



THE SABAN RESEARCH
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The Saban Research Institute Annual Symposium

HEALTH COMPLEXITIES IN PEDIATRICS: INVESTIGATING SYSTEMS IN ACTION AND INTERACTION

Feb. 19, 2020



Paul S. Viviano



Pat Levitt, PhD

WELCOME

From the moment their young lives begin, the incredibly complex functions inside children’s bodies are being carefully coordinated to maximize health, growth and development. From the activities of single cells to the coordinated efforts of each organ—their systems must work together to develop strong physical and mental health.

At Children’s Hospital Los Angeles, we are conscious that this period of development provides invaluable opportunity to positively impact the trajectory of health. Disruption of the finely tuned interactions of a child’s body can result in a breakdown of physiology and function that can lead to poor health and disease.

The Saban Research Institute Annual Symposium convenes a diverse group of internationally recognized experts on the interactions that drive children’s health. The individuals who come together examine the interplay of environment and genetics, brain processes and disease states, and the social determinants of health and disease. The promise of their efforts underscores the value of the work done here every day to advance pediatric medicine through research and clinical care. Together these experts are solving the mysteries of physical mechanisms that, once understood, will produce innovative approaches to prevention and treatment.

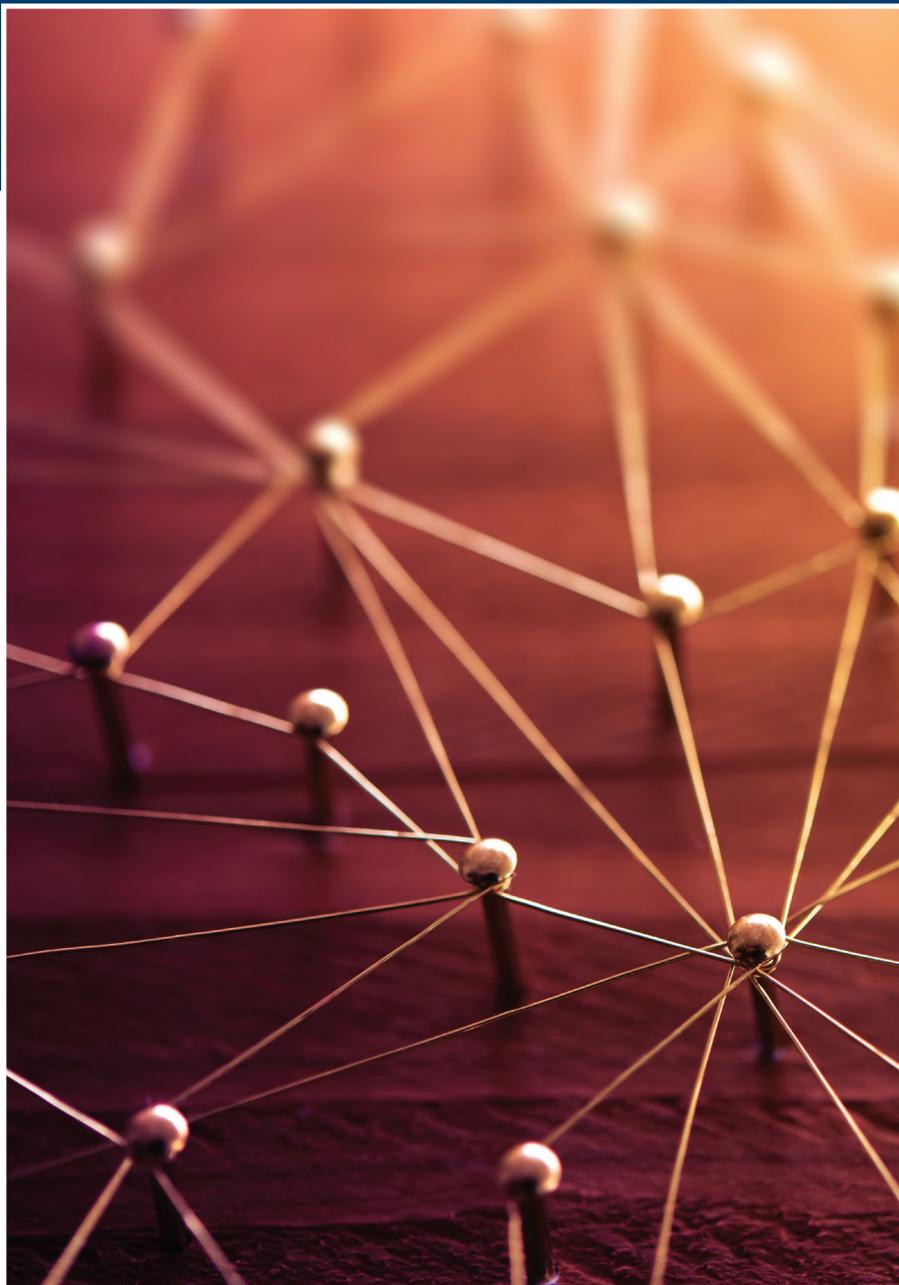
It would be impossible to host such an auspicious gathering without the work of the Symposium Committee members. This year, we have Jennifer Baird, PhD, Michael Goran, PhD, and Hugo Rosen, MD, to thank. We are also grateful to the Training, Education, Career Planning and Development team for its organizational and logistical acumen in support of this effort.

Finally, we wish to share our deep appreciation for the individuals and foundations who support research. We could not achieve our goals without their commitment. A special and heartfelt thank you is extended to philanthropists Cheryl Saban, PhD, and husband Haim Saban and The Saban Family Foundation for their ongoing leadership in supporting transformative research that is already improving the health of children here and around the world.

Warmest regards,

Paul S. Viviano
President and Chief Executive Officer
Children’s Hospital Los Angeles

Pat Levitt, PhD
Vice President and Chief Scientific Officer
Children’s Hospital Los Angeles



SYMPOSIUM OVERVIEW

Health Complexities in Pediatrics: Investigating Systems in Action and Interaction

Within pediatric care, health complexity abounds. Today's research enterprise reflects the challenges of addressing the needs of the whole child. New discoveries are generating insights on the complexity of a single organ, the interactions between organs and system functions, and the ways in which exposures early in life have a profound effect on subsequent quality of life and health outcomes. Interdisciplinary research reveals the dynamic interplay between genetics, environment, behavior and other factors unique to each individual. Each organ, each system, each interaction is part of normal development for children. The more we learn about the complexities at play, the better we can tailor prevention, treatment and structural interventions to facilitate children's health, growth and long-term well-being.

Today's symposium presentations from national and international luminaries, and from our colleagues here at CHLA and USC, center around the theme of "**Health Complexities in Pediatrics: Investigating Systems in Action and Interaction.**" Speakers will present cutting-edge research findings across basic, clinical, translational and community-based settings, highlighting achievements as well as areas where further exploration is needed. These presentations demonstrate the ways in which the gears of our pediatric research community work together to power further scientific **action, interaction** and life-changing discoveries for children and families at Children's Hospital Los Angeles.



Symposium Co-Organizer:
Jennifer Baird, PhD, MPH,
MSW, RN, CPN

Dr. Baird is a nurse scientist and Director of the Institute for Nursing and Interprofessional Research at Children's Hospital Los Angeles, an innovative program designed to support interprofessional clinician engagement in research and evidence-based practice translation. She has a doctorate in nursing from the University of California, San Francisco, a master's in public health from the Harvard T.H. Chan School of Public Health and a master's in public health from Virginia Commonwealth University. Her research focuses on developing strategies to enhance parent/provider communication in the acute care environment, to promote the safe transfer of patients from the hospital to home, and to support children with medical complexity in the home environment.

Dr. Baird is the principal investigator of the California Nurse-led Discharge Learning (CANDLE) Collaborative, a project funded by the Lucile Packard Foundation for Children's Health to enhance the quality of discharge preparation for patients and families in children's hospitals across the state. She is the co-investigator on a series of grants supporting the development and implementation of telehealth home-based palliative care model for children with medical complexity, and she serves as the senior nurse consultant and nursing lead on a master's in public health to evaluate the 21-site dissemination and implementation of Patient and Family I-PASS, a family-centered rounds intervention. I-PASS aims to improve communication and reduce medical errors in pediatric inpatient settings, ensure the safe transfer of patients from the hospital to home, and support children with medical complexity in the home environment.



**Symposium Co-Organizer:
Michael I. Goran, PhD**

Dr. Goran is Professor of Pediatrics at Children's Hospital Los Angeles and the Keck School of Medicine of USC and serves as Program Director for Diabetes and Obesity at The Saban Research Institute. He also holds the Dr. Robert C. and Veronica Atkins Endowed Chair in Childhood Obesity and Diabetes and serves as co-Director of the USC Diabetes and Obesity Research Institute. Dr. Goran is a native of Glasgow, Scotland, and received his doctorate from the University of Manchester in the United Kingdom prior to completing postdoctoral training in the United States. He previously served on the faculty at the University of Vermont and at the Department of Nutrition Sciences at the University of Alabama at Birmingham prior to joining USC.

For 30 years, Dr. Goran has focused his research on the causes and consequences of childhood obesity. His work aims to understand the metabolic factors linking obesity to increased disease risk during growth and development, and to use this information as a basis for developing new clinical, behavioral and community approaches for prevention, treatment and risk reduction. He also studies ethnic disparities in obesity and obesity-related diseases, including Type 2 diabetes and fatty liver disease, with a special interest on the effects of dietary sugar on obesity and metabolic diseases among Hispanic populations. His work covers maternal-infant nutrition and identifying modifiable factors that can be targeted for interrupting the developmental programming of obesity, including bioactive elements of breast milk and infant microbiome development. For more information about Dr. Goran's research, please visit GoranLab.com.



**Symposium Co-Organizer:
Hugo R. Rosen, MD**

Dr. Rosen is the Norris Chair of Medicine and Professor of Medicine, Immunology and Molecular Microbiology at the Keck School of Medicine of USC. A physician-scientist, he has published approximately 200 original peer-reviewed manuscripts investigating the cellular and molecular underpinnings of liver diseases. He is an elected member of the American Society for Clinical Investigation and the American Academy of Pediatrics, and has received numerous awards including the Senator Hatfield Award for Research.

Among Dr. Rosen's early seminal contributions, he identified epidemiologic factors that shape the variable natural history of hepatitis C virus infection. The originality, scope and impact of his research has advanced scientific thought by identifying many aspects of the division of labor played by different immune cells in liver diseases, including a recent focus on nonalcoholic fatty liver disease. Dr. Rosen's work has been funded continuously for more than 20 years, and his research program trains the next generation of translational scientists, including doctoral and MD-PhD candidates, postdoctoral fellows and faculty.

SCHEDULE

8 – 8:45 a.m.

Continental Breakfast and Check-in

The Saban Research Building lobby

8:45 – 9 a.m.

Symposium Welcome

Pat Levitt, PhD, The Saban Research Institute of Children's Hospital Los Angeles; Keck School of Medicine of USC

Paul S. Viviano, President and Chief Executive Officer, Children's Hospital Los Angeles

SESSION 1

9 – 9:50 a.m.

Microbes in the Environment, Genes and Childhood Asthma: Biology Is Context

Fernando D. Martinez, MD, University of Arizona

9:50 – 10:20 a.m.

From Neurons to Neighborhoods: New Frameworks for Understanding and Supporting Pediatric Health and Development

Michele D. Kipke, PhD, The Saban Research Institute of CHLA; Keck School of Medicine of USC

10:20 – 10:40 a.m.

Morning Break

SESSION 2

10:40 – 11:30 a.m.

CNS-Directed Therapy for Childhood Leukemia: Cognitive Decline and Biomarkers of Neurologic Injury

Ki Moore, PhD, RN, FAAN, University of Arizona College of Nursing

11:30 a.m. – noon

Neonatal Hypoxic-Ischemic Encephalopathy: Novel Biomarkers and a Roadmap to Advance Neuroprotection

Jessica L. Wisnowski, PhD, The Saban Research Institute of CHLA; Keck School of Medicine of USC

Noon – 1:15 p.m.

Lunch

Anita S. Watson Courtyard of The Saban Research Building

SESSION 3

1:15 – 2:05 p.m.

Dissecting the Human Liver Using ScRNA-seq

Sonya MacParland, PhD, University of Toronto

2:05 – 2:35 p.m.

Fusion Oncogene Sarcomas: Scientific and Clinical Challenges

James Amatruda, MD, PhD, The Saban Research Institute of CHLA; Keck School of Medicine of USC

2:35 – 2:55 p.m.

Afternoon Break

SESSION 4

2:55 – 3:45 p.m.

Programming by Maternal Over-Nutrition: A Developing Obesity Crisis

Susan Ozanne, PhD, University of Cambridge

3:45 – 4:15 p.m.

Western Diet Consumption and Memory Impairment: What, When and How?

Scott Kanoski, PhD, USC Dornsife College of Letters, Arts and Sciences

4:15 – 4:30 p.m.

Closing Remarks

4:30 – 6 p.m.

Reception

Anita S. Watson Courtyard of The Saban Research Building



Pat Levitt, PhD

Dr. Levitt is Chief Scientific Officer, Vice President and Director of The Saban Research Institute of Children's Hospital Los Angeles. He is the Simms/Mann Chair in Developmental Neurogenetics at Children's L.A. and the W.M. Keck Provost Professor of Neurogenetics at the Keck School of Medicine of USC.

In addition to holding previous leadership positions at the University of Pittsburgh and Vanderbilt University, Dr. Levitt has served as a member of the U.S. National Advisory Mental Health Council for the National Institute of Mental Health, a member of the National Academies of Science, Engineering and Medicine Committee, and on the editorial boards of 10 scientific journals, including his current role as Editor-in-Chief of *Mind, Brain and Education*. He is an elected member of the National Academy of Medicine and an elected fellow of the American Association for the Advancement of Science Fellow and the Dana Alliance for Brain Initiatives. He is also a senior fellow at the Center on the Developing Child at Harvard University and serves as co-Scientific Director of the National Scientific Council on the Developing Child, a policy council that assists policy makers, service providers and business leaders in making decisions regarding child brain and physical health program investments. Dr. Levitt has spoken to these groups in 42 states, Mexico and Canada.

Dr. Levitt has been funded continuously by the National Institutes of Health and numerous private foundations since 1982. His laboratory conducts both translational and clinical research, focusing on identifying factors that assure healthy development of brain architecture that control learning and emotional and social behavior. His clinical research studies address how toxic stress responses in infants and toddlers may be detected as early as possible to develop best practices for promoting resilience and better prevention and intervention. He also conducts research on families who have a child with autism spectrum disorder and co-occurring medical conditions, such as gastrointestinal disorders. He has published over 300 scientific papers.



Paul S. Viviano

Paul S. Viviano joined Children's Hospital Los Angeles as President and Chief Executive Officer in 2015 and serves as a member of the Board of Directors and Foundation Board of Trustees.

Prior to coming to Children's Hospital Los Angeles, Viviano served as CEO and Associate Vice Chancellor of the UC San Diego Health System, an institution renowned for medical research and patient care. Viviano previously served as President of USC University Hospital and USC Norris Cancer Hospital, and President and Chief Operating Officer within the St. Joseph Health System. He also served for 10 years as Board Chair and CEO of Alliance HealthCare Services, the nation's largest provider of outpatient diagnostic imaging and radiation oncology services.

As part of his ongoing advocacy, Viviano is Board Chair of the California Children's Hospital Association and co-Chair of the Medicaid CEO Advisory Council for the national Children's Hospital Association (CHA), two organizations committed to protecting and supporting pediatric health care. He is a member of the CHA Public Policy Committee and the former LA Central Area Chair of the Hospital Association of Southern California. Additionally, Viviano chairs the Board of Trustees of Loyola Marymount University and is a board member of the UCLA Health Policy and Management Alumni Association.

In 2020, Viviano was honored with the Partners in Care Foundation Vision & Excellence in Healthcare Leadership Award and the Archdioceses of Los Angeles' Cardinal's Award. He was named the 2016 Leader of Today Honoree by the UCLA Fielding School of Public Health and one of the Los Angeles Business Journal LA500, the city's most influential Angelenos, in 2017 and 2018.



Fernando D. Martinez, MD

Dr. Martinez is a Regents' Professor and Director of the Asthma & Airway Disease Research Center at the University of Arizona in Tucson. A world-renowned expert and a highly regarded researcher in his field, Dr. Martinez's primary research interests include the natural history, genetics and treatment of childhood asthma.

His groundbreaking research has had an impact in numerous ways, most prominent among them being the development of the concept of the early origins of asthma and chronic obstructive pulmonary disease (COPD). This concept is now widely accepted as the potential basis for designing new strategies to prevent these illnesses, which affect millions of children and adults. In addition, Dr. Martinez has contributed to the scientific community's understanding of the role of gene-environment interactions in the development of asthma and allergies. He has been a principal investigator as part of the National Heart, Lung and Blood Institute (NHLBI) Asthma Treatment Networks, which have contributed fundamental evidence on which to base national guidelines for treating the disease.

Dr. Martinez serves on the National Scientific Council on the Developing Child and was a member of the National Asthma Education and Prevention Program, which was responsible for publishing the "Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma" in 1997 and its first revision in 2001. He has been a member of the FDA Pulmonary-Allergy Drugs Advisory Committee and the Board of Extramural Advisors of the National Heart, Lung, and Blood Institute.

Dr. Martinez's research is well-detailed in more than 250 original research papers and editorials, many in collaboration with investigators worldwide. He is frequently invited to give keynote presentations at national and international meetings.



Michele D. Kipke, PhD

Dr. Kipke is a Professor of Pediatrics and Preventative Medicine at the Keck School of Medicine of USC and serves as the Vice Chair of Research in the Department of Pediatrics at Children's Hospital Los Angeles. She is also co-Director of the Southern California Clinical and Translational Science Institute (SC CTSI) at USC, overseeing clinical research at Children's L.A.

A nationally known pediatric health researcher and policy expert, Dr. Kipke has been intimately involved in the HIV/AIDS epidemic since its onset in the U.S. and has made significant scientific contributions to the field of HIV prevention. Early in her career, she studied risk for substance use, mental health problems and HIV exposure among homeless youth and injection drug users; developed and conducted the first formal evaluation of an HIV prevention intervention for adolescents in Harlem, New York; and evaluated one of the first needle-exchange programs in Los Angeles.

Dr. Kipke's current research is focused on biobehavioral and sociocultural risk factors among African American and young Latino males who have sex with men, trans and gender-nonconforming youth, interventions to promote uptake of antiretrovirals for HIV prevention, and ways to improve the care delivered to children with autism and other neurodevelopmental disorders.



Ki Moore, PhD, RN, FAAN

Dr. Moore is Dean of Nursing at the University of Arizona's College of Nursing and is also the Anne Furrow Endowed Professor at the college. She has focused her research program on the impact of central nervous system (CNS)-directed treatment for pediatric acute lymphoblastic leukemia (ALL) and brain tumors on cognitive outcomes and on mechanisms of tissue injury. She has conducted studies to gain a better understanding about the mechanisms of treatment-related injury and gene-expression changes associated with chemotherapy. Dr. Moore translated these findings into clinically focused studies. She and her research team developed and tested an intervention that improved academic math abilities and quality of life for children receiving CNS treatment for ALL. Her current work focuses on biomarkers of oxidative stress and apoptosis as mechanisms of chemotherapy-induced neurologic injury.



Jessica L. Wisnowski, PhD

Dr. Wisnowski is an Assistant Professor of Research in Radiology and Pediatrics at the Keck School of Medicine of USC who specializes in perinatal brain injury. She holds a doctorate in clinical psychology from the University of Iowa and completed postgraduate training in neuropsychology, neuroimaging and neuroscience at Rancho Los Amigos National Rehabilitation Center, USC and Children's Hospital Los Angeles. Dr. Wisnowski's research focuses on the development and application of novel neuroimaging biomarkers to aid in diagnosing perinatal brain injury and managing neuroprotective therapies. She has published numerous peer-reviewed publications about hypoxic-ischemic encephalopathy (HIE), bilirubin encephalopathy, kernicterus, prematurity and normal brain development. She is currently Chairwoman of the Neuroimaging Core for a National Institutes of Health (NIH)-funded multicenter trial centered around erythropoietin neuroprotection for neonates with HIE.



Sonya MacParland, PhD

Dr. MacParland is a basic scientist and immunologist in Toronto General Hospital's Soham & Shaila Ajmera Family Transplant Centre and also serves as Assistant Professor in the University of Toronto's Departments of Laboratory Medicine and Pathobiology and Immunology. Dr. MacParland's research program focuses on translating fundamental knowledge about the immune biology of the liver into clinical applications. She and her research team are using advanced genomics, including single cell RNA sequencing, to describe the microenvironment of the healthy human liver, and they recently developed the first transcriptomic map of the human liver as a platform to examine how immune dysregulation drives liver diseases. Her team is also examining how the liver immune environment can be therapeutically targeted and manipulated using nanoparticles to slow or reverse ongoing damage.



James F. Amatruda, MD, PhD

Dr. Amatruda holds the Endowed Chair of Sarcoma Research in the Cancer and Blood Disease Institute and the Division of Hematology-Oncology at Children's Hospital Los Angeles. He also serves as Professor of Pediatrics and Medicine at the Keck School of Medicine of USC. Dr. Amatruda is a physician-scientist with a primary research and clinical focus on solid tumors of childhood including sarcomas, germ cell tumors and Wilms tumor. His lab has developed zebrafish models of genetic subtypes of pediatric solid tumors to better define their biology and to use that knowledge to identify and validate novel approaches for improved therapies. He has held longstanding leadership positions in the Children's Oncology Group (COG), serving as Chair for the Germ Cell Tumor Biology Committee and the Rare Tumors Biology Committee. He also serves as a member of the COG Solid Malignancies Integrated Translational Science Center Steering Committee, and on the Scientific Advisory Boards of the William Guy Forbeck Foundation, the Osteosarcoma Institute, the Pablove Foundation, Curing Kids Cancer and the 1 Million 4 Anna Foundation.

Dr. Amatruda received his bachelor's degree in biochemical sciences from Harvard University and his medical and doctoral degrees from the Washington University School of Medicine. He did internship and residency training in internal medicine at the Brigham and Women's Hospital, followed by fellowship training in medical oncology at Dana-Farber/Partners Cancer Care, both in Boston. He was a postdoctoral fellow in the laboratory of Dr. Leonard Zon at Boston Children's Hospital, Harvard Medical School. Prior to coming to Children's L.A., Dr. Amatruda was on the faculty at UT Southwestern Medical Center in Dallas.



Susan Ozanne, PhD

Dr. Ozanne is Professor of Developmental Endocrinology at the University of Cambridge Institute of Metabolic Science Metabolic Research Laboratories and heads the Programme on Epigenetic Programming across the Life Course at the MRC Metabolic Diseases Unit. She is also a fellow of Churchill College, Cambridge, where she teaches first-year medical students. She obtained a first-class honors degree in biochemistry from the University of Edinburgh before attending Christ's College at the University of Cambridge where she obtained her doctorate. Prior to her current appointment she was a British Heart Foundation senior fellow and a Wellcome Trust Career Development Fellow.

Dr. Ozanne's research interests are focused on understanding the underlying mechanisms by which suboptimal nutrition in early life impacts long-term cardio-metabolic health and applying this knowledge to optimize intervention strategies. In 2013 she received the Nick Hales Award from the International Society for the Developmental Origins of Health and Disease for outstanding contributions to the field by an investigator under the age of 45. She has mentored 20 graduate students to successful completion of their doctoral degrees. Dr. Ozanne has authored more than 200 peer-reviewed papers on the early origins of health and disease and is an elected member of the council of the Society for the Developmental Origins of Health and Disease.



Scott Kanoski, PhD

Dr. Kanoski is an Associate Professor in the Department of Biological Sciences at USC. He studies the neurobiology of obesity onset, treatment and pathophysiology, with a research focus on discovering the underlying neural systems that regulate higher-order aspects of feeding behavior and understanding how these neural systems are negatively impacted by dietary and metabolic factors. Drawing on his training in psychology and behavioral neuroscience from the University of Illinois, Purdue University and the University of Pennsylvania, Dr. Kanoski's research applies multiple levels of analysis in animal models, including behavioral, neuroanatomical, molecular, viral-based genetic and neuropharmacological approaches.

Dr. Kanoski has received several awards from The Obesity Society and the Society for the Study of Ingestive Behavior—two premier scientific organizations centered on obesity research—and has served in leadership roles on multiple committees for these organizations. Dr. Kanoski's NIH-funded research has identified the hippocampus, a brain region most famously associated with memory function, as a critical neural substrate responding to endocrine and neuropeptide signals to regulate higher-order aspects of feeding behavior. His work has further revealed that the hippocampus is highly vulnerable to neurobiological insults, such as neuroinflammation and blood-brain barrier disruption, and functional disruption following consumption of Western diets that contain high levels of simple sugars and saturated fatty acids, particularly during adolescence.

Dr. Kanoski's recent advances in these areas have been published in leading journals, including *Cell Metabolism*, *Nature Communications*, *Molecular Psychiatry*, *Biological Psychiatry*, and *eLife*. Dr. Kanoski's ongoing research is advancing knowledge of the neurobiological antecedents and consequences related to excessive food intake and weight gain.

A HISTORY OF RESEARCH AT CHILDREN'S HOSPITAL LOS ANGELES

The research program at Children's Hospital Los Angeles began in 1952. At that time, resources were allocated on a project-by-project basis with equipment being borrowed from clinical laboratories. In the late 1950s, a decision was made to develop a strong basic research program, and several highly capable investigators were recruited to lead work in the areas of pathology, hematology-oncology and infectious diseases. During the 1960s those initial areas of inquiry expanded to include endocrinology, virology and genetics. The research program also began gaining national reputation for its success at securing federal funding, receiving its first endowment in 1965. Over the next three decades, the institution continued to expand its research enterprise with new areas of focus, increases in National Institutes of Health funding and purpose-built research facilities.

Established in 1992, the Research Institute became The Saban Research Institute in 2003 following a \$40 million gift in support of pediatric research made by Cheryl Saban, PhD, Haim Saban and The Saban Family Foundation.

Over the course of its evolution, The Saban Research Institute has recruited transformative faculty members dedicated to basic, clinical and translational research to further our understanding of the developmental origins of health and disease. Researchers at The Saban Research Institute are committed to the health of the whole child, working in collaborations designed to accelerate the discovery, development and delivery of innovative preventive, diagnostic and treatment options. The Institute works with the local community as well as with colleagues around the globe, focusing on individualized health and medicine, the developing mind, and regenerative medicine and cellular therapies.



CHILDREN'S HOSPITAL LOS ANGELES FOUNDATION BOARD OF TRUSTEES 2020 RESEARCH AND INNOVATION COMMITTEE



The Research and Innovation Committee cultivates philanthropic support for Children's Hospital Los Angeles' research enterprise and innovation priorities.

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Children's Hospital Los Angeles is ranked No. 1 in the Western U.S., No. 1 in California and Foundation Board of Trustees nationwide on the U.S. News & World Report Honor Roll of pediatric hospitals. The hospital is home to The Saban Research Institute, one of the largest and most productive pediatric research facilities in the United States. Children's L.A. is also one of America's premier teaching hospitals through its affiliation with the Keck School of Medicine of USC since 1932.

For more information, visit **CHLA.org**. Follow us on **Twitter**, **Facebook**, **YouTube** and **LinkedIn**, or visit our hospital blog, **CHLA.org/blog**, and our research blog: **ResearCHLAblog.org**.