendation is driven by the overwhelming evidence of

the deleterious influences of both chronic and acute hyperglycemia, the decrease in overall incidence of severe hypoglycemia, the waning association between lower A1C target and hypoglycemia, and newer insulins and technological advances that have increased the feasibility of minimizing out-of-range glucose levels. The recent adaptation of a lower target for children by the ADA reflects similar guidance from other societies worldwide. Specifically, the International Society for Pediatric and Adolescent Diabetes (ISPAD) proposed <7% in 2018, The National Institute for Health and Excellence (NICE) in the UK <6.5% in 2015

(<https://www.nice.org.uk/guidance/ng18>), and the Swedish National Diabetes Register 6.5% in 2018.

The historical evidence highlights the detrimental effects of hyperglycemia in children and adolescents. These conditions may include "increased likelihood of brain structure and neurocognitive abnormalities, microvascular and macrovascular complications, and increased mortality." Data also support a decreased risk over time for youth with T1D of developing severe hypoglycemia and the weakened association

between lower A1C and risk of developing severe hypoglycemia.

Of concern are barriers to achieving the goal of near-normalization of A1C in children. One is the fear of hypoglycemia developing. Other barriers are biological such as lack of residual B-cell function, glucagon abnormalities, behavioral, familial, health-care system related, and societal.

Current gaps in knowledge include the risk factors for poor diabetes outcomes (related to hyper- or

hypoglycemia) that may allow identification of high-risk individuals for targeted interventions. Additionally, it will be important to understand the pathophysiology of the deleterious consequences of hypo- and hyperglycemia

(e.g., effects on the brain; relative contribution of the degree and duration of hyperglycemia; etc.) that can be leveraged for prevention and treatment. A key gap area is socioeconomic and racial/ethnic disparities in diabetes outcomes and inequality in access to diabetes care and technology; this recognized need is fueling multiple initiatives at the research level, including trials to translate efficacious interventions to real-world settings, advocacy and public policy. Furthermore, the implementation of strategies proven effective to optimize diabetes outcomes will be facilitated by ongoing behavioral research to address difficulties following treatment plans, concerns about quality of life, undue burden of care, and therapeutic inertia. International data indicate that lower A1C can be achieved safely in pediatrics and there are ongoing efforts to utilize quality improvement methodology to implement proven efficacious strategies to optimize A1C and other measures of glucose control in the U.S.





Research Focus on Plants Aims for Future Improved Health Options

Dr. Kendal Hirschi and colleagues in his laboratory work to integrate fundamental plant science with basic nutrition research. Located in the USDA/ARS Children's Nutrition Research Center, the laboratory focuses on finding ways to make plants healthier so they grow more effectively during difficult situations and so they contain extra minerals and vitamins and fewer anti-nutrients.

One priority is to sustain plants' health during heavy and extended periods of rain, when oxygen is less available and when some plants cannot tolerate the water, especially if they get emerged. Hence, the focus is on developing a new mechanism that might help plants grow stronger under conditions of limited oxygen. Especially relevant is that when plants are submerged, they tend to close their pores, further inhibiting intake of oxygen, resulting in death. Contrariwise, if the plant is able to keep energy reserves active, it may survive.

Similarly, if a plant survives submergence in water, it can be equally stressed by a sudden change to a very dry environment. Compounding the problem is the instance of repeated on/off of submergence and then dryness, exposing the plant to repeated shocks that may overwhelm it. Recognizing that some plants are more tolerant to submergence than are others, Dr. Hirschi's lab is investigating whether plants actually altered some of their genes, by studying those properties in transgenic plants.

One area that they are exploring is the controversial concept that nutrition may include the digestion of genetic information. Dr. Hirschi noted that "perhaps part of what we eat, and what makes us healthy, isn't just elements that come from plants, but maybe there's genetic information in the plant that's communicating to the genetic information in our bodies." If food contains genetic information that controls human microbiomes or the digestive system,



where malnutrition contributes to nearly half of all deaths in children younger than 5 years of age. Recently, the gut microbiome has been implicated in childhood malnutrition, and investigations may reveal important aspects of malnutrition-related deficiencies that can be targeted by therapeutic foods. Plant diets in other settings have been associated with intestinal health and development of a diverse and stable microbial system. Preliminary studies in the Hirschi lab have shown that specific gut microbes appear to be competent in exosome-like

then researchers possibly could use a plant's natural carrier materials in various capacities, including developing vaccines. Further, plants could be designed to improve their bioavailability, thereby providing nutrients that would have a greater effect on the consumer.

They also are working on bringing together plant biology and nutritional sciences. Nutritional scientists have long demonstrated the nutrients found in foods, and in the last several decades, plant genome projects have developed genetic tools to manipulate nutrient content, but only a few studies have sought to determine the impact that genetic modifications have on nutrient bioavailability. The Hirschi lab is hoping to define the relationship between nutrient partitioning in the plant matrix and nutrient absorption. They are using transgenic approaches to systematically repartition various nutrients among isogenic crop lines, with the goal of visualizing how genetic and environmental alterations redistribute nutrients inside plants cells, and ultimately optimize an assortment of technologies to provide a scalable model to help remedy the nutrient deficiencies that exist around the world.

Currently, increased awareness has been raised concerning the value of a plant diet and the impact it could have worldwide,

nanoparticles (ELNs), which communicate to microbes and fungi through the transport of various lipids, proteins, and RNAs. The continued work will identify the role of therapeutic plant-based diets and their associated ELNs on gut microbiome composition and function.

A distinct advantage that the Hirschi lab has is its location, where researchers and students have access to greenhouse and animal facilities. The building also houses clinical researchers who are engaged in studies involving people and food.

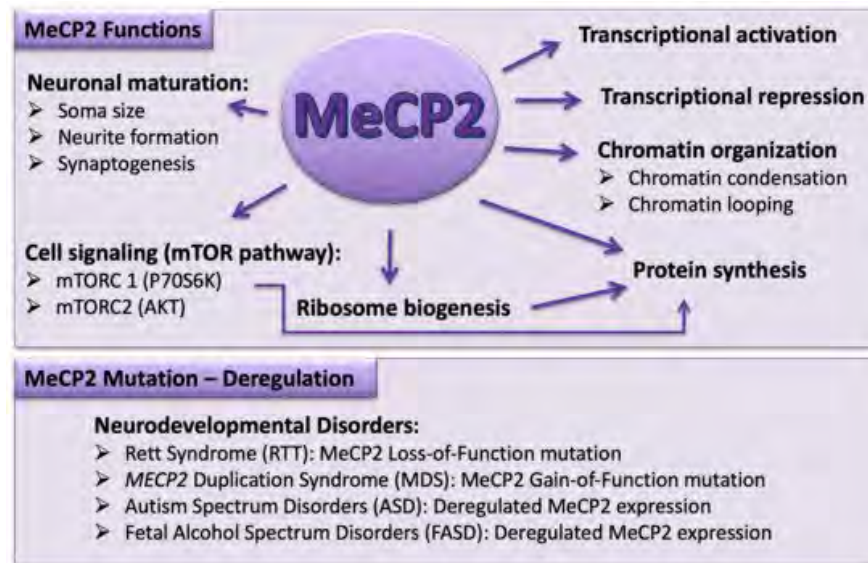
A photo slide show and video tour of the green house can be seen online:

<https://www.bcm.edu/research/labs-and-centers/faculty-labs/kendal-hirschi-lab/greenhouse>

(Photos courtesy of the Hirschi laboratory)



Study Demonstrates Effects of Deleting *Mecp2* on Motor Learning in Mice



Dr. Huda Zoghbi, Professor, was senior author on a recently study that revealed three important features of cerebellar dysfunction that occur after loss of *Mecp2* from the cerebellum. The first observation was that no non-motor phenotypes in the cerebellar knock-out (KO) mice, despite the cerebellum being implicated in non-motor behaviors including social interaction and cognition. The finding suggests that non-motor phenotypes in Rett syndrome, for which Dr. Zoghbi is recognized as discovering its cause, are probably not caused by cerebellar dysfunction. They also did not observe any motor deficits in any of the cell type-specific KO mice, noting in the study published in *elifesciences* that “the same phenomenon is seen for the sensorimotor gating deficits of *Mecp2* null mice, which are present in mice lacking *Mecp2* in all inhibitory neurons but not in individual subtypes of inhibitory neurons.” The authors’ conclusion was that the finding suggests that cerebellar-related motor deficits result from combined dysfunction in the entire circuit, not from a single cell type. Their third finding was that behavior deficits in cerebellar KO mice were milder than those of mice lacking *Mecp2* in the cortex and basal ganglia. Phenotypes of cerebellar KO mice were restricted to motor learning, appearing in 6-month-old mice, in contrast to motor deficits in mice lacking *Mecp2* in the cortex and basal ganglia, which are more profound and occur in mice 2 months old. This finding also attests to their contention that

motor symptoms in Rett syndrome are caused by a combination of cerebellar, cortical, and basal ganglia dysfunction.

The study also describes the improvement in motor learning after additional training in cerebellar KO mice, a finding not published previously and not observed, in their knowledge, in other *Mecp2* KO mice. A related effect has been reported in female *Mecp2* heterozygous mice in which memory deficits were rescued with fornical deep brain stimulation. Activation of the cerebellar circuitry during training may improve the motor phenotypes in cerebellar KO mice by enhancing synaptic function in a manner similar to the proposed mechanism of deep brain stimulation. It also may mean that repetitive circuit activation resulting from training could improve other behavioral deficits in *Mecp2* KO mice.

Their conclusions were that “even though *Mecp2* is broadly expressed throughout the brain, neuronal subtypes between brain regions, and even those within a brain region, respond differently to the loss of *Mecp2* . . . and [that] it is important to keep in mind that the functional consequences of *Mecp2* loss are context specific.”

Other authors on the study were Achilly NP, He L-j, Kim OA, Ohmae S, Wojaczynski GJ, Lin T, Sillitoe RV, and Medina JF. The full report is available at <https://elifesciences.org/articles/64833>

“End with Good Stuff”



*“Lady & the Tramp”
aka*

*Belle (D&D Borden’s Lady Plurabelle of the Liffey) & Omri
AKC Canine Good Citizens – Licensed Pet Therapy Dogs*