The future starts now.
Academic Annual Report 2012
VISION: Children's National Medical Center aspires to be a top five academic pediatric medical center that is recognized as leading the quest to prevent or cure many of childhood’s most serious and prevalent disorders. We will achieve this vision through a unique collaboration between clinical and research programs, innovative educational programs, enhanced academic partnerships, improved infrastructure, and a stable base of financial support. Through this approach, our role as a national and international leader in the research and treatment of childhood diseases will be significantly strengthened.
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MISSION: Children’s Research Institute will conduct novel basic, translational, clinical, and community research and education programs within Children’s National Medical Center that improve the well-being of children throughout their lives.

FROM THE DIRECTORS

Highlights

This year has been exciting with the recruitment of exceptional investigators, especially in the area of Cancer and Immunology Research. Three faculty have won national awards for research excellence in pediatric residency training program has received its strongest class yet. Despite the increased competition for NIH funding, we have had the highest funding of the Children’s Research Institute in its history. A brief summary of these achievements follows.

Welcomes New Center Directors and Principal Investigators

Dr. Guay-Woodford, MD, joined CRI as Director of the newly re-named Center for Translational Science (formerly the Center for Clinical and Community Research). Dr. Guay-Woodford also serves as the Director of the Clinical Translational Science Institute at Children’s National (CTSI-CN). The CTSI-CN provides the structure to quickly translate research findings from the lab (or bench) to the patient’s bedside and community. It is funded by an NIH Clinical and Translational Science Award (CTSA) for which Dr. Guay-Woodford serves as Principal Investigator. Dr. Guay-Woodford is an internationally known pediatric immunologist and his work focuses on gene therapy for Wiskott-Aldrich Syndrome, a disease characterized by recurrent infections and the absence of cell-mediated immunity. He has published extensively in leading journals such as Cell and Nature.

Yang Liu, PhD, has been appointed as Director of the Center for Cancer and Immunology Research. Dr. Liu came from the University of Michigan where he was a Professor in the Departments of Internal Medicine, Pathology, and the Division of Immunology and co-Leader of the Tumor Immunology and Host Response Program. Dr. Liu is the Principal Investigator of several NIH research awards in the area of cancer immunology and immunotherapy. He has published more than 130 papers in prestigious journals including Nature, Science, Proceedings of the National Academy of Sciences and the Journal of Clinical Investigation.

Yuan Zhu, PhD, has been appointed as Research Director of the Gilbert Family Neurofibromatosis Institute and Senior Scientist in the Centers for Cancer and Immunology Research. Dr. Zhu was also recruited from the University of Michigan where he was an Associate Professor in the Departments of Internal Medicine and Cell and Developmental Biology. Dr. Zhu’s research focuses on the role of tumor suppressor genes on tumor stem cells. He is the Principal Investigator of two NIH grants related to neurofibromatosis and has published in prestigious journals including Cell and Nature Genetics.

Pan Zheng, MD, PhD, was appointed Senior Scientist in the Sheik Zayed Institute for Pediatric Surgical Innovation and the Center for Cancer and Immunology Research. Dr. Zheng is a pathologist and was trained for the University of Michigan. His research focuses on the role of tumor suppressor genes on tumor stem cells. He is the Principal Investigator of two NIH grants related to neurofibromatosis and has published in prestigious journals including Cell and Nature Genetics.
umor evasion of host immunity, its molecular
mechanisms and signaling pathways and biology of
cells. Dr. Zheng currently holds an NIH R01
grant on signaling in inflammation and stem cell
research. She has published more than 80 peer-
reviewed papers in journals including Science and
Proceedings of the National Academy of Sciences.

Aline Bollard, MD, PhD, is the Director of the
Immunology Initiative at the Sheikh Zayed Institute,
senior investigator in the Center for Cancer and
Immunology Research. Dr. Bollard’s clinical and
research interests focus on cellular immunotherapy
defeat in pediatric cancers and other immunological
diseases. Dr. Bollard is the Principal Investigator
on several federal and foundation grants on topics
to cellular immunotherapy and stem cell
transplantation. She has published more than 60
publications.

A. Penn, MD, PhD, is Director of the Fetology
Laboratory in the Division of Neonatology and Center
Neuroscience Research. She is a neonatologist and
researcher moving from Stanford University School of
Medicine. Her research interests focus on the fetal
brain and placenta interactions and how these
interactions, when perturbed, can result in brain
damage. She holds a prestigious NIH Director’s New
Investigator Award for research on this topic.

National Awards for Faculty

Himi Luban, MD, Chief of the Division of
Pediatrics and Vice Chair of Pediatrics
Academic Affairs, received the Tibor Greenwalt
Memorial Award from the American Association
of Blood Banks. This award recognizes Dr. Luban’s
pioneering research in pediatric hematology
transfusion medicine with a focus on neonates
with transfusion and other disease, and abrogation of transfusion-associated
graft versus host diseases, which set FDA standards
of practice.

David Wessel, MD, received a career achievement
award from the American Heart Association,
recognizing his contributions in pediatric heart
health. Dr. Wessel currently serves as Principal
Investigator for the Collaborative Pediatric Critical
Therapies for newborns with congenital heart disease,
as well as advances in the treatment of pulmonary
hypertension. Dr. Wessel was also recently promoted
to Executive Vice President and Chief Medical Officer
for Hospital and Specialty Services. He is the Ikaria
Distinguished Professor of Critical Care Medicine.

Roger Packer, MD, Senior Vice President of the
Center for Neurosciences and Behavioral Medicine,
Children’s National Medical Center, recently
received the American Heart Association’s
Distinguished Research Scientist Award for
his work in understanding and treating children
with neurological disorders.
al who has performed leading research in
ence with relevance to the care of children
urological disorders. It recognizes Dr. Packer's
onal status as a clinical investigator in pediatric
otor research who has applied research to
ical care. Dr. Packer oversees clinical
ence and behavioral medicine and directs
Brain Tumor Institute and the Gilbert
erofibromatosis Institute. He leads clinical
ational and international level for a
of childhood brain tumors through the
Brain Tumor Consortium and Children's
y Group of the NIH.

Research in Research Funding
yer was marked by continued growth in our
portfolio, with the total annual research
creasing from $64 million in 2011 to $73
n 2012. This increase resulted from research
of the Sheikh Zayed Institute through a
it from the Government of Adu Dhabi.
itted approximately 300 grants and saw a
ate of 54 percent for non-federal grants and
ent for federal grants, both higher than the
verage. In assessing the efficacy of our pilot
rogram we found that 20 percent of these
ere subsequently converted to externally
rojects, providing a 2.6 fold return on
ent. Our bridge funding program was even
ccessful with 57 percent of investigators who
one year of interval funding converting the
ward to funded NIH grants.

Matriculating class chosen, including five MD/PhDs, four MD/MPH, seven members of the AOA medical student honorary society, and a Fulbright Scholar. Congratulations goes to our residency director, Dewesh Agrawal, MD.

Research Round Up
While most of the wonderful work taking place at
RI is covered in this annual report, we want to
ention a few highlights:
• The muscular dystrophy program continues
grow with collaborative cross-center efforts
cluding a P50 Center of Research Translation
directed by Eric Hoffman, PhD, and Avital Cnaan,
PhD; a U54 Pediatric pharmacology center in
muscular dystrophy drug development directed by
John van den Anker, MD, PhD, and Ed Connor,
MD; a Network for Excellence in Neuroscience
ical Trials (NEXT) directed by Roger Packer,
MD (the only pediatric site funded in the United
ates); an IND-enabling toxicity program
on exon skipping; and an R01 on molecular
dagnostic methods.
• The Rare Disease Clinical Research Center for
Cycle Disorders led by Mark Batshaw,
D, Mendel Tuchman, MD, and Marshall
mar, MD, continues to grow, now including
academic centers from the United States and
rope. The Urea Cycle Disorders Consortium
ducts clinical trials for bringing new drugs
to patients and studies to better diagnose and
nderstand these rare disorders. Dr. Tuchman
so received an R01 to fund a trial of a novel
treatment approach to urea cycle disorders.
• Our nursing research investigators, led by Pamela
inds, PhD, RN, are studying important pediatric
health issues including identifying disruptions
patient care processes, family decision making,
In summary, this has been another successful academic
ear for Children's Research Institute and we are
leased and grateful to all our dedicated faculty and
staff who worked hard to make this happen.

Mark L. Batshaw, MD
Chief Academic Officer
Children's National Medical Center
Director
Children's Research Institute

Mendel Tuchman, MD
Chief Research Officer
Children's National Medical Center
Scientific Director
Children's Research Institute

Pamela Hinds, PhD, RN
Children's National Medical Center
Research Institute

In summary, this has been another successful academic
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NIOR LEADERSHIP

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Pamela S. Hinds, PhD, RN, FAAN
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John van den Anker, MD, PhD
Associate Director, Center for Clinical and Translational Science

Peter C.W. Kim, MD, CM, PhD
Senior Vice President, Sheikh Zayed Institute for Pediatric Surgical Innovation

Peter C.W. Kim, MD, CM, PhD
Senior Vice President, Sheikh Zayed Institute for Pediatric Surgical Innovation

Kurt D. Newman, MD
President and CEO
Children’s National Medical Center

Elizabeth Singer
Chair of the CRI Board
Honoring Excellence in Research and Education

One of the core pillars to the mission of Children’s National, research is integral to all that we do to support and improve the lives of children and families. But how much do we and even staff know about all of our own edge research? A few years ago, Children’s National sought to answer that question by hosting a Research Day to display and showcase a variety of projects. It also was a chance for students and learn about science. Now that one-day event has evolved into Research and Education Day, a showcase of the strength and diversity of Children’s National research and education. The day is sponsored by Children’s Research Institute, Department of Medical Education, the Department of the Clinical and Translational Science Institute, Children’s National, and the Sheikh Zayed for Pediatric Surgical Innovation.

“Faculty, trainees, fellows, affiliates, and others are invited to participate in a variety of activities including poster presentation sessions, speaker presentations, and panel discussions on a variety of topics,” stated Kerstin Hildebrandt, Executive Director of Operations and Affi Li for Children’s National Institute.

Dr. Batshaw helps one of the students who took part in one of the many “Being Me” activities organized by the National Children’s Museum through the Children’s Science Education Partnership Award from the A.A. Milani for Pediatric Surgical Innovation.
The goal is to inform the academic community, collaborative institutions, community partners, and partners along with government agencies about significant research projects and educational programs at Children's National.”

This year, Research and Education Week boasted more than 250 posters during the two-day presentations. Judging panels evaluated the posters in five different categories including clinical research, community based research, basic and translational research, education, training, and program development, and quality and performance improvement. Altogether, 30 different winners and honorable mentions were chosen from faculty, staff, fellows, post docs, trainees, and students from high school through graduate school.

Additionally, this year included an expanded presentation and visiting speaker component that featured three different guests and a panel discussion geared towards talking about innovative pediatric research projects:

Robert Engleman, MD, helped to kick off the week-long engagements at the Medical Education and Rounds Greenberg Lectureship.

Dr. Susan Shurin, MD, then Acting Director of the National Heart, Lung, and Blood Institute spoke about the field of pediatric research and the collaborations between the institute and Children’s National.

Nathan Moreno, PhD, the author of *Biomedical Research, Bioethics, and Biopolitics: Shaping Our Present and Future* was the keynote speaker for the week and gave a rousing presentation on ethics and research.

Wrapping up the week was a panel discussion that took place at IMPACT DC, the Washington, DC, metro community. The panel featured local and national research collaborators, community partners, and Children’s National Board members, who reflected on a decade of collaborative asthma care and research at Children’s National and where this work will go in the future. It was a rousing discussion on the importance of community education and meeting the needs of patients and families.

Throughout the entire week, conversations between families, staff, students, researchers, and clinicians could be seen inside the Sheikh Zayed Campus walls. It was both exciting and telling of how Research and Education Week has become an integral part of Children’s effort to promote cutting-edge research that will help to improve the health and quality of life for children.
In ensuring they’re as healthy as can be, we see the need to inspire and invigorate their minds in science and biotechnology. Encouraging children and families to learn about science, technology, engineering, and mathematics (STEM) is one of the important initiatives at Children’s National Institute. This past year, Children’s National participated in the 2nd USA Science and Engineering Festival, the nation’s largest celebration of science and engineering. The gathering is the country’s only science festival, and was developed in response to President Obama’s “Educate to Innovate” campaign to support STEM education, increase the number of U.S. students in science and math, and to encourage children, from elementary school to high school, to pursue careers in STEM by fostering discovery and innovation.

The presence at this event became a true partnership between the Sheikh Zayed Institute for Pediatric Innovation, Children’s Research Institute, the Bone Health Program, and the “Being Me” gathered to attend the event. Laura Tosi, MD, Director of the Bone Health Program, said, “As part of its commitment to STEM education, volunteers from Children’s National Bone Health Program talked to attendees about bone health with the help of the following partners: Mid-Atlantic Dairy Association, the National Dairy Council, and the American Dairy Association Maryland.”
Pretending they were physicians and scientists and learning about how the human body works through art-focused, hands-on activities. Children explored their dexterity by performing minimally invasive surgery inside a life-sized dummy, using robotic tools.

Learning about the respiratory and digestive systems, by looking at lungs in “action,” and understanding the role of the environment in asthma. The participants also decorated crowns to serve as a daily reminder about the benefits of a balanced diet.

Gathering friendship cards, which were used as a method to avoid bullying.

Recognizing the key ingredients needed to build the best possible skeleton and how bone strength is measured, as well as exploring new technologies that help repair bone and other musculoskeletal injuries. Specimens loaned from the Smithsonian Institute, taught participants how infection, injury, and disease severely impacted patients’ bone health and quality of life in previous generations.

“One of the most amazing things I saw that weekend were the countless groups of kids, faces lit with excitement, running from station to station, asking pointed questions with lots of “hows” and “whys” and competing,” reflected by Naomi L. C. Luban, MD, Division Chief of Laboratory Medicine. “It’s that kind of excitement and thrill that is motivating and reminds you that pediatric healthcare and research goes beyond disease and is really about encouraging children to develop a desire to answer questions and make them aware of the importance of science in improving the health of the nation.”

—Naomi L.C. Luban, MD

George Washington University's Graduate School of Education and Human Development. As Science Education Partnership Award from the National Institutes of Health and with Naomi L.C. Luban, MD, as the Principal Investigator, “Being has developed an art-based science and health curriculum.

During the course of three days, our researchers, medical students, National Children’s Museum and Children’s Research Institute staff engaged more than 50 children and families from around the country. Some of the activities included:

- Pretending they were physicians and scientists and learning about how the human body works through art-focused, hands-on activities. Children explored their dexterity by performing minimally invasive surgery inside a life-sized dummy, using robotic tools.
- Learning about the respiratory and digestive systems, by looking at lungs in “action,” and understanding the role of the environment in asthma. The participants also decorated crowns to serve as a daily reminder about the benefits of a balanced diet.
- Gathering friendship cards, which were used as a method to avoid bullying.

“[...]Pediatric healthcare and research goes beyond disease and is really about encouraging children to develop a desire to answer questions and make them aware of the importance of science in improving the health of the nation.”

—Naomi L.C. Luban, MD
A breakthrough in understanding a key mechanism of white matter development

Researchers at Children’s National have made inroads in better understanding the basics of a key brain developmental process: the formation of white matter, known as myelination.

Children’s National researchers identified Sox17 as a gene that helps regulate the Wnt/beta-catenin pathway during the transition of oligodendrocyte progenitor cells, or immature brain cells, into a more mature, differentiated state where they produce myelin.

“This is the first time the Sox17 gene has been identified as a regulator of the Wnt/beta-catenin pathway during myelination,” said Li-Jin Chew, a co-author of the study. “Our findings suggest that loss of Sox17 over-stimulates the Wnt/beta-catenin pathway and keeps oligodendrocyte progenitors from maturing and producing myelin.”

Myelination, white matter growth and repair, and the study of complex mechanisms of prenatal brain development are a key focus of the Center for Neuroscience Research at Children’s National, which also houses the White Matter Diseases Program one decade of life. Myelination can be impaired for a number of reasons, most commonly intrauterine infection, reduced or interrupted blood flow (which carries oxygen and nutrients) to the forming infant brain, or perinatal injury. As a result, white matter doesn’t develop the way that it should or is somehow damaged, resulting in mental retardation and developmental disabilities.

“For the first time, we’ve identified Sox17 as a key regulator of the Wnt/beta-catenin pathway during myelination,” said Li-Jin Chew, a co-author of the study. “Our findings suggest that loss of Sox17 over-stimulates the Wnt/beta-catenin pathway and keeps oligodendrocyte progenitors from maturing and producing myelin.”

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“From here we plan to look more closely at the parts of the pathway that Sox17 regulates. We’ll be able to understand the crucial molecular events that occur during oligodendrocyte development and disease,” stated Vittorio Gallo, PhD, Director of the Center for Neuroscience Research. “This is an incredibly exciting discovery that puts us closer to figuring out the underlying cause of white matter diseases. It also means that we may eventually understand how we could influence these pathways and possibly ease white matter damage or deficiency in our patients.”

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Li-Jin Chew, PhD, and Vittorio Gallo, PhD, from the Center for Neuroscience Research at Children’s National. Photo taken by Michael Leong, George Washington University
Introducing a New Center Director

**OCTOBER 2012,** Yang Liu, PhD, joined Children's Research Institute at Children's National Medical Center as the Director for the Center for Cancer and Immunology Research. The addition of this leading researcher will be instrumental in continuing the development of quality research at Children's National Medical Center.

Dr. Liu's goal is to create a nationally recognized research center in cancer biology and immunology, building stronger connections among and between research scientists and clinicians. Dr. Liu envisions a center in which the clinical and laboratory-based investigators can interact effortlessly to identify and solve the mysteries of cancer biology and immunology. He particularly wants to emphasize the cross-fertilization of two research fields within the center. The long-term goal is to receive recognition as a National Cancer Institute-designated cancer center, and to produce groundbreaking publications that impact basic concepts and practical applications in the field of cancer and immunology.

Dr. Liu highlights some of his previous work in translational research:

- **The interest in cancer biology concerns the therapeutic targeting of cancer stem cells and revealing the X-linked tumor suppressor genes within those cells. Cancer stem cells are responsible for cancer relapse. Dr. Liu's laboratory has identified a method to selectively eliminate cancer stem cells in an experimental setting and our work moving forward will be to test the notion in pediatric cancer patients.**

- **The effort in immunology focuses on understanding how the immune system fine-tunes its response to tissue injuries. It is well established in this field that an injured tissue releases its intracellular component which is inflammatory. Limited inflammation is required for tissue repair, but strong inflammation can be detrimental to the tissue in question. Dr. Liu's research has identified a novel pathway that limits this inflammation to harmless levels, stimulating tissue repair. This means stimulating this pathway can encourage tissue repair and thus protect against autoimmune diseases like rheumatoid arthritis and multiple sclerosis.**

Dr. Liu is excited about his opportunity at Children's, saying, “The impact of an individual is always modest. However, our hope as a team is that we will have a positive impact. Children's National Medical Center is currently ranked among the top five pediatric institutions in the country, but we need our research to match our national reputation. The same is true for other blood disorders. Strengthening the research program will bolster the institution’s reputation while propelling the clinical program to a new level of excellence.”
Research Funding

Research Funding by Sponsor

- NIH $39,022,610.87
- Sheikh Zayed Research Center $12,061,791.00
- Other Non-Federal $6,666,348.00
- HRSA $5,466,720.00
- Department of Defense $5,067,236.00
- Other Federal $2,501,174.00
- Internal Awards $2,295,927.00

Total $73,081,806.87

6-Year Growth in NIH Funding

<table>
<thead>
<tr>
<th>Year</th>
<th>NIH Funding (in Millions)</th>
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<tbody>
<tr>
<td>FY07</td>
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<tr>
<td>FY12</td>
<td>$39.20</td>
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</table>

Total $73,081,806.87

Research Funding by Center

- Center for Translational Science $19,824,823.50
- Genetic Medicine $17,779,071.87
- Sheikh Zayed Research Center $13,648,882.00
- Neuroscience $9,202,767.00
- Cancer and Immunology $9,167,603.50
- Molecular Physiology $3,458,659.00

Total $73,081,806.87
The word philanthropy derives from philos, the ancient Greek word for “loving” and anthropos for “human being.” The term is believed to have been coined by the playwright Aeschylus, who sought to evoke the gift of fire, which has benefited humanity in countless ways. The generous support that sustains Children’s Research Institute and Children’s National Medical Center exemplifies this original idea. Philanthropy lights our path toward clearer scientific understanding, new knowledge, and improvements to the health of children everywhere.
Gilbert Family Neurofibromatosis Institute

and Dan Gilbert are visionary entrepreneurs, philanthropists and incredible advocates for pediatric research. During the past seven years, they have come extraordinary partners to Roger Packer, Senior Vice President for Neuroscience and Behavioral Medicine and Director of The Gilbert Neurofibromatosis Institute.

Gilbert is founder and chairman of Quicken and majority owner of the Cleveland Cavaliers. Gilbert is the founder and CEO of Doodle. Jennifer and Dan Gilbert have five children, the oldest of whom was born with neurofibromatosis (NF), a difficult-to-predict and extremely variable genetic disorder that has complex manifestations including tumors of the brain, optic nerve, nervous system and body, learning disabilities, sleep disorders, and depression.

Through their philanthropy, the Gilberts have enabled Dr. Packer and Children’s National to build a team of talented physicians, nurses, genetics counselors, therapists, and investigators who are leaders in NF clinical care and medical research. The Gilbert Family Neurofibromatosis Institute has become internationally respected for its real-time integration of innovative research into the best healthcare for children with NF. Since its inception, The Gilbert Family Neurofibromatosis Institute has contributed greatly to the field, including the establishment of standards of care for children diagnosed with NF, new therapies for NF tumors, and exciting laboratory discoveries about the cellular and sub-cellular activities of NF tumor cells, which will lead to new treatments and, perhaps one day, cures for NF.

During the coming years, Dr. Packer and Yuan Zhu, PhD, the newly appointed Scientific Director of the Institute, will continue to translate these discoveries into immediate solutions at the bedside. Together, the Gilberts and Dr. Packer are expanding the Institute’s scope to include people affected by other rare genetic disorders.

“IT has been exciting, more than words can express, living in this great country and being able to start, develop, and grow businesses. It will be even more exciting to deploy the wealth these businesses created to improve our world, which I feel confident will be a much better place in the years and decades ahead.” —Dan and Jennifer Gilbert

NF patient family, Carrie Baker and her daughter, Brooke.
Shirley Howard is an 87 years-young wonder who has been the driving force behind the Children's Cancer Foundation (CCF) for approximately 30 years.

Shirley started her career in radio and TV and quickly realized that she had a talent for connecting with people through the media. At the same time, Shirley and her husband Bill, now deceased, began volunteering for children's cancer causes. They combined their passion with their networks and the Children's Cancer Foundation was formed.

Over the years the Howards raised between $2 million and $3 million annually. They focused their grants on pediatric cancer research projects to advance clinical care, as well as clinical care facilities in the more and Washington regions. Altogether, they contributed more than $4 million to Children's National. In recent years, CCF has funded research projects for Stephan Ladisch, MD, and Jeffrey Me, MD, PhD, as well as clinical spaces including the Center for Cancer and Disorders and the Bone Marrow Transplant Patient Clinic.

The proposed research will allow Children's National to collaborate with the American Academy of Pediatrics, to determine the relative effectiveness of the different dissemination strategies to increase uptake by pediatricians of immunization best-practice recommendations.

The Pfizer Investigator Initiated Research mechanism provides support to advance scientific and medical knowledge including studies that contribute to improved health and wellness for people. They believe that working with healthcare professionals is essential to gaining the real-world information needed to deliver better treatment choices.

We are grateful for the generosity of Pfizer and for their support of our work that has the potential to improve early childhood immunization rates.

Pfizer, Inc. has provided generous support to fund the research of Linda Fu, MD, MS. Her project seeks to compare immunization quality improvement dissemination strategies for increasing immunization rates among a national sample of diverse pediatric practices. The proposed research will allow Children's National to collaborate with the American Academy of Pediatrics, to determine the relative effectiveness of the different dissemination strategies to increase uptake by pediatricians of immunization best-practice recommendations.

The goal of this intervention is to help empower minority parents to communicate with primary care providers, which will increase their utilization of primary care providers for asthma care, facilitate more effective visits, increase medical adherence, reduce emergency department visits, and improve their children's asthma health outcomes.

The Verizon Foundation partnered with Children's National, providing support to the research of Ivor Horn, MD, with the goal of improving health outcomes for children with asthma in the District of Columbia. The proposed study, Text2Breathe, uses Short Messaging Service (SMS/text messaging) technology to provide health education information designed to equip parents in urban, low-income underserved communities with tools and techniques for communicating effectively with their children's primary care providers.

The goal of this intervention is to help empower minority parents to communicate with primary care providers, which will increase their utilization of primary care providers for asthma care, facilitate more effective visits, increase medical adherence, reduce emergency department visits, and improve their children's asthma health outcomes.

The Verizon Foundation is focused on using technology to solve critical issues in the areas of sustainability, education and healthcare. They aim to reduce the impact and disparities of chronic conditions and improve the quality of healthcare for underserved populations through technology deployment and behavioral interventions.

Through their support, The Verizon Foundation is enabling Children's National to address the critical needs of our patient population and improve health and social outcomes by using innovative methods to enhance patient care and outcomes.
Children’s National Endowed Professorships

L. Batshaw, MD
Thomas Willson and Lenore Williams McKnew Professor of Pediatric Oncology

Jeffrey Dome, MD, PhD
Ruth Pack Wolf and William B. Wolf, Sr. Professor of Neuroscience

Vittorio Gallo, PhD
Richard L. and Agnes F. Hudson Professor of Health Services Research

Paramjit T. Joshi, MD
Dr. Robert J. and Florence T. Bosworth Professor of Cancer and Transplantation Biology Research

Yang Liu, PhD
C. Richard Beyda Distinguished Professor of Cardiology

Lisa Guay-Woodford, MD, PhD
Robert H. Parrott Professor of Pediatric Research

Eric Hoffman, PhD
A. James Clark Professor of Molecular Genetics

L. A. Jonas, MD
Hon-Funker Distinguished Professor of Academic Medicine

Patricio Ray, MD
Robert H. Parrott Professor of Pediatric Research

Jeffrey Dome, MD, PhD
Thomas Willson and Lenore Williams McKnew Professor of Pediatric Oncology

Mendel Tuchman, MD

Marshall L. Summar, MD

John N. van den Anker, MD, PhD

David L. Wessel, MD
CENTER'S MULTIDISCIPLINARY RESEARCH investigates childhood cancers, their origins, immune responses, and therapy, through nationally known programs in pediatric oncology clinical trials. The Center also investigates bone marrow and stem cell transplantation, hematologic disorders, including sickle cell disease, and infectious diseases that affect children.

VISION STATEMENT: To develop the foundation for the best and most compassionate care of children with cancer, immunologic, hematologic, rheumatologic, infectious, and allergy related disorders, through basic, translational, epidemiologic, and population-based research.

Center for Cancer and Immunology Research

Mendel Tuchman, MD
Interim Director
Professor of Pediatrics, Biochemistry, Molecular Biology & Integrative System Biology

Yang Liu, PhD
Designate Director
FACULTY

Anne Angiolillo, MD  
Oncology

Patrick Chang, MD  
Hematology, Oncology

Lawrence J. D’Angelo, MD, MPH  
Adolescent Medicine

Roberta L. DeBiasi, MD  
Infectious Disease

Jeffrey Dome, MD, PhD  
Oncology

Leslie Doros, MD  
Oncology

Cynthia Gingalewski, MD  
General Surgery

Eugene Hwang, MD  
Oncology

David Hyun, MD  
Infectious Disease

Shana Jacobs, MD  
Oncology

David A. Jacobsohn, MD  
Blood and Marrow Transplantation

Marina Jerebtsova, PhD  
Nephrology

Lawrence Jung, MD  
Rheumatology

Naynesh R. Kamani, MD  
Blood and Marrow Transplantation

Lindsay Kilburn, MD  
Oncology

AeRang Kim, MD, PhD  
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Stephan Ladisch, MD  
Oncology

David Leitenberg, MD, PhD  
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Yihui Liu, PhD  
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Allergy and Immunology

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Holly Meany, MD  
Oncology

Parvathi Mohan, MBBS  
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Evelio Perez-Albuerne, MD, PhD  
Blood and Marrow Transplantation

Patricio Ray, MD  
Nephrology

Gregory H. Reaman, MD  
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Brian R. Rood, MD  
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Reuven Schore, MD  
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Sadhna Shankar, MD  
Hematology, Oncology

Nalini Singh, MD, MPH  
Infectious Disease

Xiaoyan Song, PhD, MB, MSc  
Infectious Disease

Pingtao Tang, MD, PhD  
Nephrology

Amanda Thompson, PhD  
Hematology, Oncology

Shamir Tuchman, MD, MPH  
Nephrology

Steve Zeichner, MD, PhD  
Infectious Disease
Section: Childhood Cancers

Center’s researchers in pediatric oncology conduct basic, translational, and clinical research. Current areas of focus include brain tumors, retinoblastoma and Wilms tumors, and new drug development (telomerase inhibitor).

Brain Tumors

Brain tumors are the most common solid tumor in children, with about 3,750 new patients diagnosed every year. Children’s National has one of the largest most active programs in the United States for diagnosis and treatment of children with brain tumors. Through a multidisciplinary team approach including the specialties of neuro-oncology, neurosurgery, neuropathology, psychology, and neuroradiology, Children’s National not only provides state-of-the-art clinical care but also performs cutting-edge research investigating the genetic causes, biology, and new treatments of these tumors.

Tumor Biomarkers

- Brian Rood, MD
- Yetrib Hathout, PhD (Center for Genetic Medicine Research)
- Javad Nazarian, PhD (Center for Genetic Medicine Research)

Drs. Rood and Hathout work to characterize the cerebrospinal fluid (CSF) proteome in patients with medulloblastoma. CSF is uniquely suited to this due to its continuous turnover, ready availability, and its relatively low protein complexity. Current diagnostic and therapeutic monitoring studies are limited in their ability to accurately characterize a brain tumor’s biological response to therapy and detect tumor recurrence. Using cutting-edge proteomics technology, they are working to develop a means to:
  - Augment the ability of MRI scanning to differentiate tumor tissue from post-surgical or post-radiation effects
  - Assess treatment response to small molecule inhibitors and anti-angiogenic agents
  - Detect early disease recurrence
  - Identify pharmacodynamic biomarkers that predict response to specific molecularly targeted therapies

The systematic evaluation of CSF of patients with brain tumors is building the foundation for reliable biomarker discovery. In collaboration with investigators from the National Institutes of Health and other institutions, the research team is identifying novel biomarkers that could improve diagnostic and treatment outcomes. The systematic evaluation of CSF of patients with brain tumors is building the foundation for reliable biomarker discovery. In collaboration with investigators from the National Institutes of Health and other institutions, the research team is identifying novel biomarkers that could improve diagnostic and treatment outcomes.

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  - Identify pharmacodynamic biomarkers that predict response to specific molecularly targeted therapies

Through proteomic and genomic analyses, the research team has identified NG2 as a potential biomarker and therapeutic marker of DIPG. Studies have shown that human primary cells express high levels of NG2 and that NG2 downregulation in vitro retards cellular migration. Studies are being conducted on the role of NG2 in vivo and its potential role as a therapeutic target. The hypothesis being tested is that specific targeting of NG2 in vivo will reduce cellular proliferation and migration and will be effective in the treatment of BSG and DIPG.

The Collaborative Ependymoma Research Network (CERN)

- Roger Packer, MD (Senior Vice President, Center for Neuroscience and Behavioral Medicine)
- Eugene Hwang, MD

CERN is a consortium of six adult and seven pediatric hospitals that lead the nation in research to find a cure for ependymoma. CERN members are chosen for their scholarly excellence and commitment to working cooperatively. CERN members collaborate by sharing research findings, responses to new treatment regimens and other new developments in a comprehensive effort against this brain cancer. CERN sponsors clinical trials specific to ependymoma that are only conducted at CERN consortium hospitals.
Goldie Dome, MD, PhD (Chief of Oncology, or, Solid Tumor Program)

Ashley Hill, MD (Chief of Anatomic Pathology, or for Genetic Medicine Research)

Tara Hinds, RN, PhD (Center for National Science)

Angiolillo, MD (Director, Leukemia/Therapy Program)

Derek Dean, MD

Eugene Hwang, MD

Amanda Jacobs, MD

Kelly, RN, PhD (Center for Translational Science)

May Kilburn, MD

Aung Kim, MD, PhD

Christopher Lawlor, MD

Marcus, MD

Meany, MD

Roger Packer, MD

Lindsey Ronnell-Wallace, MD, PhD

Scotty Reaman, MD

Rood, MD (Director, Neuro-Oncology Program)

Steven Schore, MD

Shana Shankar, MD

Sandra Thompson, PhD

Varela, MD

Dr. Dome serves as the COG Principal Investigator for Children's National, Chair of the COG Renal Tumor Committee, and Chair of a study for high-risk renal tumors. Dr. Hill is the Vice Chair of the Pathology Committee and Dr. Kelly is the Co-Chair of the Nursing Research Committee. Dr. Hinds serves on the COG Scientific Review Committee and co-chairs a task force to develop and incorporate patient reported outcomes in COG clinical trials. Dr. Angiolillo and Dr. Schore serve as the Study Chair and Vice-Chair for a study on standard-risk acute lymphoblastic leukemia (ALL), the largest therapeutic study within the COG. Dr. Meany is the Study Chair for the upcoming COG study for intermediate-risk neuroblastoma. Dr. Packer leads the medulloblastoma committee of COG. Dr. Jacobs is on the steering committee of the COG Cancer Control Committee. Children's National is one of a select group of 21 institutions in North America to be included in the COG Phase I consortium, allowing patients with recurrent and refractory tumors access to the newest agents. Dr. Angiolillo serves as Principal Investigator, and Dr. Kim serves as the Co-Principal Investigator.

Pediatric Brain Tumor Consortium (PBTC)

Roger Packer, MD

Brian Rood, MD

Eugene Hwang, MD

Lindsay Kilburn, MD

Children's National was one of the founding members of the Pediatric Brain Tumor Consortium (PBTC), an NIH-funded consortium consisting of eight member institutions. The PBTC develops novel therapies for children with brain tumors through innovative biology-based early phase clinical trials. In 2010-2011, Children's National enrolled 24 patients to PBTC studies than any other institution in the consortium. Drs. Rood and Packer are Co-Chairs of phase I trials on anti-angiogenic agents in children with relapsed brain tumors. Dr. Lindsay Kilburn chairs a phase II trial testing capecitabine and radiation in diffuse intrinsic pontine glioma and sits on the PBTC Data Safety Monitoring Board.

Other Experimental Therapeutics Research

Children's National investigators also develop phase I and II studies that are administrated outside the programs of COG and the PBTC. Dr. Holly Meany is the Principal Investigator of a phase I study of sorafenib and irinotecan for recurrent solid tumors and brain tumors. This study is funded by grants from the Clinical Translation Science Institute at Children's National (CTSI-CN), the American Society of Clinical Oncology (ASCO), and the Pablove Foundation. The Children's Hospital of Philadelphia, Boston Children's Hospital/Dana Farber Cancer Institute, and the National Cancer Institute are participating in this Children's National-led study. Integrated is a study of Patient Reported Outcomes, led by Dr. Pam Hinds, to provide an important adjunct to the traditional endpoints of phase I studies, thereby facilitating prioritization of new treatments for phase II and III studies. Dr. Hwang is the Principal Investigator for a multi-institutional phase II study of vinorelbine for recurrent or progressive low-grade gliomas. Dr. Rood is the Principal Investigator for a phase II study of metronomic chemotherapy for recurrent/progressive brain tumors. Children's National also participates in the Therapeutic Advances in Childhood Leukemia and Lymphoma Consortium (TACL), the Cooperative Ependymoma Research Network (CERN), and the Childhood Cancer Survivor Study (CCSS). Dr. Shana Jacobs leads the Palliative Care/Cancer Control Program and under her leadership, Children's National has the only dedicated pediatric palliative care service.
Gangliosides in Cancer

The role of gangliosides in tumor progression, particularly of some neuroectodermal brain tumors (e.g., neuroblastoma, medulloblastoma, meningioma), causes the most cancer-related morbidity and mortality. The synthesis and shedding of the membrane sphingolipids, or gangliosides, have been strongly implicated in contributing to tumor progression. Dr. Ladisch’s laboratory delineated basic mechanisms by which tumor gangliosides modulate the behavior of cells in the tumor microenvironment, such as cell signaling and subsequent cell growth responses. To test these findings in vivo, they developed a novel animal model system of specific constitutive inhibition of ganglioside synthesis. They are now comprehensively determining how ganglioside knockout in these tumor systems affects tumor progression, providing the first unambiguous insights in a genetically controlled and stable system.

Some studies have revealed a striking dependence of tumor angiogenesis in vivo upon the synthesis and shedding of tumor cell gangliosides.

Gangliosides and antitumor immune response (human neuroblastoma)

Stephan Ladisch, MD

Lisa Radoja, PhD

Ladisch’s laboratory also focuses on characterizing the effect of tumor gangliosides on the biology of neuroblastoma, specifically the antitumor immune response. This research is based upon the hypothesis that specific gangliosides shed by tumors are intercellular signaling molecules and protect tumor cells from immune recognition.

Conclusions: Gangliosides play a critical role in the processes facilitating tumor growth, and their elimination should be considered as a potential therapeutic target in the treatment of cancer.

Tumor ganglioside depletion impedes tumor growth and angiogenesis

105 cells wild type (WT) or genetically (constitutively) ganglioside-depleted (DKO) tumor cells were implanted in syngeneic mice. Top panels: DKO cells exhibit strikingly impeded tumor and tumor vessel growth; arrows indicate tumor; the left panel is a saline (no tumor cells) control. Bottom panels: Ganglioside-depleted DKO tumors exhibit impeded angiogenesis (no large vessels seen) compared to WT tumors (H&E stain, 400X).
Shedding and potent immunosuppressive properties of human neuroblastoma tumor gangliosides have been shown to inhibit murine antitumor responses, identified antigen presenting cell targets, and most recently uncovered a link between tumor gangliosides and the accumulation of immune cells in the tumor microenvironment.

In collaboration with Dr. Radoja, Dr. Ladisch's lab has shown inhibition of murine antitumor responses, identified antigen presenting cell targets, and most recently uncovered a novel mechanism by which gangliosides interfere with the cytotoxic function of macrophages that is important for tumor cell elimination.

Ladisch, MD

Ganglioside expression and neuroblastoma differentiation

It has been speculated that specific gangliosides are linked to the clinical and biological behavior of many types of tumors, including neuroblastoma (NB). Recent work by Dr. Ladisch indicated that low or absent expression of complex gangliosides (GD1b, GT1b and GQ1b, CbGs) correlates with unfavorable clinical features and an aggressive biological phenotype in NB tumors, while high CbG expression is predictive of a favorable disease outcome. The rationale for testing the hypothesis that CbGs ameliorate or modulate tumor progression is supported by the observation that CbGs ameliorate the malignant behavior of NB cells in vivo.

Dome, MD, PhD

Recovery of telomeres using telomerase as a therapeutic target for pediatric cancer

Telomerase is a nuclear enzyme that replenishes telomere repeats that are lost during DNA replication. Because telomerase is relatively specific to cancer cells and is critical to cancer cell immortality, it represents a highly attractive therapeutic target. The laboratory of Dr. Dome focuses on telomere biology of osteosarcoma, the most common bone tumor of children and teenagers. Osteosarcoma is distinct from most cancers in that only 50 percent of tumors express telomerase. The remaining tumors utilize a poorly characterized recombination-based telomere maintenance mechanism called “ALT” that distinguishes ALT-dependent osteosarcomas from their telomerase-dependent counterparts. In addition, the laboratory is evaluating the efficacy of GRN163L, a small molecule telomerase inhibitor, in preclinical models of osteosarcoma, malignant rhabdoid tumor, neuroblastoma, and Wilms tumor. The preclinical studies have yielded promising results that will allow researchers to rationally design clinical studies of agents that target telomeres and telomerase. Dr. Dome's laboratory recently demonstrated that telomere shortening alters the kinetics of the DNA damage response, as measured by γH2AX staining, in malignant rhabdoid tumor cells.
Cancer Immunology

Cancer immunology focuses on studying the interaction between the immune system and cancer. In particular, our investigators seek to take advantage of the fact that the immune system is able of recognizing cancer specific antigens. Two avenues are being pursued, one seeking to optimize patients’ own immune system to recognize and consequently destroy cancer cells, the other seeks to provide a patient with a new immune system (from a donor) capable of destroying cancer cells.

Marrow Transplantation (BMT)

David A. Jacobsohn, MD (Chief, Division of Blood and Marrow Transplantation)

Jacobsohn’s interest is graft-versus-host disease (GVHD), the main complication after bone marrow transplantation. One of the main barriers has been to develop effective therapy for GVHD as well as tests to diagnose and grade GVHD. Dr. Jacobsohn has led and designed a number of clinical trials looking at various therapeutic agents to treat GVHD. Furthermore, he conducts risk factor studies to look at prognostic factors that affect outcomes of patients after having developed GVHD.

Transfusion Medicine

Naomi L. C. Luban, MD (Chief, Division of Laboratory Medicine)
Zohreh Tatari-Calderone, PhD (Sheikh Zayed Institute)
Yaser Diab, MD (Hematology)
Ross Fasano, MD (Laboratory Medicine/Hematology)
Richard Levy, MD (Anesthesiology)
An Massaro, MD (Neonatology)
Wendy Paul, MD (Laboratory Medicine)
Lillian Su, MD (Critical Care Medicine)
Edward C. C. Wong, MD (Laboratory Medicine)

Dr. Luban leads a team whose overall goals are to investigate the adverse consequences of transfusion through epidemiological, clinical, and device/laboratory methods development and evaluation. Our multidisciplinary team works in concert with colleagues in the divisions of Hematology, Blood and Marrow Transplantation, Critical Care Medicine, Center for Genetic Medicine Research and the Sheikh Zayed Institute and colleagues at NHLBI, NIDDK and the Division of Transfusion Medicine, NIH Clinical Center, the American Red Cross, and the Food and Drug Administration.

Sickle Cell Disease Immunopathology

We continue our studies on the immunologic basis of red blood cell (RBC) alloimmunization in Sickle Cell Disease (SCD). Drs. Zohreh Tatari-Calderone, Ross Fasano, and Edward Wong have expanded patient enrollment, evaluated serial cytokine profiles, and abstracted patient-specific data on more than 300 SCD patients to correlate the development of RBC allo antibodies with B cell activation due to RBC antigen exposure during the inflammatory process. Dr. Fasano continues his studies on molecular RBC antigen genotyping and has developed a computer algorithm for donor/recipient RBC matching which will be matched for more than 30 RBC antigens. Dr. Fasano, in collaboration with Drs. Wong and Jacobsohn, has developed a study which will utilize Luminex methodology to quantify and categorize pro- and anti-inflammatory and pro-coagulant profiles of children undergoing extracorporeal photopheresis (ECP), a procedure used to treat Graft-vs-host disease (GVHD) following Hematopoietic Stem Cell Transplantation; the study will focus on children with SCD undergoing transplant who have a chronic, heightened inflammatory state.

Coagulopathy and Necrotising Enterocolitis Diagnosis and Treatment

Collaborative investigations with our colleagues in the Division of Neonatology were expanded this past year beyond transfusion. The effect of core body temperature and specimen handling on thromboelastogram (TEG) values in neonates requiring both ECMO and hypothermia for encephalopathy were completed. From these studies we developed the first neonatal reference ranges for TEGs; these results were presented at several meetings and are in the process of publication. TEG provides analysis of complex fibrinolytic, antifibrinolytic pathways and platelet function in a point of care device; TEG’s usefulness in neonates with critical bleeding was limited by an absence of reference ranges. With Drs. Yaser Diab, Richard Levy and American Red Cross colleagues, we completed studies to improve methods for aliquoting platelets for neonatal transfusion and established that depletion of ADP in platelet concentrates occurs due to acquired depletion of cytochrome C oxidase.

Hematology and Transfusion Medicine

Investigators in this section are involved in many aspects of hematology research, including optimization of the treatment of patients with clotting disorders, developing therapies for sickle cell disease, and improving understanding of immune perturbations associated with blood transfusions.
A multidisciplinary Special Interest Group in Necrotizing Enterocolitis, a particularly concerning disorder of the newborn. Utilizing Whole sequencing, members of the SIG hope to define the immunologic, molecular, and metabolic pathophysiologic underpinnings of this disorder, which has pathophysiologic similarities to RBC alloimmunization and postnatal microchimerism seen after massive transfusion.

Studies with the FDA on the plasticizers BPA and metabolites continue and to date, the only group to generate PK data on BPA exposed pediatric population as compared to exposed to plasticizers within the setting of the ICU. Our focus is on children undergoing extracorporeal bypass and catheterization. Ongoing health concerns over the estrogenic/anticluster effects of BPA leaching from medical devices make this work highly relevant.

Infectious Diseases

Factors in this section are primarily involved in HIV/AIDS, viral cardiomyopathy, laboratory, and research in viral myocarditis.

Research in HIV related disorders, viral pathogenesis, and viral therapeutics

In Zeichner, MD, PhD

The laboratory of Dr. Zeichner studies human immunodeficiency virus-1 (HIV-1; HIV), Kaposi’s-associated Herpes virus (KSHV), the agent of Kaposi’s sarcoma, and other agents associated with immunopathology and to develop new therapies and vaccines for these diseases. In past work the laboratory defined the gene expression program KSHV uses to reproduce. Recently, the laboratory showed that the virus can sense when the virus’ host cell is about to die and then reproduce using a new, rapid, but relatively ‘sloppy’ reproduction pathway. This knowledge may lead to innovative treatments for the cancers associated with KSHV and other Herpes viruses. One of the lab’s HIV projects involves studying how HIV remains latent and what stimuli lead to HIV activation. After HIV infects certain cells, a DNA copy of the virus can remain latent within the genome of the host cell for many years. This creates a long-lived reservoir of latently infected cells, which is the reason why HIV infection cannot be cured yet. Much recent interest has focused on working to find ways to effectively and safely activate HIV in that latent reservoir without harming other cells or organs. If a safe method could be found to activate HIV, that method could be used, along with currently available drugs that can block the new infections of cells, to attack and deplete the long-lived reservoir of cells latently infected with HIV. The lab is working on another HIV project developing novel screening methods to identify highly effective immunogens, which may be useful in the development of new HIV vaccine candidates and vaccines for other diseases.

HIV-associated renal diseases

- Marina Jerebtsova, PhD
- Jinliang Li, PhD
- Pingtao Tang, MD, PhD
- Ray Patricio, MD
- Xuefang Xie, PhD
- Natella Rakhmanina, MD, AAHIVS (Center for Translational Science)

More than 90 percent of HIV-1 positive African American children from Washington, DC, are followed at Children's National. These children are at exceptionally high risk for developing renal cardiovascular complications secondary to immune alterations, infections, cytokines, viral proteins, dyslipidemias, insulin resistance, hypertension, and a genetic predisposition to develop renal disease in the context of HIV infection. This group, in collaboration with Dr. Rakhmanina, from the Division of Infectious Disease, and Dr. D’Angelo, from the Division of Adolescent Medicine, is studying the pathogenesis of renal-cardiovascular diseases in HIV-infected children. Their main goals are to understand how HIV-1 induces renal injury, and test new therapies to prevent the renal complications induced by HIV-1. Dr. Li is exploring the role of new HIV-receptors and co-receptors that may facilitate the entry of HIV-1 into CD4 negative renal cells. Dr. Xie is investigating how lipid rafts modulate the signaling of HIV-proteins in podocytes, as well as the role of a recently discovered genetic variant of a lipid binding protein named ApoL-1, which increases the risk of development of HIV-nephropathy in African Americans. Drs. Jerebtsova and Tang are working with HIV-transgenic mice and rats to determine how HIV-1 induces renal endothelial and epithelial injury. Several adenoviral mediated gene transfer techniques have been developed to express foreign genes in developing and young rodent kidneys in vivo, and these models are being used to explore how HIV induces renal injury.

Clinical research in pediatric and adolescent HIV infection

- Lawrence D’Angelo, MD, MPH (Chief of Adolescent and Young Adult Medicine)
Even Zeichner, MD, PhD (Site Principal Investigator, International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Group, Washington, DC, is ranked first in the nation in infection and AIDS prevalence, particularly among children and youth. This is the result of an all high HIV prevalence rate in the community, high rates of perinatal transmission, and a rising number of behaviorally acquired cases of infection. Several investigators are involved in funded research looking at infection trends and responses to treatment. Dr. D’Angelo is the Principal Investigator for the Adolescent Trials Unit site in Washington, part of the national Adolescent Trials Network. The 18-site network looks at a range of behavioral, biologic factors influencing HIV disease in adolescents and young adults. Currently nine protocols are open to patient enrollment focusing on treatment interventions, adjunctive vitamin D therapy, vaginal microbicides, risk factors for HIV infection, pre-exposure prophylaxis and adherence therapy. Dr. Rakhmanina collaborates with investigators at the MedStar Washington Hospital Center to look at the current algorithm used for prenatal HIV testing during pregnancy and the use of antiretrovirals as prophylaxis of effective perinatal transmission. Specifically, Dr. Rakhmanina is interested in determining whether any differences in transmission rates between African American men of U.S. origin and African immigrant men. In addition, she leads a multidisciplinary team of clinical researchers studying the most effective screening of drug-susceptible infants born to HIV-infected mothers from acquiring the disease, and new drugs for HIV infection and the diseases that accompany HIV infection. The Children’s National IMPAACT site has sub-sites at MedStar Washington Hospital Center, where HIV-infected pregnant women are treated, and at Johns Hopkins University. Dr. Zeichner also is the Principal Investigator for an NIH-sponsored project to understand how HIV microbicides may affect the vaginal microbial flora as a way of understanding why some of the clinical trials of HIV microbicides failed. Dr. Zeichner is the local Principal Investigator for industry-sponsored studies that give HIV infected children in the Washington area access to new investigational agents that may prove useful in patients for whom conventional therapies are no longer effective.

Pharmacology of antiretroviral therapies in children and adolescents
- Natella Rakhmanina, MD, PhD (Center for Translational Science)
- Eric Hoffman, PhD (Center for Genetic Medicine Research)
- Charles Flexner, MD (Johns Hopkins University)
- Edmund Caparelli, PharmD (University of California, San Diego)

The treatment of HIV infection requires lifelong administration of multiple antiretroviral (ARV) agents. Dr. Rakhmanina focuses her research on the pharmacology of ARV therapy in pediatric patients. She specifically investigated the effects of developmental changes on the pharmacokinetics and pharmacodynamics of ARV therapy in children and adolescents. Her work in this field has contributed to the identification of saliva as a non-invasive alternative for therapeutic drug monitoring of nevirapine in children.
Featured Publications


Center for Genetic Medicine Research

VISION STATEMENT: To transform children’s health through genome-enabled research, pre-clinical studies of experimental therapeutics, and clinical trials.

The Center for Genetic Medicine houses a highly interdisciplinary faculty, with nearly half the physician-scientists from many clinical divisions in the hospital. Focusing on common health problems in Washington, DC, as well as serving as an international referral site for rare disorders, faculty and their laboratories are encouraged to be collaborative, and many of the Center’s projects bring together multiple clinical and scientific disciplines. The Center strives to provide faculty access to the latest technologies in genomics, proteomics, microscopy, bioinformatics, clinical (murine) drug trials, and multi-site clinical trial networks. The Center provides services these technologies to laboratories throughout the DC region, and internationally, through a series of NIH Core grants. Drug development and experimental therapeutics has become an increasing focus, resulting in a technology transfer to an early-stage biopharmaceutical company, EraGen BioPharma, Inc.

Eric Hoffman, PhD
Director
Chairman, Department of Integrative Systems Biology, George Washington University

Kanneboyina Nagaraju, DVM, PhD
Associate Director
Director, Murine Drug Testing Facility
Professor, School of Medicine, George Washington University
FACULTY

Nancy Bauman, MD
Otolaryngology

Charles Berul, MD
Cardiology

Kristy Brown, PhD

Michael Bukrinsky, PhD
Tropical Heath, GWU

Ljubica Caldovic, PhD

Kim Chapman, MD, PhD
Genetics

Yi-Wen Chen, DVM, PhD

Avital Cnaan, PhD

Tatiana Cohen, PhD

Anamaris M. Colberg-Poley, PhD

Laurie Conklin, MD

Edward Connor, MD

Joseph Devaney, PhD

Rohan Fernandes, PhD
Sheik Zayed institute

Robert J. Freishtat, MD, MPH
Emergency Medicine

Stanley Fricke, PhD

Heather Gordish-Dressman, PhD

Andrea Gropman, MD
Neurology, Developmental Pediatrics

Lisa Guay-Woodford, MD

Yetrib Hathout, PhD

D. Ashley Hill, MD

Monica Hubal, PhD
Anesthesiology

Juan Ibla, MD

Sabah Iqbal, MD
Emergency Medicine

Jyoti Jaiswal, PhD

Brian Kirmse, MD
Genetics and Metabolism

Susan Knoblach, PhD

Linda Kusner, PhD

Brendan Lanpher, MD

Linda Leatherbury, MD
Cardiology

Richard Levy, MD
Anesthesiology

Suresh Magge, MD
Neurosurgery

Hiroki Morizono, PhD

Evander Nadler, MD
General Surgery

Javad Nazarian, PhD

Terence A. Partridge, PhD

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Maria T. Pena, MD
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Dinesh Pillai, MD
Pulmonary Medicine

Hans George Pohl, MD
Pediatric Urology

Diego Preciado, MD
Otolaryngology

Mary Callaghan Rose, PhD

Leticia Ryan, MD
Emergency Medicine

Iman Sami-Zakhari, MD
Pulmonary and Sleep Medicine

Matthew Sharron, MD
Critical Care

Dashuang Shi, PhD

Christopher Spurney, MD
Cardiology

Marshall Summar, MD
Genetics and Metabolism

Carolina Tesi Rocha, MD
Neurology

Laura L. Tosi, MD
Orthopaedics

Mendel Tuchman, MD

John Van Den Anker, MD
Pediatric Clinical Pharmacology, Neonatology

Adeline Vanderver, MD
Neurology

Zuyi Wang, PhD

Xiaofang Wu, MD, MPharm
Muscle and Muscular Dystrophy

Biochemistry of Muscle and Membrane Transport:

Dr. Jaiswal's group focuses on understanding cell biology of muscle and degenerative diseases. The group studies the cellular and molecular mechanisms of muscle repair and the role played by these processes in helping the injured muscle cells heal and how a deficit in this process is associated with muscular dystrophies, like LGMD2B and Miyoshi myopathy, and defects in membrane transport result in a variety of degenerative diseases. His studies on understanding how injured muscle cells heal and how a deficit in this process is associated with muscular dystrophies, like LGMD2B and Miyoshi myopathy, is helping identify cellular compartments that are deficient in function in these dystrophic cells. One such study led to the identification of previously unrecognized role of mitochondria in repairing injured muscle fibers (Sharma et al. 2012).

Another study has identified a role of the intracellular protein annexin A2 in regulating repair and inflammation in injured muscle cells and muscle tissue.

Dr. Partridge's team began studying two other mechanisms involved in causing muscle disease. Dr. Cohen investigates the role of defects in sarcomeric membrane proteins in causing muscle disease. She also studies muscle diseases caused by defects in the protein called dysferlin, which is thought to be essential for membrane repair and regeneration. In one such study, her work has identified that an intrinsic inflammatory response inhibits myogenesis in dysferlin-deficient cells (Cohen et al. 2012).

Surrogate Biomarkers for Muscle Disease

Clinical Trials:

Yetrib Hathout, PhD
Kanneboyina Nagaraju, DVM, PhD
Eric Hoffman, PhD
Avital Cnaan, PhD
Linda Kusner, PhD
Laurie Conklin, MD

Biomarker discovery and validation is important for conduct of clinical trials, particularly Phase 2 trials where early serum or other markers predicting clinical response are needed. GenMed has many biomarker projects underway in muscular dystrophy and immune disorders (myasthenia gravis, inflammatory bowel disease). A NIH R01 grant to develop serum and urine surrogate biomarkers that can predict disease progression and response to treatment in Duchenne muscular dystrophy (DMD) was awarded to Drs. Hathout, Cnaan, and Hoffman (UC Davis, lead institution) for 350 DMD patients followed in the CINRG network headquartered in GenMed. Biomarker discovery assays include proteomics, microRNA, metabolomics, and cytokine arrays.

Facioscapulohumeral Muscular Dystrophy

Yi-Wen Chen, DMV, PhD

Facioscapulohumeral muscular dystrophy (FSHD) is an autosomal dominant muscle disease caused by defects in the gene DUX4, which is thought to be expressed in muscle fibers in early fetal development. Dr. Chen investigated the role of the gene PITX1 in FSHD and showed that it is expressed in muscle fibers in early fetal development. She also showed that the gene is expressed in muscle fibers in early fetal development. Her work has focused her efforts on dissecting the molecular pathophysiology of FSHD using genome-wide approaches. Her studies showed that the gene DUX4 and PITX1 were aberrantly expressed in the muscle of patients with FSHD and the PITX1 gene was transcriptionally regulated by DUX4. The up-regulation of PITX1 was specific to FSHD as its altered expression was not observed in 11 other neuromuscular disorders. PITX1 plays a critical role during embryonic development but is expressed at a very low level in postnatal muscles. To study the roles of Pitx1 in postnatal skeletal muscles, Dr. Chen generated and characterized a tet-repressible muscle-specific PITX1 transgenic mouse model (TRE-PITX1/mCK-tTA). These mice over-express a PITX1 transgene in skeletal muscles upon withdrawal of oral doxycycline, resulting in a time and muscle-specific induction of PITX1. The TRE-PITX1/mCK-tTA mice exhibited significant loss of body weight and muscle mass, reduction of muscle strength, and decrease of myofiber diameters. The most prominent pathological change was the development of atrophic myofibers with mild necrosis and inflammatory infiltration. Expression profiling and protein assays showed that p53 tumor suppressor and its downstream pathways were activated in muscles of the Pitx1 transgenic mice. The selective involvement of specific muscles, asymmetric muscle involvement, and the presence and distribution of atrophic myofibers often seen in FSHD suggest that the upregulation of Pitx1 and possibly p53-dependent pathways may play a major role in the pathogenesis of the underlying muscle phenotypes in the mouse model. A study in which morpholinos against Pitx1 were systemically administered to the transgenic mice showed that the Pitx1 expression could be blocked at the translation level by the morpholino molecules. The main goal is to increase our understanding of the molecular pathophysiology of FSHD and identify potential therapeutic targets.
\textbf{Center for Genetic Medicine Research} \\

\textbf{Inital Muscular Dystrophies and \textit{Inital Myopathies}} \\

i-Rocha and Hoffman are working closely on molecular diagnostics and clinical trial infrastructure in the congenital dystrophies and congenital myopathies. Dr. i-Rocha received funding through a Neurological Academic Development Award (NSADA) for National Institute of Neurological Disorders and Stroke (NINDS), and Drs. Hoffman and Tesi-Rocha and Hoffman are working closely on genetic medicine research.

\textbf{nis and Muscle Inflammation} \\

Kanneboyina Nagaraju, DVM, PhD & Hoffman, PhD \\

Nagaraju's group has been working on the inflammatory and metabolic pathways in dystrophin, dysferlin and calpain deficient skeletal muscle. Dr. Nagaraju's group has recently shown that Toll-like receptors (TLR) are highly up-regulated in dysferlin and dystrophin deficient skeletal muscle and endogenous TLR ligands activate the inflammasome pathway and initiate inflammatory response in skeletal muscle. Studies are currently underway to block this inflammatory pathway in the skeletal muscle and contribute to the initiation of inflammatory muscle diseases.

Drs. Nagaraju and Hoffman's groups study the inflammatory and metabolic pathways in dystrophin, dysferlin and calpain deficient skeletal muscle. Dr. Nagaraju's group has recently shown that Toll-like receptors (TLR) are highly up-regulated in dysferlin and dystrophin deficient skeletal muscle and endogenous TLR ligands activate the inflammasome pathway and initiate inflammatory response in skeletal muscle. Studies are currently underway to block this inflammatory pathway in the skeletal muscle and contribute to the initiation of inflammatory muscle diseases.

The most prominent pathological change was the development of atrophic myofibers with mild necrosis and inflammatory infiltration (panel A). The affected myofibers stained heavily with NADH-TR with the strongest staining in those angular-shaped atrophic fibers (panel B). Immunoblotting revealed that the p53 tumor suppressor was up-regulated in the muscles over-expressing Pitx1. The selective involvement of specific muscles, asymmetric muscle involvement, and the presence and distribution of angular atrophic myofibers often seen in FSHD suggest that the up-regulation of Pitx1 and possibly p53 may play a major role in the pathogenesis underlying muscle phenotypes in the mouse model.

\textbf{Pre-clinical Drug Testing Facility} \\

Kanneboyina Nagaraju, DVM, PhD
conducted for Center faculty, biotechnology, pharmaceutical companies. He led an international effort to develop standard operating procedures, either with TREAT-NMD, a European network for the neuromuscular field. Recently he received a muscular dystrophy translational research grant to support the preclinical phenotyping and drug testing at Children’s. In 2011, he received a NIH award for the training of faculty and students in disease pathobiology.

**Clinical Trials and Cooperative International Neuromuscular Research Group (CINRG)**

Vital Cnaan, PhD
Eric Hoffman, PhD
Kanneboyina Nagaraju, DVM, PhD
Terence Partridge, PhD
Jyoti Jaiswal, PhD

CINRG Coordinating Center is directed by Dr. Cnaan through a joint appointment with CRI’s Center for Translational Science, and Dr. Hoffman as the elected Scientific Director of the CINRG group (www.cinrgresearch.org). CINRG currently has 26 clinical research sites in more than 10 countries. CINRG is a very active clinical trial network which has launched three new studies in 2012 and is following the largest cohort of patients Duchenne muscular dystrophy (DMD) in a longitudinal natural history study. This study received NIH ancillary grants to support the development of new strength and function outcome measures to aid key data for clinical endpoints in clinical trials as well as the development and validation of markers.

Two clinical projects funded by the NIH for a P50 center grant were developed and will be initiated at all CINRG centers in the coming year. An observational study on Becker muscular dystrophy (BMD) will be the first BMD study with a focus on studying the natural history presentation of participants with specific in-frame mutations that would result from exon-skipping therapies. The second project is a tissue bank of blood and skin biopsies on DMD participants with specific out-of-frame mutations that are currently being studied in exon-skipping drug development programs. The P50 grant also includes molecular studies of variable response of patients to semi-functional (Becker-like) dystrophin conducted by the Hoffman and Partridge labs, with Core support by Drs. Nagaraju, Hathout, and Jaiswal.

A completed clinical trial of Pentoxifylline as a rescue treatment for DMD was published in *Neurology*.

The CINRG Coordinating Center and CINRG sites remain an active clinical trial network and continue to collaborate with other neuromuscular research networks such as TREAT-NMD, Neuro-NEXT, and Parent Project Muscular Dystrophy.

**Systemic Anti-sense Drug Development**

- Kristy Brown, PhD
- Yetrib Hathout, PhD
- Eric Hoffman, PhD
- Kanneboyina Nagaraju, DVM, PhD
- Terence Partridge, PhD
- Jyoti Jaiswal, PhD

Exon-skipping is perhaps one of the most promising approaches for treatment of Duchenne muscular dystrophy. The approach uses antisense-oligonucleotide dystrophin expression in animal models and stabilized their muscle. However the doses used in preclinical trials are 100 times higher than those used in humans.

Drs. Hoffman, Nagaraju, Hathout, Brown, Partridge, and Jaiswal initiated a series of research projects aiming to test different doses of morpholino in preclinical setting and monitor both efficacy in restoring dystrophin and its function. Through support by a U54 on pediatric pharmacology (Drs. van den Anker PI, Drs. Nagaraju, Hoffman, and Hathout PIs on Project 1, 2, and 3) the team is treating a rodent model with varying doses of morpholino to define the optimal dose and time that sustain dystrophin expression while keeping potential kidney toxicity to a minimum. In this context the team has developed a highly specific and sensitive mass spectrometry technique to quantify dystrophin in human muscle biopsies. The technique uses stable isotope labeled dystrophin as a spike in internal standard with targeted mass spectrometry analysis. The technique was found perfectly linear over a large dynamic range of three orders of magnitude. A manuscript is under preparation about the technique. The goal is to use this technique to not only quantify dystrophin in phase II clinical trials of DMD patients receiving morpholino drugs but also in Becker's dystrophy patients whose disease severity depends on the amount of expressed dystrophin.

Additionally through support by a U54 pilot study Dr. Brown has developed a mass spectrometry method to accurately detect and quantify the morpholino drug in body fluids and tissue of animal models treated. The study was presented at the 60th Conference on Mass Spectrometry and Allied Topics May 20–24, 2012, in Vancouver, Canada.
Innovative Steroid Drug Development

Hoffman, PhD
Deboyina Nagaraju, DVM, PhD
Freishtat, MD
Conklin, MD

aGen Biopharma, Inc.

Understanding the molecular mechanisms underlying the efficacy of glucocorticoid drugs, prednisone and dexamethasone, has been an exciting area of interest to many of the disease groups in the Center, including the asthma, mor, inflammatory bowel disease, and muscle groups. Drs. Nagaraju and Hoffman worked with medicinal chemist John McCall to develop live steroids, a new series of drugs that are able to increase the efficacy and decrease the side effects of traditional glucocorticoid drugs. This technology transfer company, ReveraGen, was the lead compound for ReveraGen, and was recently named as one of a few NIH awardees for Rare and Neglected Diseases as Phase I and Phase awarded of the Muscular Dystrophy Association Philanthropy group.

To many of the research projects on corticoids and VBP15 is uncovering the mechanism of action of these drugs. A model developed by Drs. Freishtat and Hoffman that these drugs synchronize mitosis and cell signaling after tissue injury.

Asthma

Robert J. Freishtat, MD, MPH
Monica Hubal, PhD
Sabah Iqbal, MD
Evan Nadler, MD
Perry W. Payne, Jr., MD, JD, MPP
Dinesh Pillai, MD
Mary Rose, PhD
Stephen Teach, MD, MPH
Zuyi Wang, PhD

Asthma has become considerably more prevalent and severe in the United States during the last 40 years, yet the reasons for this are not clear. It remains one of the most significant childhood illnesses, disproportionately affecting urban youth, especially African Americans, who have among the highest asthma-related morbidity and mortality rates of any United States racial/ethnic group. The asthma research group's work is focused in Washington, DC, where the target population is largely minority and disadvantaged: 71 percent of youth younger than 18 years and 52 percent of adults are non-Hispanic African Americans. Addressing this poorly-served population is significant and representative of urban settings around the country. The majority of Washington, DC, African American youth with asthma are seen at Children's National, including more than 85 percent of all acute or emergency department visits and more than 95 percent of all hospital admissions. Studies are urgently needed to identify effective and sustainable strategies for reducing the dramatic health disparities experienced by disadvantaged, urban, and minority youth with asthma.

The Center’s airway biology group continues to rapidly expand its translational and multidisciplinary approaches to asthma research, which are on the cutting edge of the field. The foundation for this program is Dr. Freishtat’s Asthma Severity Modifying Polymorphisms (AsthMaP®) Project (www.AsthMaPKids.org), which began in 2007 and was recently funded for a 5-year second phase.
Teach, Wang, Nadler, and Hubal, AsthMaP®2 provide novel generalizable insights into the distribution of vitamin D deficiency and obesity to
ma disparities in urban children and adolescents. nately, this will inform asthma intervention
of vitamin D supplementation currently under
dopment. In addition, The AsthMaP® Project
ues to serve as a central resource for many of
sthma studies in the Center.

of these studies is an exciting collaborative effort
ling all of the members of the Center’s asthma
p, the Dissociative Steroid Drug Development
and, ReveraGen BioPharma, Inc. Since
ma is an inflammatory condition where steroids
mainstay of care, Drs. Freishtat and Wang
are directing a collaborative effort to build data-
driven systems biology models that incorporate stem
biology (led by Dr. Freishtat), steroid biology
(led by Dr. Hoffman), and cellular signaling and
differentiation (led by Dr. Rose). As a result, we are
beginning to show the true connections among these
multiple asthma-related factors.

Mucous and Airway Disease
■ Mary Rose, PhD
■ Maria T. Peña, MD
■ Dinesh K. Pillai, MD
■ Diego Preciado, MD
■ Xiaofang Wu, MD, MPharm

The overproduction of mucus and mucins in the
upper and lower respiratory tracts contributes to
the morbidity and/or mortality rates of pediatric
airway diseases, including asthma, cystic fibrosis
(CF), chronic rhinosinusitis (CRS) and otitis media
(OM). Dr. Rose’s research on down-regulation
of secretory mucin genes by dexamethasone
(classical glucocorticoid) and VBP15 (dissociative
glucocorticoid) has shown that repression by
dexamethasone is transcriptional and mediated by the
glucocorticoid receptor and histone deacetylase 2.

Mucus/mucin hypersecretion in the sinus mucosa is
driven by submucosal gland hyperplasia. The question
of how mediators triggered by inflammation or
cigarette smoke activate the mechanisms that lead to
glandular hyperplasia and mucin gene upregulation
are being addressed by Drs Peña, Preciado, Wu,
and Rose using three types of in vitro models that
were recently developed. Mucin hypersecretion also
contributes to the pathology of otitis media (OM) in
children. Dr. Preciado is investigating the mechanisms
that lead to OM and upregulation of MUC5B (major
mucin in chronic OM effusion) in a newly-funded
R01 using expression array and proteomic approaches
to look at the effect of cytokines, bacterial products,
and tobacco smoke on middle ear epithelial cells in
vitro and in vivo.

Proteomic analyses are being carried out on
differentiated human bronchial epithelium from
asthmatic (Pillai) and CF (Rose) cells, as well as on
bronchial casts (from patients with sickle cell disease,
genital ear disease and respiratory disorders), and
lung mucus from patients with Hyper IgE syndrome
(Rose and Pillai). Secretome data will be used to
interrogate and compare lung mucosal components
from pulmonary patients to elucidate the underlying

Representative micrographs of
immunofluorescent double staining of
MUC5AC and MUC5B mucins in the
sinus mucosa. Images of (A) MUCSAC;
(B) MUC5B; (C) nuclear marker DAPI
are shown separately, then merged in
(D). Scale bar: 50 μm. (Wu X, et al.
Arch Otolaryngol Head Neck Surg. 2011 Apr;
137(4):383-389.)
Dr. Sharron. The efforts of Dr. Ibla are focused on understanding the impact of environmental hypoxia on pulmonary epithelial cell cycle and dysynchronous tissue remodeling. Drs. Leatherbury and Sami, in collaboration with Dr. Cecilia Wu’s group at the University of Pittsburgh, have shown that congenital heart disease patients with heterotaxy have a substantial risk for ciliary dyskinesia and increased respiratory disease and are enriched in mutations in primary ciliary dyskinesia genes. This work is now being expanded to examine ciliary function in other conditions that encompass chronic lung disease.

Dr. Colberg-Poley’s group studies how human cytomegalovirus (HCMV), a lung pathogen, reprograms cellular metabolism. HCMV infection targets mitochondria-associated membranes (MAM), an endoplasmic reticulum (ER) subdomain that contacts mitochondria. The MAM provides sites for calcium (Ca\(^{2+}\)) signaling to mitochondria (required for cellular metabolism), senses and responds to ER stress, coordinates mitochondrial antiviral signaling, and induces mitochondrial-mediated programmed cell death. Her group found that an HCMV protein (pUL37x1) traffics through the ER, MAM, and to mitochondria. Further, her group found that pUL37x1 recruits the proapoptotic protein Bax to the MAM and targets it for proteasomal mediated degradation. In collaboration with Drs. Yetriib Hathout and Kristy Brown, her group performed quantitative proteomic analyses on the MAM in normal human fibroblasts and at late times of HCMV infection. The studies generated the first global definition of human MAM proteome and found that HCMV dramatically changes the MAM proteome.

Dr. Geovanny Perez, a pulmonary fellow, has joined Dr. Colberg-Poley’s group to define the microbiome is challenging. The lung microbiome is complex and dynamic. As most bacteria will not grow under standard conditions, culture conditions of lung microbiome in cystic fibrosis patients required special (anaerobic) conditions and extended incubation times. Recently, next generation sequencing has been successfully used to identify bacteria in the lung microbiome of patients with chronic obstructive pulmonary disease (COPD). In collaboration with Drs. Eric Hoffman, Joseph Devaney, and Dinesh Pillai, Dr. Colberg-Poley will use next generation sequencing to determine microbial populations in bronchiolar lavages from cystic fibrosis patients.

**Related Diseases**

- M. Colberg-Poley, PhD
- J. Freishtat, MD, MPH
- Ibla, MD
- Leatherbury, MD
- Sami-Zakhari, MD
- Sharron, MD

Related research at CRI continues to increase. That leads efforts on behalf of NIH-funded inter studies of genetic changes in overwhelming Drs. Leatherbury and Sami, in collaboration with Dr. Cecilia Wu’s group at the University of Pittsburgh, have shown that congenital heart disease patients with heterotaxy have a substantial risk for ciliary dyskinesia and increased respiratory disease and are enriched in mutations in primary ciliary dyskinesia genes. This work is now being expanded to examine ciliary function in other conditions that encompass chronic lung disease.

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often expressed in temporal and organ-specific terms. miRNAs appear to be very important in human developmental timing events, stem cell proliferation, cell cycle control, and oncogenesis. Recently, somatic missense mutations in the wild-allele of DICER1 have been identified in PPB, shaping the hypothesis that DICER1 loss/attenuation predisposes these children to cancer by altering the miRNA regulatory mechanisms that control the balance between rapid proliferation and differentiation in the growing lung and other affected organs. The long-term goal of the research program is to use the familial PPB model to understand the role of DICER1 and miRNAs as molecular controls of growth factors during organ development and organogenesis. With a better understanding of the regulatory effects on growth factor expression, with normal and abnormal development, we hope to identify natural molecules that could be converted to therapeutic agents for cancers that arise in the lung of growth factor dysregulation.

Urea Cycle Disorders (UCD)

UCD Cycle Disorders Institute
Mark Batshaw, MD
Ljubica Caldovic, PhD
Andrea Gropman, MD
La Lithert Konecki, MD, PhD
Lauren Krivitzky, PhD
Hiroki Morizono, PhD
Dashuang Shi, PhD
Marshall Summar, MD
Mendel Tuchman, MD

UCD's National is considered the world leader in nation-wide research and clinical programs for these disorders. The Center for Genetic Medicine Research and the Center for Translational Science continue to collaborate on the NIH-funded Rare Diseases Clinical Research Center for the study of UCD. The strength of this program was acknowledged by CRI and the Children's National Board of Trustees, through the establishment of the Urea Cycle Disorders Institute, directed by Dr. Tuchman. The Institute brings together clinical practice and translational research and is funded by six NIH grants on urea cycle disorders and nitrogen metabolism and philanthropy. The UCD clinical research faculty includes Drs. Batshaw (Developmental Pediatrics), Tuchman (Metabolism), Gropman (Neurology), Lichter (Metabolism), Krivitzky (Neuropsychology), McCarter (Biostatistics) and Summar (Genetics). This Center is following more than 500 individuals with UCD in 15 sites across the United States, Canada, and Europe in a 5–10 year longitudinal study to understand the medical and cognitive outcome of these devastating disorders. As part of this program Dr. Gropman is using neurocognitive and neuroimaging techniques to assess the cognitive deficits associated with these disorders. Additionally, Dr. Lichter assembled a multicenter trial to study the value of hypothermia as neuroprotection during hyperammonemic coma. The UCD program is also collaborating with several biotechnology and pharmaceutical companies to test new treatments for these disorders.

N-Acetylglutamate Synthetase (NAGS)

Ljubica Caldovic, PhD
Mendel Tuchman, MD
Dashuang Shi, PhD

In a project funded by the NIH, Dr. Tuchman and colleagues identified DNA sequences, promoter and enhancer, and transcriptional factors that regulate expression of the NAGS gene. They have shown that transcription factor called hepatic nuclear factor 1 (HNF1) binds to the NAGS enhancer and directly regulates expression of the NAGS gene. This allowed identification of a disease causing mutation in the HNF1 binding site in patient with NAGS deficiency.

Ornithine Transcarbamylase (OTC)

Mark Batshaw, MD
Hiroki Morizono, PhD

Drs. Morizono and Batshaw, along with long-term collaborator, Dr. Wilson, at the University of Pennsylvania, tested the efficacy of adeno-associated virus based gene therapy for treatment of OTC N-carbamyl glutamate and supplementation of L-citrulline. This is the only mouse model of a urea cycle defect that can be rescued to reach adulthood and to reproduce. It represents an important breakthrough in the production of an inducible mouse model of high blood ammonia level which can now be investigated for various aspects of elevated ammonia, especially the effect of ammonia on the brain and mitigations of its toxicity.

In another project funded by the NIH, Dr. Dashuang Shi was successful in solving the crystal structure of a bacterial NAGS/NAGK protein that resembles mammalian NAGS and was able, based on this structure, to create a reliable model of human NAGS. This work provides a long sought after answer to the question of how the regulatory L-arginine effect on NAGS was reversed during evolution from inhibition to activation.

Dr. Caldovic’s laboratory identified DNA sequences, promoter and enhancer, and transcriptional factors that regulate expression of the NAGS gene. They have shown that transcription factor called hepatic nuclear factor 1 (HNF1) binds to the NAGS enhancer and directly regulates expression of the NAGS gene. This allowed identification of a disease causing mutation in the HNF1 binding site in patient with NAGS deficiency.
Vanderver also works on white matter diseases, including leukodystrophies, using novel technologies, including whole exome sequencing, to identify novel nosologic groups.

Brain Tumors and Neurofibromatosis

- Javad Nazarian, PhD
- Yetrib Hathout, PhD

Dr. Nazarian has continued his efforts in tackling pediatric brain tumors in a quest for biomarker identification and discovery of therapeutic targets. Dr. Nazarian's laboratory is supported by the Isabella Kerr Molina Foundation, Musella Foundation, Clinical and Translational Science Institute at Children's National (CTSI-CN) award, and generous funds from the Zickler family.

In an effort to expand collaboration on pediatric brain tumor research, Dr. Nazarian had formed the Mid-Atlantic DIPG (diffuse intrinsic pontine glioma) Consortium (MADC) consisting of the National Cancer Institute and the Johns Hopkins Medical Center. Dr. Nazarian's multidisciplinary team of experts includes neurologists, neurosurgeons, bioengineers, and oncologists. One of the team members involved in generating the complete protein profile of CSF from children with brain tumors.

Their work has been recently published as the first protein profiling of cerebrospinal fluid from children with brainstem glioma. This study is part of a larger effort in Dr. Nazarian's laboratory to understand the molecular makeup of pediatric brain tumors. Dr. Rohan Fernandes is a bioengineer that has begun collaboration with Dr. Nazarian's laboratory to use Dr. Fernandes' expertise to utilize nanoparticles for treating brain cancers.

Dr. Hathout has been involved in several collaborative projects using proteomics and mass spectrometry approaches including the characterization of the molecular mechanisms of CMV infection (Zhang et al. 2011), defining novel CSF biomarkers associated with medulloblastoma (Rajagopal et al. 2011), and leukodystrophies (Brown et al. 2011).

Spinal Cord Damage and ALS

- Susan Knoblach, PhD
- Zuyi Wang, PhD

Dr. Knoblach continues her analysis of a spinal cord injury expression profiling data set. This year she has been involved in generating the complete protein profile of CSF from children with brain tumors.
suggested that MRI and histological changes are still occurring at the site of impact months after spinal trauma, but to date, research has not examined all molecular changes. To that end, the database contains gene expression profiles taken at three and six months after injury. By sorting these data according to the functional status of the profiled animals, Drs. Knoblach and Wang identified specific genes that are associated with poor recovery and permanent paralysis, other genes that are associated with a return toward normal function. The plan is to focus on some of these molecular changes to determine what role they may play in secondary injury mechanisms and in neurological impairment.

Dr. Knoblach has continued her work on the role of galectins in amyotrophic lateral sclerosis (ALS). Last year, she determined that galectin-3 likely acts as an endogenous anti-inflammatory immunomodulator during the progression of chronic motor neuron degeneration, and that mice with motor neuron disease that do not express galectin-3 develop paralysis and succumb to the disease earlier than mice that express galectin-3. Recently, her group found that galectin-3 is directly neuroprotective, because it prevents the death of neurons even when immune cells are not present.

Dr. Knoblach also is working with ReveraGen BioPharma, Inc. to investigate the benefits of their lead compound, VBP15, in both ALS and neuronal damage. Promising preliminary results have been obtained.

Nitric Oxide Metabolism

- Marshall Summar, MD

Dr. Summar, who is Chief of the Division of Genetics and Metabolism, brought research on nitric oxide metabolism and urea cycle function to Children’s Research Institute. His research examines how dysfunction in the production of nitric oxide precursors affects patients under stressful conditions. This currently involves projects in neonatology, critical care medicine, neurology, fetal and translational medicine, and cardiac surgery and has led to an ongoing multisite FDA clinical trial (Phase II) using citrulline. The clinical trial is currently funded by two NIH grants and is an active collaboration between Children’s National, Vanderbilt University, Cincinnati Children’s Hospital, and the University of Vermont.

Glutathione Metabolism

- Marshall Summar, MD

Dr. Summar and his laboratory work on glutathione metabolism in oxidant injury, including the genetic and enzymatic components of the oxidant response pathway involving glutathione. This work involves close collaborations with critical care medicine, neonatology, fetal and translational medicine, neurology, and cardiac surgery. An intervention trial in animals of a glutathione precursor as an injectable antioxidant is ongoing with cardiac surgery in a brain damage model.

Organic Academia

- Kimberly Chapman, MD, PhD

Dr. Chapman is engaged in work examining bioenergetics in patients with the organic academia, propionic academia. She studies the blockade of classic energy metabolism in these patients which is closely related to effects on energy metabolism from high-dose chemotherapy and certain seizure medications. Her research has resulted in close collaborations with the NIH and international centers. It has led to a pre-clinical therapeutic consideration for the amino acid leucine in patients with propionic academia. In her first year with the Center, Dr. Chapman has been named the recipient of a K award grant.

Fatty Acid Oxidation, HIV Drugs

- Brian Kirmse, MD
- Marshall Summar, MD

Dr. Kirmse is engaged in work on fatty acid oxidation and newborn screening. He examines the effects of drugs used in the treatment of HIV and congenital exposure to HIV. His work has already shown that infants exposed to these drugs have lower levels of fatty acids in their plasma.
International AIDS Society meeting in Rome, his first year at Children’s National, he has a K award, as well as HIV funding through CFAR. This work has the potential to lead to improvements in growth and development in children exposed to AZT and related drugs. This potentially affects 3-4 million children in sub-Saharan Africa.

Sommar and Lanpher are examining patients with Down Syndrome (DS) as a model of chronic injury. Looking at cardiac disease effects, one metabolism, and secondary genetic factors, they have found roles for each in the acquisition of chronic injury and oxidative injury seen in DS. His work should lead to interventions in capacity in patients with DS and has resulted in collaboration with Johns Hopkins University regarding cardiac outcomes in DS patients.

Clinical Aspects of Pediatric Kidney Disease
- Hans Pohl, MD

Dr. Pohl (Division of Urology) continues to pursue his interest in the pathogenesis of renal injury from urinary obstruction and urinary tract infection (UTI). He has applied his growing expertise to various clinical research trials, receiving NIH or other external funding, as co-Investigator or collaborator: (1) RIVUR (Randomized Intervention for Vescoureteral Reflux), (2) CUITE (Cautious Urinary Tract Infection Evaluation), (3) STARRS (Steroids to Reduce Renal Scarring), (4) Biomarkers (Biomarkers in UTI Evaluation), and (5) GENUSCIS (Personalized GEnitoUrinary Health Care: A Longitudinal Study of the Urine Microbiome after Spinal Cord Injury).

Drug- and Genotype-Associated Kidney Toxicity
- Yetrib Hathout, PhD
- Eric Hoffman, PhD
- Kanneboyina Nagaraju, DVM, PhD

Drs. Hathout, Hoffman, and Nagaraju have received a NIH U54 pediatric pharmacology grant to look at kidney toxicity that may result from long-term systemic treatment with morpholino anti-sense drugs. This very competitive award, one of only four in the United States, was done in partnership with the Center for Translational Science (Drs. van den Anker and Connor). The Center’s effort will focus both on dose-optimization of drug delivery using rodent models, and kidney toxicity biomarkers.

Health Disparities and Type 2 Diabetes, Inactivity, and Obesity
- Eric Hoffman, PhD
- Joseph Devaney, PhD
- Heather Gordish-Dressman, PhD

Both inactivity and obesity are major health problems in Washington, DC, children, and this problem is
A key study is the AIMMY protocol, where university students enrolled into a baseline assessment of metabolic syndrome risk factors. About 1,000 students have enrolled into AIMMY from the University of Calgary, Howard University, University of Massachusetts Amherst, and East Carolina University. Population-based cohort functions as a clinical network, where pre-phenotyped students can be rolled into different interventions stratified by ethnicity, or genotype. One such ancillary study recently funded by the CTSA, where Howard University students with a specific genotype will be rolled into a prospective study of muscle function.

MY is supported by a NIH P20 Health disparities Center grant, as well as philanthropic donations from the Clark Family in Washington, DC, Maryland, and donations in Calgary, Canada.

A second large population-based study is called CHIP and this is in collaboration with Paul Visich at Michigan University, and Paul Gordon at University of Michigan. CHIP has enrolled about 30 fifth-grade children, where the classrooms are linked to a local hospital for metabolic syndrome studies. Center investigators have carried out type/phenotype associations in the CHIP cohort, published a paper in *Pediatrics Research* showing some heart disease genetic risk factors are much rarer in children than in older more sick adults.

Dr. Devaney continues his work on the genetics of coronary heart disease with Drs. Epstein and Burnett at the MedStar Washington Hospital Center. Their group was involved in a large genetic study to investigate a coding SNP located in the kinesin-like protein-6 gene and coronary heart disease. The work involved 19 other centers and did not find any association with the SNP (Assimes et al. 2010). The study was published in the *Journal of the American College of Cardiology*.

### Technology Development

The Center for Genetic Medicine Research is a technological hub for advanced research methods for the Washington, DC, region, nationally, and internationally. Technologies are developed as pilot projects by Center investigators, then delivered to the wider research community through Core functions. Core grants include a Genomics/Proteomics Core of the NIH Intellectual and Developmental Disabilities Research Center, the Genomics/Proteomics Core of the NIH CTSA, and Genomics, Proteomics, Bioinformatics, and Clinical Outcomes Cores of the National Center for Medical Rehabilitation Research. During the last year, there have been many new technologies delivered and/or developed by the Center.

### Imaging Technologies

- Stanley Fricke, PhD
- Jyoti Jaiswal, PhD
- Kanneboyina Nagaraju, DVM, PhD

Dr. Fricke was recruited to Children’s National as a MRI physicist from Georgetown University. He has demonstrated a 128,000 fold gain in slew rate, which promises to take the MRI exam session from the current one hour to a few minutes. This will help eliminate the need for anesthesia in young children as well as permits top motion for cardiac studies. Dr. Fricke is under a contract with Johns Hopkins’ Applied Physics Laboratory to study inflammation due to traumatic brain injury. Here nanoparticle technology is employed to track diffuse neuronal damage via MRI and optical microscopy. Finally Dr. Fricke is developing equipment systems for multi-modality pre-clinical imaging that allow for the placement and tracking of nanoparticles into cells, the placement of those cells in a body, tracking the movement of the same through the body and finally exact stereolocation of the same for biopsy.

Dr. Jaiswal has constructed a state-of-the-art live cell imaging microscope, and is delivering services through the Intellectual and Developmental Disabilities Research Center grant. The imaging core, led by Dr. Jaiswal, is a collaboration between the Center for Neuroscience Research and Sheikh Zayed Institute.

Dr. Nagaraju offers imaging technology development using caged near infra-red compounds through his Murine Pre-Clinical Drug Testing Facility. A key methods paper was published in 2011 showing feasibility of this approach for testing efficacy of drugs.

### Genomics

- Eric Hoffman, PhD
- Susan Knoblach, PhD
- Joe Devaney, PhD

The Center collaborated with the Sheikh Zayed Institute to obtain three next-generation sequencing libraries.
Center for Genetic Medicine Research

The Center for Genetic Medicine Research employs a RainDance unit, capable of 1 million PCR reagents per patient in an hour. Genomics profiling and Illumina bead arrays are technologies that are now routinely offered to investigators at Children’s National and elsewhere. Numerous exomes or targeted resequencing of exomes or targeted resequencing has been done on nearly 200 patients.

Selected Publications


Faculty

- Chapman, MD, PhD, specializes in medical genetics with a focus on inborn errors of organic metabolism.

- Guay-Woodford, MD, is the director of the National and Translational Science Institute at Children’s National and specializes in polycystic kidney disease.
Center for Neuroscience Research

VISION STATEMENT: To understand the development of the central nervous system and the cellular, molecular, synaptic, and network mechanisms of brain dysfunction to prevent or treat neurological, developmental, and behavioral disorders of childhood.

The Center for Neuroscience Research comprises an expanding group of highly productive lab-based developmental neuroscientists and clinical investigators who have established ongoing research programs and collaborations in the area of neurodevelopmental disorders. While some investigators have distinct expertise and research programs, their research as a whole is used on childhood neurological disorders, from early stages of when the nervous system is established, to postnatal stages that include the formation of neuronal connections and wrapping of neuronal processes by the myelin insulator. The unique and exciting setting of the Center has supported and promoted a large number of research projects that span basic, translational and clinical research in neurodevelopmental disorders. The Center includes 11 major areas of research, including neural stem cells, developmental neurobiology, birth defects, fetal alcohol syndrome, brain injury and brain protection, perinatal hypoxia and hyperoxia, epilepsy, neuro-oncology, neurofibromatosis, attention deficit hyperactivity disorder, and autism.

Vittorio Gallo, PhD
Director
Wolf-Pack Chair in Neuroscience, Professor of Pediatrics, Pharmacology and Physiology

William Davis Gaillard, MD
Associate Director
Professor of Pediatrics and Neurology
Center for Neuroscience Research

FACULTY

Maria T. Acosta, MD
Neurology

Candice A. Alfano, PhD
Psychology

Laura Anthony, PhD
Neuropsychology

Robert Avery, MD
Neurology

Madison M. Berl, PhD
Neuropsychology

Jessica Carpenter, MD
Epilepsy, Neurophysiology, Critical Care Neurology

Taeun Chang, MD
Epilepsy, Neurophysiology, Critical Care Neurology

Li-Jin Chew, PhD
Developmental Neurobiology

Cedric Clouchoux, PhD
Diagnostic Imaging and Radiology

Joan Conry, MD
Epilepsy, Neurophysiology, Critical Care Neurology

Joshua Corbin, PhD
Developmental Neurobiology

Adré du Plessis, MBChB
Fetal and Transitional Medicine

Gerard Gioia, PhD
Neuropsychology

Penny Glass, PhD
Psychology

Andrea Gropman, MD
Neurology, Developmental Pediatrics

Kristina Hardy, PsyD
Neuropsychology

Nobuyuki Ishibashi, MD
Cardiovascular Surgery

Beata Jablonska-Gierdalska, PhD
Developmental Neurobiology

Jyoti Jaiswal, PhD

Richard A. Jonas, MD
Cardiac Surgery

Parmajit T. Joshi, MD
Psychiatry

Nadja Kadom, MD
Radiology

Lauren Kenworthy, PhD
Neuropsychology

Lauren Krivitzky, PhD
Neuropsychology

Tarannum Lateef, MD
Neurology

Uta Lichter-Konecki, MD

Catherine Limperopoulos, PhD
Diagnostic Imaging and Radiology

Judy S. Liu, MD, PhD
Developmental Neurobiology, Epilepsy

Dilip Nath, MD
Cardiovascular Surgery

Karin Nelson, MD
Neurology

An Nguyen-Massaro, MD
Neonatology

Roger J. Packer, MD
Neurology

Phillip L. Pearl, MD
Neurology

Jay A. Salpekar, MD
Psychiatry

Joey Scafidi, MD
Epilepsy, Neurophysiology, Critical Care Neurology

Billie Lou Short, MD
Neonatology

Jason Strang, PsyD
Neuropsychology

Kazue Hashimoto-Torii, PhD
Developmental Neurobiology

Masaaki Torii, PhD
Developmental Neurobiology

Jason Triplett, PhD
Developmental Neurobiology

Tammy N. Tsuchida, MD, PhD
Epilepsy, Neurophysiology, Critical Care Neurology

Chandan J. Vaidya, PhD
Neuroscience

L. Gilbert Vezina, MD
Radiology

Karin Walsh, PsyD
Neuropsychology

Elizabeth Wells, MD
Neurology

Steven Weinstein, MD
Epilepsy, Neurophysiology, Critical Care Neurology

Christopher Vaughan, PsyD
Neuropsychology

Irene Zohn, PhD
Developmental Neurobiology
stem cells are present in both the embryonic and postnatal brain, can self-renew, and are able to regenerate all the major cell types within the central nervous system. Dr. Corbin is interested in understanding the relationship between gda progenitor cell specification, neuronal genies and their physiology. He continued a productive collaboration with Dr. Huntsman, an experienced electrophysiologist, whose work focused on the physiological characterization of gda inhibitory neurons. Their studies identified previously unknown progenitor pool dedicated to the formation of specific neural circuits in the mammalian brain. Dr. Gallo studies cellular signals that regulate the development of neural stem cells and progenitors in the perinatal and adult brain. The laboratory is extending these studies to animal models of brain injury and disease, including demyelinating disorders of the white matter and matter lesions, it is hoped that therapeutic targets may be identified for strategies of pharmacological intervention.

Myelin and White Matter Development
- Li-Jin Chew, PhD
- Vittorio Gallo, PhD

Myelin formation during postnatal brain development represents one of the most crucial steps in the establishment of mature white matter and of fully functional connections between neurons. Drs. Gallo and Chew continue to study new cellular and molecular approaches that promote oligodendrocyte maturation, myelination, and oligodendrocyte development in cultured cells and in transgenic mice. The focus of these studies is on mechanisms that promote oligodendrocyte progenitor differentiation and developmental myelination under pathological conditions. Dr. Gallo continues to study oligodendrocyte progenitor cell migration during normal development and after white matter injury. A focus of Drs. Gallo and Chew's studies is the function of Sox transcription factors in oligodendrocyte development and pathology. They identified downstream signaling pathways of Sox transcription factors that are involved in regulating specific phases of oligodendrocyte development. Additionally, Dr. Chew studies how inflammation impacts oligodendrocyte progenitor cell function in cellular maturation, myelination, and repair after demyelination injury. Recent studies have revealed roles for mitogen-activated protein kinase activity in cytokine control of white matter development and repair by oligodendrocyte progenitor cells. Current research in cultured cells and transgenic mouse models investigates the involvement of cytokine-induced kinase activation in the inhibition of proper oligodendrocyte progenitor cell maturation. By understanding the effects of chronic inflammation on the progenitor cells of developing white matter and in white matter lesions, it is hoped that therapeutic targets may be identified for strategies of pharmacological intervention.

Cerebral Cortex, Development, and Epilepsy
- Judy Liu, MD, PhD

It is widely accepted that proper cognitive development in humans occurs through the interdependent interactions between genetic, epigenetic, and environmental factors. Both
neural tube demonstrating aberrant activation of the heat shock pathway outside of the cell and potentially providing a drug target to prevent neural tube defects. Other studies in Dr. Zohn’s lab demonstrate that iron, in addition to folic acid, is an important nutrient to prevent neural tube defects. Iron deficiency is one of the most common nutritional deficiencies among women of childbearing age and has not been previously implicated as contributing to neural tube defect incidence. The involvement of iron in human neural tube defects will be validated with epidemiological studies and clinical trials to determine if dual supplementation could further reduce the incidence of neural tube defects worldwide.

**Development and Dysfunction of the Social Brain**

- **Joshua Corbin, PhD**

The mammalian basal telencephalic limbic system is comprised of a number of structures that are involved in the regulation of complex emotional and social behaviors. The most prominent of these is the amygdala, which regulates specific aspects of emotional memory, attention, and appropriate responses to environmental stimuli. The laboratory of Dr. Corbin studies the link between neurodevelopmental events and the formation of amygdala circuitry and related behavior. He also models the underlying defects in these processes that occur during developmental disorders, such as autism spectrum disorders. Using animal models of amygdala development and malformation, the Corbin lab has recently identified specific genetic mechanisms that underlie the formation of complex amygdala neural circuits. Additionally, using specific animal models, Dr. Corbin and his team have revealed potential avenues of pharmacological intervention for autism spectrum disorders, such as these findings from animal models to the clinic, in order to address the major social deficits found in autism spectrum disorders. Thus, through combined basic and translational research efforts, the Corbin lab aims to improve the quality of life for individuals with developmental disorders.

**Sensory System Development**

- **Jason Triplett, PhD**

We utilize our senses to understand the world around us, often seamlessly integrating information from different senses to create a robust representation of the world. This essential function of the nervous system requires precise neuronal connectivity, much of which is established early in development. In addition to the precise wiring within a single sense, information from multiple senses must be brought together in a coherent way in associative areas of the brain. Unfortunately, this complex process is disrupted in developmental disorders such as autism spectrum disorders. Using animal models with specific sensory impairments, Dr. Triplett and his team have identified potential therapeutic approaches that may be used to treat these disorders.

**Subsets of excitatory neurons in the mouse olfactory bulb marked by state of the art optogenetic tools.**

Center for Neuroscience Research
Developmental Disabilities

Intellectual and Developmental Disabilities Research Center (IDDRC)

- Vittorio Gallo, PhD
- William D. Gaillard, MD
- Gerard Gioia, PhD
- Jyoti Jaiswal, PhD (Center for Genetic Medicine Research)

This National Institute of Child Health and Human Development funded center, directed by Dr. Gallo, continues to support five scientific core resources used by more than 90 NIH funded investigators studying brain development and function, and various aspects of neurodevelopmental disorders at George Washington University, Georgetown University, center has become a hub in the Washington, DC, metropolitan area for studies in developmental disabilities and related disorders. The activities of IDDRC investigators are distributed among seven areas of research, corresponding to different IDD-associated conditions: autism, brain tumors, epilepsy, neuromuscular disease, brain injury, urea cycle disorders, and white matter disorders. In each of these areas, genetic, translational neuroscience, and behavioral science programs are integrated to provide a multidisciplinary approach to each research theme. The seven areas of research are supported by Children’s National infrastructure and by the following scientific cores: the Molecular Genetics and Proteomics Core, the Cellular Imaging Core, the Neuroimaging Core, the Neurobehavioral Evaluation Core, and the Biostatistics and Informatics Core. Each of these cores has grown based on steady institutional investment on infrastructure, personnel, state-of-the-art equipment, and software. The Cellular Imaging, Neuroimaging, and Neurobehavioral Evaluation Cores are all part of the Center for Neuroscience Research and are directed by Drs. Jaiswal, Gaillard, and Gioia, respectively.

Brain Injury and Brain Protection

- Gerard Gioia, PhD
- Adré DuPlessis, MD
- Vittorio Gallo, PhD
- Nobuyuki Ishibashi, MD
- Richard Jonas, MD
- Catherine Limperopoulos, PhD
- Ann Massaro, MD
- Joey Scafidi, MD

Traumatic brain injury (TBI) is the leading cause of acquired brain damage in children, producing...
image from TBI is determined not only by mechanical injury to neural structures, but also axonal degeneration and neuronal is. The overall goal of this research project is to determine if fundamental differences in the pathways that produce neuronal death are due to brain maturity and the consequences of trauma on brain structure and function. Dr. Massaro, who directs the radiology imaging research program, and her team, including Dr. Cedric Clouchoux, have delineated the consequences of chronic intracerebral ischemia on tissue volume and morphology. Drs. Jonas and Scafidi, in collaboration with Drs. Gallo and Jablonska, have continued their program investigating protection during congenital heart surgery, with models of premature brain injury, he studies the effect of epidermal growth factor receptor signaling on recovery and whether pharmaceutical manipulation of these pathways promotes cellular and functional recovery. He uses multidisciplinary techniques to assess recovery such as cellular and ultrastructural imaging, behavior, neuroimaging, and physiology. Drs. Gallo and Chew continue their studies of the cellular effects of hyperoxia on white matter development, in particular on axonal pathology with the goal of identifying molecular and cellular therapeutic targets that attenuate the effects of hyperoxia on the developing white matter.

Perinatal Hypoxia and Hyperoxia

- Li-Jin Chew, PhD
- Vittorio Gallo, PhD
- Beata Jablonska, PhD
- Joseph Scafidi, MD

Preterm birth is a major pediatric public health concern. Today, as many as 1 to 2 percent of all live births are preterm; the survival rate of these infants is 85 to 90 percent, however as many as 30-50 percent of children that survive preterm birth have a high incidence of cerebral palsy, intellectual disability, and other cognitive handicaps. While some prematurely-born children progressively improve, a significant percentage still suffer major cognitive deficits, as many have repeated a grade by age 8, and more than 50 percent receive special help at school. Circulatory disturbances and oxygen deprivation are two major causes of neurodevelopmental impairments in these children. Hypoxia, due to lung immaturity and respiratory disturbances, is an important mechanism underlying these devastating neurological complications at this critical time in development. The research program on perinatal hypoxia and brain injury is a collaborative effort between Dr. Gallo’s research team (Drs. Jablonska and Scafidi) and Flora Vaccarino, MD (Child Study Center, Yale University), together with a group of investigators at Yale. Dr. Scafidi (supported by a K08 Award from NINDS) and Dr. Jablonska are using a clinically relevant mouse model of chronic sublethal hypoxic injury to study the developing brain. This model reproduces all the brain injury hallmarks found in children, including cognitive behavioral abnormalities. Animal studies are combined with clinical research on premature babies and with post-mortem human brain tissue. Dr. Scafidi is a clinician-scientist and his research is focused on understanding

Epilepsy

- Madison Berl, PhD
- William Davis Gaillard, MD
- Gerard Gioia, PhD
- Molly Huntsman, PhD
- Judy Liu, PhD
- Phillip Pearl, MD
- Tammy Tsuchida, MD
- Chandan Vaidya, PhD
- Amanda Yuan, MD
- Steve Weinstein, MD

The lifetime risk of experiencing epilepsy is one in 27. Epilepsy has far reaching consequences on brain structure and function, as well as significant morbidity and mortality. The epilepsy program at Children’s National continues to play a leading national and international role in the evaluation, care, and investigation of children with epilepsy in the Children’s Pediatric Epilepsy Program (CPEP). Drs. Pearl and Tsuchida lead the pediatric initiative in a phase II clinical trial of leviteracitam to protect and prevent post-traumatic epilepsy. Dr. Tsuchida played
Epilepsy (ADHD, anxiety, depression) play an important role in the quality of life in children with epilepsy. Dr. Gaillard along with Barbara Kroner, (RTI International), launched a CDC study to investigate access to care and to identify co-occurring disorders in children with epilepsy who live in the District of Columbia. Dr. Berl designed probes of verbal working memory to study the functional and structural anatomy of working memory systems in children with focal epilepsy. Dr. Berl is examining cognitive efficacy, and with fMRI the functional sequences, of computer-based programs to improve working memory in children with epilepsy. In studies of the interaction of cognitive systems, Dr. Leigh Sepeta, under the mentorship of Berl and Gaillard, is designing age appropriate paradigms to investigate the consequences of epilepsy on memory systems. Dr. Gaillard has extended NSF NINDS supported work to model heterogeneity among language systems using fMRI. CPEP also plays a critical role into national initiatives and repositories for pediatric status epilepticus, infantile epilepsy, and infantile spasms.

Cortical dysplasias (FCD), a non-genetic malformation, is one of the most common causes of intractable epilepsy and tuberous sclerosis. Although cortical dysplasia is the most common cause of medically refractory epilepsy in children, little is known about the physiology and genetics, let alone drug resistance of these entities. Dr. Liu is collaborating with the clinical epilepsy service and neurosurgery service to obtain surgical samples from patients who are having epilepsy surgery to remove normal brain tissue that generates seizures. Her goal is to collect this epileptogenic brain tissue and to develop transcriptional profiles of the regions of the brain that cause seizures in an effort to find molecules associated with genetic studies, enabling tailoring of treatments. A translational team of Drs. Huntsman and Liu from basic neuroscience in conjunction with Dr. Gaillard from the CPEP have conducted preliminary studies of resected brain tissue. The effort has identified unsuspected potential genes and pathways that may prove to be targets for novel treatment. Children’s National Medical Center is now one of only a handful of centers worldwide that is capable of performing this type of research. Dr. Weinstein continues his collaborative studies with Dr. Steven Schiff (Penn State University) of seizure prediction and neural control in animal models of epilepsy.

Neuro-Oncology/Neurofibromatosis (NF)

- Maria Acosta, MD
- Robert Avery, MD
- Kristina Hardy, PsyD
- Roger Packer, MD
- Karen Walsh, PsyD
- Elizabeth Wells, MD

Brain tumors are the most common solid cancers of childhood. Directed by Dr. Packer, Children’s National’s Brain Tumor Institute continues to be a leading program with continuous funding through the Pediatric Brain Tumor Consortium (PBTC), which received a new five-year funding agreement from the National Cancer Institute (NCI) and Children’s Oncology Group. The program also received a $2 million gift to undertake research in the molecular biology of medulloblastoma. The neuro-oncology program is pursuing innovative translational research in childhood low-grade gliomas, brain stem gliomas, medulloblastomas, ependymomas, and malignant glial tumors. New open studies through the consortium are attempting to inhibit aberrant cell signaling. This includes selecting and testing new molecules.
to malignant peripheral nerve sheath tumors, utilizing mouse modeling. He also will continue his research on medulloblastoma and glial tumor development. He will work with the team to translate these investigations into novel treatment and preventive approaches, as well as biomarker discovery. The Neurocognitive Program, led by Dr. Acosta and with collaboration from Drs. Walsh and Hardy have become a model for the development of biological tested interventions, implementation of neuro-rehabilitation programs and tailored of interventions as age, clinical needs, family and environmental conditions. The Department of Defense (DOD) supported the NF Clinical Trail Consortium (chaired by Dr. Packer), which is currently conducting three protocol studies for Plexiform Neurofibromas, Optic Nerve Glioma and Cognitive deficits. Dr. Acosta’s phase II DOD consortium randomized double blind placebo control trial of lovastatin is nearing completion for enrolling patients. From the phase I study using lovastatin for cognitive deficits in NF1, Dr. Acosta observed that brain functional connectivity in NF1 patients is abnormal compared with normal controls, but that after treatment with Lovastatin a more similar pattern to normal controls was observed in patients with NF1. Continuing studies now employ resting state fMRI as a potential biomarker for intervention response.

Attention Deficit Hyperactive Disorder (ADHD) and Mood Disorders

- Maria Acosta, MD
- Adelaide Robb, MD *(Center for Translational Science)*
- Chandan Vaidya, PhD

Mood disorders are increasingly being recognized as having their onset in (early) childhood. Dr. Robb}

The figure shows connectivity maps from a seed voxel in the posterior cingulate cortex (top image) in typical developing children (“controls”) and children with NF1 (TDC) [Off drug (lovastatin) and on drug].

The figures and box plots show the normalization of connectivity in children with NF when treated with lovastatin.
ADHD is the most common cognitive disorder of childhood and is overexpressed in children with neurological disorders such as epilepsy, neurofibromatosis, and Down syndrome. Dr. Acosta and her collaborators reported the identification of a gene LPHN3 (located on chromosome 11q) that is associated with a very high risk of ADHD. Furthermore, LPHN3 variants interact with a haplotype on chromosome 11q, doubling ADHD susceptibility. Current investigations include the development of non-invasive techniques (fMRI, SPECT) in addition to demographic and environmental factors to correlate genetic markers with diagnosis and prognosis in this condition.

**New Faculty**

- Cedric Clouchoux, PhD, Diagnostic Imaging and Radiology. Dr. Clouchoux is a Research Faculty at the Advanced Pediatric Brain Imaging Research Laboratory. His background is in biomedical engineering and image processing. His research interests are the characterization and the quantification of the in vivo fetal brain development, and more specifically focused on the cerebral cortex. The two main aspects of this work are developing advanced image processing tools to evaluate brain growth, and quantifying the evolution of anatomical structures and cortical folding during the antenatal life for both normal and high-risk fetuses.

- Kazue Hashimoto-Torii, PhD, Developmental Neurobiology, was recruited from Yale University as a tenure track Assistant Professor of Pediatrics, Pharmacology, and Physiology. Her research focuses on understanding how prenatal environmental influences, such as nutrition, medication, and alcohol intoxication, in combination with genetic risk factors, lead to functional impairment of the developing brain in mental disorders, including autism, fetal alcohol syndrome, and schizophrenia. She uses various modern experimental methods, including patient-derived inducible Pluripotent Stem (iPS) cells and mouse genetic models, towards the goal of preventing and treating these disorders.

- Dilip S. Nath, MD, Cardiovascular Surgery, focuses on examining the effects of gamma-glutamylcysteine on reducing oxidative injury to developing white matter. A mouse brain slice in vitro model for cardiopulmonary bypass induced stress is studied and further validated with magnetic resonance imaging technology utilizing a mouse hypoxic stress in vivo model. The results of the study will provide preclinical data for an important and relevant neuroprotective strategy to improve clinical outcomes in patients undergoing pediatric cardiac surgery.

- Elizabeth Wells, MD, Neurology, completed her neurology training at Children’s National last year and has joined the Brain Tumor Institute under an NSADA. She is examining the effects of brain tumor treatment on brain structure and function.
Selected Publications

Center for Translational Science

VISION STATEMENT: To promote innovation that improves child, family, and community health. Our MISSION is to foster broad collaborative investigation that accelerates discovery across the continuum of the bench, the bedside, and the community.

SED ON A CENTER-WIDE STRATEGIC PLANNING PROCESS that was initiated in Spring 2, the Center for Clinical and Community Research (CCCR) was re-organized into the Center Translational Science (CTS), to more accurately reflect the broad portfolio of our investigator-related research; our involvement in a diverse set of national consortia; and the establishment of key infrastructure resources, including the highly prestigious Clinical and Translational Science Institute at Children’s National (CTSI-CN), that is funded by an NIH Clinical and Translational Science Award (CTSA).
FACULTY

EXECUTIVE COMMITTEE

John van den Anker, MD, PhD
Director, Pediatric Clinical Pharmacology
Vice Chair of Pediatrics for Experimental Therapeutics
Evan and Cindy Jones Professor of Pediatric Clinical Pharmacology
Professor of Pediatrics, Integrative Systems Biology, Pharmacology and Physiology

Stephen Teach, MD, MPH
Chief, Division of Pediatric Allergy and Immunology
Associate Chief, Division of Emergency Medicine
Professor of Pediatrics
The George Washington University

Randi Streisand, PhD, CDE
Associate Professor, Psychiatry and Behavioral Sciences, Pediatrics Diabetes
Team Director of Psychology Research and Service
The George Washington University

Claude Abdallah, MD, MSC
Nicholas Ah Mew, MD
Shireen M. Atabaki, MD, MPH
Oluwakemi Badaki, MD
Mark L. Batshaw, MD
Stephen Baumgart, MD
Lee Beers, MD
John Berger, MD
Kathleen Brown, MD
Randall S. Burd, MD, PhD
Elizabeth Carter, PhD, MPH
James M. Chamberlain, MD
Hollis Chaney, MD
Irene Chatooir-Koch, MD
Avital Cnaan, PhD
Edward Connor, MD
Denice Cora-Bramble, MD, MBA
Michele Dadson, PhD
Nathan Dean, MD
Nina Deutsch, MD
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Linda Yu-Sing Fu, MD, MSc
Cathehine Gillespie, PhD, MPH
Monika Goyal, MD
Ellen Hamburger, MD
Raafat S. Hannallah, MD
Ivor Braden Horn, MD, MPH
Brian Jacobs, MD
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Anitha John, MD
Yewande Johnson, MD
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Richard Kaplan, MD
Paul Kaplowitz, MD
Kanwal Kher, MD
Terry Kind, MD, MPH
Catherine Klein, PhD, RD
Anastassios Koumbourlis, MD
Karen Simpson Kuehl, MD, MPH
Ricardo LaGrange, PhD
Amy B. Lewin, PsyD
Uta Lichter-Konecki, MD
Naomi L.C. Luban, MD
Lori Luchtmaman-Jones, MD
Maureen E. Lyon, PhD
Eleanor Mackey, PhD
William Madigan, MD
Darlene Mansoor, MD
Gerard Martin, MD
David Mathison, MD, MBA
Robert J. McCarter, Jr., ScD
Emily Meier, MD
Chaya Merrill, DrPh
Michele Mietus-Snyder, MD
Nazar M. Mirza, MD, ScD
Maureen Monaghan, PhD
Jeffrey Moak, MD
Rachel Y. Moon, MD
Asha Moudgil, MD
Karen O’Connell, MD
Tessie W. October, MD, MPH
Mary Ottolini, MD, MPH
Judith Owens, MD, MPH
Kavita Parikh, MD
Sophie Pestieau, MD
Khodayar Rais-Bharami, MD
Natella Y. Rakhmanina, MD, PhD
Adelaie S. Robb, MD
Leticia Ryan, MD, MPH
Craig Sable, MD
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David Wessel, MD
Edward Wong, MD
Angela Wratney, MD, MHS
Joseph L. Wright, MD, MPH
Overview: The Center for Translational Science

Center for Translational Science (CTS) organized into three major sub-themes that reflect the broad base of our investigator-initiated research: Molecular Pathogenesis and Experimental Therapeutics; Patient Oriented Research; and Behavioral and Community Research. These sub-themes include investigator-initiated programs, as well as NIH-funded consortia, in which Children's national researchers play leadership roles. In addition, in the Behavioral and Community sub-theme, there is a particular emphasis on pediatric health services and health disparity research.

Investigators are supported by three cross-disciplinary programs: the Division of Biostatistics and Study Design; the Center for Pediatric Informatics; and Office for Grants Enhancement, which provides support for junior faculty in writing and mentoring career development awards; a mechanism for monitoring the progress of early-stage investigators; a venue for review/critique of grant applications; and a mechanism for review/critique of grant applications. In addition, the Office of Innovation Development works with investigators at Children's National and their outside collaborators, funders, and sponsors to advance product development, such as new therapies and devices.

Molecular Pathogenesis and Experimental Therapeutics

Hepato-Renal Fibrocystic Disease Core Center (HRFDCC)

Lisa M. Guay-Woodford, MD

The HFRD Translational Core Center was founded in 2005 by the new Director Dr. Guay-Woodford during her tenure at the University of Alabama at Birmingham and funded through an NIH P30 mechanism. Autosomal recessive polycystic kidney disease (ARPKD) and other hepato-renal fibrocystic diseases are relatively rare recessive disorders, but constitute an important set of childhood nephropathies. Rare disease research requires greater collaboration than the efforts in common diseases where patient resources are routinely available and large repositories can be built locally, as well as nationally.

Within the HRFDCC, Dr. Guay-Woodford established the Hepato-Renal Fibrocystic Diseases Translational Resource (Core A) that features a longitudinal clinical database; a database for genetic mutations; a human tissue repository; and a DNA Bank for patients with hepato-renal fibrocystic diseases drawn from tertiary care centers throughout the Americas (North, Central, and South). In addition, she has developed a portfolio of ARPKD-
In addition Children’s National has become the official pediatric clinical pharmacology training site for the NIGMS funded T32 in clinical pharmacology at Johns Hopkins University allowing additional physicians to receive training in both adult and pediatric clinical pharmacology. The program has supported several investigators such as Drs. Chamberlain, Robb, and Rakhmanina in securing NIH funding. All these studies will result in findings that will improve the safe and effective use of medicines in newborn infants and children with HIV, seizures, psychiatric disorders, and pain-related issues.

The Collaborative Pediatric Critical Care Research Network (CPCCRN)

- John Berger, MD (Medical Unit Director, Cardiac Intensive Care)
- David Wessel, MD (Chief Medical Officer and Sr. Vice President, Hospital-Based Specialties)

This network was initially funded by the NIH in 2005 and competitively refunded in 2009 to investigate the safety and efficacy of treatments, management strategies and outcomes of critically ill children in intensive care units. The network consists of seven clinical sites and a data coordinating center. Led at Children’s National by Drs. Wessel (PI) and Berger, CPCCRN has completed six observational studies on diverse subjects including cortisol response in critical illness, near-fatal asthma, and opioid tolerance, as well as a randomized controlled trial of metoclopramide, glutamine, zinc, and selenium to prevent nosocomial infection in critically-ill children (CRISIS). The CPCCRN research team consists of two physician investigators and five research coordinators and research assistants.

An additional four studies are ongoing, including interventions to reduce pathologic grief in parents after the death of a critically ill child, development of a functional outcome predictors from critical...
Pediatric Emergency Care Applied Research Network (CPCCRN) and the National Heart, Lung, and Blood Institute (NHLBI), CPCCRN is conducting a randomized trial of therapeutic hypothermia after traumatic cardiac arrest (THAPCA).

Dr. Teach collaborates with Dr. Freishtat from the Center for Genetic Medicine Research with special focus on the role of steroid hormones in synchronizing the repair of injured respiratory epithelium and on the role of vitamin D on respiratory infections and asthma morbidity. Of note, Dr. Freishtat recently received R01 funding from the NIMHD to study the association of vitamin D with asthma morbidity in an African American population of children with asthma. At the other end of the translational spectrum, Dr. Teach collaborates with Dr. Horn to improve the way urban and minority parents communicate with their practitioners about asthma care. Dr. Horn herself is leading exciting efforts, in collaboration with IMPACT DC, that focus on leveraging mobile devices ("mHealth") to improve the chronic disease management of inner-city families struggling with asthma. Her model may be applicable to other models of chronic pediatric disease.

Improving Pediatric Resuscitation
■ Randall Burd, MD, PhD

Dr. Burd is the Chief of the Division of Trauma and an Associate Professor of Surgery and Pediatrics whose main research interest is in improving teamwork during trauma resuscitation and improving pre-hospital pediatric trauma triage. He leads a team of collaborators in emergency medicine and surgery, human factors, informatics, computer science, and biomedical engineering. His research in trauma resuscitation is now funded by an R01 from the NIH to develop statistical approaches for real-time prediction of outcome after pediatric injury and an EMSC Targeted Issues grant from HRSA to develop, test, and implement a novel checklist strategy for improving pediatric trauma resuscitation. Dr. Burd and his collaborators were recently awarded a grant from the NIH-National Library of Medicine to develop an approach for automatic information capture, processing and display during trauma resuscitation.

Bone Health in African American Children
■ Leticia Ryan, MD, MPH
■ James M. Chamberlain, MD
■ Stephen J. Teach, MD, MPH

As a pediatrician with training in emergency medicine, Dr. Ryan is concerned with issues related to bone health and risk of fracture in inner-city African American children. Specifically, she investigates the role of inadequate levels of vitamin D (which requires sun exposure) and bone density. Funded by a career development award from NIH, she is comparing bone health in children who have sustained a fracture and those who have not, and then comparing the levels of vitamin D in their blood and various other risk factors. Dr. Ryan’s work is the first to identify an association between both lower bone mineral density and vitamin D deficiency and increased odds of forearm fracture in African American children. Her research, published in Pediatrics in October 2012, has the potential to guide interventions for pre-pubertal African American children with evidence of poor-bone health.
including reduced risk for osteoporosis and fractures in late adulthood.

**Funded Consortia**

**City Asthma Consortium (ICAC)**
- Jennifer J. Teach, MD, MPH
- Jorn Freihshtat, MD, MPH (Center for Genetic Research)
- Shant Sharma, MD (Division of Allergy and Immunology)
- Jh Pillai, MD (Division of Pulmonary and Critical Care Medicine)

The City Asthma Consortium (ICAC) is funded by the National Institute of Allergy and Infectious Diseases (NIAID) and the ICAC consists of multiple clinical and research sites and provides infrastructure for investigator-initiated studies of multiple clinical and translational aspects of immuno-monitoring and immunotherapy among urban, disadvantaged, and minority children with moderate to severe asthma. Led by Dr. Teach, the ICAC provides workforce support to its Steering Committee, a 15-person team of principal investigators (including Dr. Teach) who plan and implement its studies.

**Pediatric Emergency Care Applied Research Network (PECARN)**
- M. Chamberlain, MD (Chief of Pediatric Emergency Medicine)

One of the group's six national Principal Investigators, Dr. Chamberlain, PECARN supports clinical and translational efforts dedicated to improving care and outcomes for acutely ill and injured children. In the past two years the PECARN has published a decision rule for use of head imaging in children with minor head injuries in the emergency department, has established national guidelines for selecting children for head imaging in the emergency department, and has established national guidelines for the treatment of acute head injuries in the emergency department. In the last 12 months, PECARN began two large randomized clinical trials, one testing optimal fluid therapy for diabetic ketoacidosis, and the other testing the use of novel pain therapies for sickle cell pain crisis.

**Behavioral and Community Research**

**Improving Care of Youth with Type 1 Diabetes**
- Randi Streisand, PhD

Families of children diagnosed with type 1 diabetes confront daunting tasks every day: administering insulin injections, monitoring blood glucose levels, and paying careful attention to diet and physical activity. While adhering to a complex diabetes regimen, parents also try to assure that their children have normal childhood activities and opportunities. Working with clinicians, Dr. Streisand is NIH-funded to conduct two randomized trials of new ways to support families and optimize diabetes management. Dr. Streisand is specifically investigating a parent-based intervention aimed at parents of very young children with diabetes, and a parent-teen intervention for early adolescents. These interventions are designed to improve family care, reduce parent and child stress, and ultimately ensure that children with type 1 diabetes are in better health.

**Transition from Pediatric to Adult Care for Adolescents with Complex Chronic Conditions**
- Lisa Tuchman, MD, MPH

Dr. Tuchman draws upon her clinical and advocacy experiences with adolescents and young adults with chronic health issues to help adolescents and their families overcome the challenges of transitioning from pediatric-oriented care to adult-oriented care for this population. Her research aims to improve the quality, safety, efficiency, and effectiveness of the delivery of chronic care management in the setting of healthcare transition. In the past year, she was awarded an AHRQ R44 Maternal and Child Health Bureau grant to implement a randomized controlled trial intervention for minority youth with special healthcare needs. She serves as Co-Investigator on multiple federally funded projects aimed at improving care transitions and self-management skills for chronically ill adolescents including those with cystic fibrosis, survivors of childhood cancer, and sickle cell disease. She serves as an expert consultant responsible for contributing to the development of evidence-based transition programs nationwide.

**Sudden Infant Death Syndrome (SIDS)**
- Rachel Moon, MD

An increasing, significant, and highly troubling racial disparity continues to exist in rates of infant mortality attributable to SIDS and other types of sleep-related sudden unexpected infant death (SUID), such as suffocation. Bed-sharing is a risk factor for such deaths and therefore requires thoughtful study. Dr. Moon's NIH K24 study has found there are many factors affecting African American parental intention to bed share, including cultural norms, with some parents believing that they are a "bad" parent if they do not sleep with their infant, the advice of healthcare professionals, and the belief that it is not possible to prevent SIDS or accidental death. Finally, many parents believe that they could best prevent SIDS or accidental death in their infant by constant vigilance, and bed sharing was a method to maintain vigilance. In response to these findings, Dr. Moon is currently...
more effective in convincing parents to change infant sleep practices. In addition, Dr. Moon just awarded an R01, entitled Social Media and -reduction Training for Infant Care Practices (ART), to study a four-armed intervention to move sleep-related infant care practices.

Genital Heart Disease Screening Program
Gerard R. Martin, MD
Elizabeth A. Bradshaw, MSN, RN, CPN

During the past year, the team at Children's National contributed to advances in research, advocacy, education, and implementation of screening for congenital heart disease (CCHD). The publication on implementation of CCHD screening in a community hospital was written by team and published in the Journal of Perinatology. In addition, a nursing research study to evaluate nurses' knowledge and satisfaction was approved by the Children's National and MedStar Washington Hospital Center IRBs and nursing research councils. The team has continued to assist hospitals in the implementation of CCHD screening on the local, regional, and international levels through participation in state advisory committees (New Jersey, Maryland, Indiana), providing leadership on the Health Service Administration’s Technical Assistance team and collaborating with the Health Authority of Abu Dhabi to implement CCHD screening in all birthing facilities in the region (13 cases with CCHD detected to date). In September, the team hosted the first CCHD Screening Workshop bringing together state departments of health and hospitals to learn about and discuss implementation. The team has written two continuing nursing education series for nurses and is participating in Center investigations are conducting highly impactful health services research.

Healthcare Communication
Ivor B. Horn, MD, MPH

Ineffective healthcare communication with racial/ethnic minority patients and their parents results in disparities in satisfaction with care, adherence to treatment plans, and quality of healthcare. Dr. Horn's research employs a framework of self-efficacy and empowerment to improve racial/ethnic minority parents’ interactions with the healthcare system. With NIH American Recovery and Reinvestment Act (ARRA) funding as principal investigator of a pilot randomized controlled trial, she applied this framework to test the effects of a healthcare communication education program for parents on child asthma outcomes. With funding from the Verizon Foundation, Dr. Horn's team is transforming that intervention into a mobile health (mHealth) platform to be delivered via text messaging. As part of AHRQ's Accelerating Change and Transformation in Organizations and Networks, Dr. Horn was awarded a subcontract in partnership with the Lewin group, Cincinnati Children's Hospital, Nemours, and the National Institute for Children's Healthcare Quality to develop technology-enabled tools to facilitate transitions in care for sickle cell patients. Dr. Horn works with Drs. Lisa Tuchman and Emily Meier on this project.

Health Services Research to Improve Healthcare for Children and Adolescents
Pamela S. Hinds, RN, PhD

Directed at Children's National by Dr. Hinds, Nursing Research supports a collection of more than 30 clinical studies led by nurse investigators. Studies include behavioral interventions, instrumentation testing, evaluation of nursing care procedures, and systematic assessments of child and family responses to illness threat from diagnosis to health recovery or to end of life. In the past year, example study outcomes include establishing the feasibility of children with incurable illness being able to report on their symptoms and functioning while receiving experimental treatments, the feasibility of implementing an anti-bullying community intervention for the inpatient adolescent psychiatric unit, and the feasibility of an anticipatory palliative care program for bone marrow transplant patients. A separate category of studies includes a focus on the work environment in healthcare; an example finding from such studies is the influence on nurses’ role satisfaction of certain leadership characteristics, with motivational leadership having the strongest influence on nurse satisfaction. Nurses’ trust of pump technology has been examined this year with findings including high levels of trust; younger nurses had the highest levels of trust of pump technology. A new category of studies is examining family outcomes of care. An example study is the individual family members’ reports of inclusiveness in discussions about stem cell transplantation and donor decisions in which all eligible family members participated in interviews and their perceptions were analyzed by family member and across family members. Early findings of the work include the diversity of family member responses to participation in decisions about transplantation and donor decisions.
sions about stem cell transplant as a treatment option for families with a child who has certain types of cancer.

**Crossing the Needs of Children with Threatening Illness**

Gaen Lyon, PhD

LaS. Hinds, RN, PhD

Dr. Lyon and Dr. Hinds conduct studies funded by the National Institutes of Health (NIH) and the American Society to develop disease-specific Family Advance Care Planning (FACE) Advance Care Planning to facilitate communication between families and teens with life-limiting conditions about their wishes for their own care, if they could not speak for themselves. The protocol has demonstrated benefits for both parents and their children, and Dr. Lyon and her team are investigating long-term outcomes and their impact on quality of life and spiritual struggle. The CE protocol is the first family-centered protocol designed to help families of adolescents living with life-limiting conditions speak directly and uniformly about their end-of-life care. Dr. Hinds is the principal investigator for this NIH P20-funded program of research, which is funding work by Dr. Ryan on the impact of a mentoring program on violence exposure in high-risk adolescents and work by Dr. Streisand on type 2 diabetes in adolescents. Dr. Horn is the Assistant Director of the Research Core and director of the Child Health Disparities Research Consortium. Dr. Cora-Bramble is working with community members to inform the direction of new research particularly relevant to minority populations. Together, they collaborate with investigators in the Goldberg Center, and at both Howard University and Johns Hopkins to mentor junior faculty and develop new areas of child health disparities research.

**DC-Baltimore Center for Research on Child Health Disparities**

- Rachel Moon, MD
- Denice Cora-Bramble, MD, MBA
- Ivor B. Horn, MD, MPH
- Leticia Ryan, MD, MPH
- Randi Streisand, PhD

Dr. Moon serves as the PI for this NIH P20-funded program of research, which is funding work by Dr. Ryan on the impact of a mentoring program on violence exposure in high-risk adolescents and work by Dr. Streisand on type 2 diabetes in adolescents. Dr. Horn is the Assistant Director of the Research Core and director of the Child Health Disparities Research Consortium. Dr. Cora-Bramble is working with community members to inform the direction of new research particularly relevant to minority populations. Together, they collaborate with investigators in the Goldberg Center, and at both Howard University and Johns Hopkins to mentor junior faculty and develop new areas of child health disparities research.

**Obesity**

- Denice Cora-Bramble, MD, MBA
- Yolanda Hancock, MD, MPH
- Robert McCarter, ScD
- Michelle Mietus-Snyder, MD
- Nazrat Mirza, MD
- Evan Nadler, MD

The prevalence of obesity and its health complications in the United States continues to rise among minority children at socioeconomic disadvantage and the Obesity Institute has expanded its multifaceted efforts to meaningfully address this complex problem. A clinical database that comprises the continuum of care from medical to surgical weight management has been developed and is maintained in real time. This both informs best practices locally and enhances the national evidence base via our participation in a multi-site Pediatric Obesity Weight Evaluation Registry (POWER), funded by the Children’s Hospital Association. Several community outreach programs also continue to thrive and to demonstrate encouraging outcomes. Fit Family Jr/Juntos Podemos, a program funded by community grants for early intervention to prevent and treat obesity in Latino families has been shown to significantly improve parental fund of knowledge and to stabilize child weight trajectories. A program modeled after this successful preschool intervention has been enthusiastically received within the federally funded DC Promise Neighborhood Initiative and is in its second year now with outcomes data pending.

Step-Up-To-Health is an after school wellness and mentoring program entering its third fully subscribed year in a private school in Ward 8, the Washington Middle School for Girls, to engage young girls at risk for overweight and obesity to participate in the African American tradition of stepping as a healthy form of vigorous exercise. To date, BMI has either been stabilized or reduced in 79 percent of participants and these encouraging data form the basis of a national step alliance funding initiative. Finally, the Obesity Institute has launched novel academic-community collaborative with Safeway Foundation funding to accelerate and support the pioneering legislation in the DC Healthy Schools
state-of-the-art online health curriculum), and
ical student mentors from George Washington
ersity (GW) School of Medicine and Health
ces who will help teach and model healthy
ior in three pilot schools within the DC
side neighborhood.

-AIDS
wrence D’Angelo, MD (Center for Cancer and
unology Research)
cardo LaGrange, PhD
tella Rakhmanina, MD, PhD
ashington, DC, has the highest rates for HIV
tion in the United States, particularly among
an American residents. Early identification of the
fection in adolescents and youth, linkage to
and timely initiation of antiretroviral therapy are
ally important in curbing the District epidemic.
for young people living with HIV is challenging,
 high levels of adherence to antiretroviral therapy
quired to ensure optimal outcome of HIV
ction and high quality of life. Reaching desired
s of adherence is often difficult for HIV-positive
, particularly those residing in disadvantaged
ner city communities. Dr. LaGrange conducts
IH-funded research career development
igations specifically focused on coping behavior
psychological adjustment in urban teens infected
 HIV, and the implications for treatment
ence. Because the most commonly reported
ssors are related to taking medication and
tence, Dr. LaGrange is developing interventions
pply innovative approaches to easing the burden
herence, thereby potentially improving illness
agement and overall quality-of-life.

Rakhmanina focuses her research on the effect
in children and adolescents. She is a Principal
vestigator of the NICHD sponsored study of the
fect of puberty on therapeutic targets of pediatric
V infection. Dr. Rakhmanina is a Principal
vestigator of the several industry-sponsored
tials of antiretroviral drugs in children and
adolescents. In addition, Dr. Rakhmanina leads
multidisciplinary team of clinical researchers
landing the most efficient mechanism of screening
adolescents and youth in pediatric emergency
departments for HIV. Dr. Rakhmanina is a Principal
vestigator of the National Institute of Allergy and
fectious Diseases “HPTN 065: TLC-Plus protocol
 Children's National, which is the only pediatric
site within this NIH sponsored study, which
aimed to determine the feasibility of a community
ocused enhanced test and link-to-care strategy in
the United States. The study will assess the feasibility
and effectiveness of different strategies for assuring
aximum initiation of antiretroviral treatment
and for promoting high treatment adherence
and maintenance of HIV suppression. Both Drs.
akhmanina and D’Angelo are the Principal
vestigators of the NIH/GW sponsored city-wide
Cohort study of HIV-infected persons in care
in the District of Columbia, which involves the
stablishment of a clinic-based city-wide longitudinal
cohort describing clinical outcomes in outpatients
with HIV/AIDS receiving care in Washington, DC,
with the goal of improving HIV/AIDS care in DC.

Teen Pregnancy
Amy Lewin, PsyD
Teen pregnancy disproportionately affects
disadvantaged and minority youth in the local
Washington, DC, community, particularly African
Americans and Hispanics. Teen pregnancy is,
children. Dr. Lewin conducts research that informs
and guides the development of effective interventions
to strengthen adolescent-headed families. She works
closely with the Generations Program in the Goldberg
Center for Community Pediatric Health, which
provides family-centered comprehensive primary
care, mental health, and social services to adolescent
parents and their children. She is evaluating the
effectiveness of the Generations model in improving
health and behavioral outcomes for both parents and
children and is working to establish a "best practices"
model of care for teen parent families. This major
HRSA-funded project is the first study to rigorously
investigate the benefits of a "teen-to-tot" model of care.
Findings from Dr. Lewin's previous research indicate
that both adolescent mothers and fathers want fathers
to be involved with their children, even when they
are no longer romantically involved with the mothers.
She has therefore developed an intervention to foster
and strengthen supportive co-parenting between teen
parents, and has received federal funding to support
its evaluation.

Centralized Support of
Clinical and Translational
Research

NIH grants that provide centralized support for
research (such as cores) and multi-center consortia in
which novel, rigorous research can be conducted have
contributed significantly to the impressive growth of
research at Children's National in the past decade.
Such grants provide approximately 20 percent of all
CRI funding (as compared to less than 5 percent at
most institutions); support the career development
of many junior faculty; and facilitate the work of a
diverse spectrum of investigators. In addition, the
Center for Translational Science

...more recently, informatics. The highly competitive Clinical and Translational Science Award at Children’s National (CTSI-CN) is the most prominent of these infrastructural programs, reflecting the organization’s emphasis on discovery through implementation science.

Components of our collaborative Center structure, as well as the CTSI-CN, are described below.

Division of Biostatistics and Study Methodology

Cnaan, PhD
Robert McCarter, ScD
Grégoire Gillespie, PhD, MPH
Cynthia Wang, PhD

Division of Biostatistics and Study Methodology, organized in 2012 by combining the Biostatistics and Informatics Unit and the Multi-Studies Section into one Division with extended depth and breadth. The Division is led by Al Cnaan, a biostatistician with more than 30 years of experience in the clinical and translational sciences. Dr. Robert McCarter, an epidemiologist and informatician with more than 30 years of experience, directs the Division. The Division provides statistical support to investigators, investigators from the Sheikh Zayed Institute, and other researchers across Children’s National. The Division supports the Office for Grants Enhancement and the Office of Biostatistics and Study Methodology.

Center for Pediatric Biomedical Informatics

Brian Jacobs, MD

The Center for Pediatric Informatics was organized in 2006 as a multidisciplinary group comprised of faculty and staff with informatics background, and an interest and/or vision to optimally develop and use the electronic health medical record to both understand and improve the quality of healthcare delivery and research in children. The Center’s primary goals are to utilize novel information technology, computer science, and knowledge management methods to: deliver safer and more effective care; increase the efficiency of care delivery; improve disease prevention; increase the effectiveness of translational research; improve knowledge access and technology-enhanced education; and enhance regulatory compliance.

Other Center objectives include:
- Development of metrics to assess quality and variance in care delivery at Children’s National
- Provision of a home for the Clinical Decision Support and Reporting Group
- Provision of an academic and administrative home for faculty from each Center with interest in informatics quality and research
- Improvement in system access and education for patients, families, and community physicians
- Analysis of population trends
- Automated surveillance for adverse events
- Optimization of the computer-user interface
- Dissemination of knowledge through presentations and publications

Since the Center’s inception in 2006, center members have been active at regional, national, and international levels in information technology and informatics meetings and workshops, with multiple presentations and peer-reviewed publications.

Office for Grants Enhancement

Peter Scheidt, MD, MPH

Building on the program of research support for junior faculty led by Dr. Scheidt the past two years, in 2012 an Office for Grants Enhancement was established under the CTSI-CN. The goal of this program is to improve grant applications submitted by Children’s National investigators in order to maximize the chance of success. The Office is comprised of Dr. Peter Scheidt, Director (60%), and Drs. Stephan Ladisch (30%), Jill Joseph (10%), and Cynthia Rand (10%). The Office conducts a variety of activities to support and encourage junior and mid-level faculty in development of competitive proposals and obtaining funding. Providing internal review of grant proposals and training activities are conducted by the Office. The Office is a key component of the grant support offered by Children’s National to developing investigators.
The Grants Enhancement office. Reviews and consultations are available and conducted at any time in the course of developing a proposal from the initial of specific aims to a final proposal.

In addition, when appropriate subject-matter expertise is not available at Children’s, the Office states and obtains in-depth external review of well developed proposals by carefully selected experienced external reviewers. The Office also organizes and schedules monthly group meetings with peer investigators who are “in the same boat” for those seeking Career Development Awards (the K12) and for those seeking R01 type funding (the Emerging Independent Investigator–E2I–Group). Through these group activities, participants share updated information on the whole process of preparation, access examples of successful applications and other supporting materials, and in peer review and feedback on their evolving proposals. Finally, the Office organizes both study-group-like reviews of proposals in a conference setting with multiple reviewers for feedback and for national benefit and seminar like sessions for investigators who are seeking broad input, creative guidance, and collaboration opportunities early in project development.

Of the drafting of this report the Grants Enhancement office and its predecessor have carried out reviews of proposals in various phases. A total of 50 Grants Enhancement reviewed proposals have been submitted for funding. Of the 40 submitted applications that have been reviewed, 7 were not scored, 17 were scored not funded and 16 (40 percent) were funded. Of the funded, there are four KL2s, three R40s, two CTSI-CN pilot studies, one K23, one P20, K12, one HRSA Faculty Development Award, and five others.

Office of Innovation Development (OID)
- Edward Connor, MD, MBE

This office was established in 2008 with the mission to facilitate translation of biomedical discoveries into innovative products that improve the health and well being of children. Dr. Connor, the Director of OID, has more than 25 years of experience in product development for children in academia and biotechnology. The Office provides strategic and operational assistance in intellectual property management and technology transfer, opportunity assessment and partnerships, drug, biologics and device development, regulatory planning and interactions, critical path and commercialization assessment, innovation and product development policy and ethics, and entrepreneurship. Since its inception the Office has worked with investigators and academic entrepreneurs throughout Children’s National and their external collaborators, stakeholders, and sponsors to advance product development. For example, OID works closely with Dr. Hoffman in the Center for Genetic Medicine Research and leading companies in the field in the development of antisense oligonucleotides for exon skipping as a treatment for Duchenne muscular dystrophy. Dr. Connor serves as President and CEO of a company formed from a Children’s National technology transfer initiative, engaged in the discovery, development, and commercialization of small molecule therapeutics for neuromuscular disorders. The company (ReveraGen Biopharma, Inc.) is partially supported by parent and foundations and MDA Venture Philanthropy and is partnered with NIH’s Therapeutics for Rare and Neglected Diseases program. OID works closely with the Sheikh Zayed Institute on a number of high potential emerging products, including a device being developed by Dr. John Fishel for stroke patients.

Clinical and Translational Science Institute at Children’s National (CTSI-CN) 2012 Leadership
- Lisa M. Guay-Woodford, MD: Principal Investigator
- Vincent Chiappinelli, PhD (The George Washington University): Co-Principal Investigator
- Pamela Hinds, RN, PhD (Nursing Research Leadership): Executive Committee
- Mendel Tuchman, MD: Executive Committee
- Lisa Schwartz, EdD (The George Washington University): Executive Committee
- Edward Connor, MD, MBE: Executive Committee
- Paula Lantz, PhD (The George Washington University): Executive Committee
- Marshall Summar, MD: Executive Committee
- Brian Jacobs, MD: Director of Biomedical Informatics
- Avital Cnaan, PhD: Director of Design, Epidemiology, and Biostatistics
- Naynesh Kamani, MD: Director of Research Ethics and Regulatory Support
- Naomi Luban, MD, and Joseph Bocchino, PhD (The George Washington University): Co-Directors of Research Education, Training, and Career Development
- Stephen J. Teach, MD, MPH: Director of the Pilot Studies Programs
- Marshall Summar, MD: Director of the Clinical Studies Resource
- Edward Connor, MD, MBE, and Eric Hoffman, PhD: Co-Directors of the Innovative Development office.
The Clinical and Translational Institute at Children's National (CTSI-CN)

The CTSI-CN is composed of a set of eight “working units” that are organized to optimize success achieving our five strategic priorities: 1) enhancing the research infrastructure; 2) promoting investigator education, training and career development; 3) accelerating discovery across the T1 interface; 4) building community partnerships; and 5) expanding value-added partnerships. All the resources of the CTSI-CN can be accessed through a system of senior staff guides and a web-based access portal (PIBEAR).

The working “units” of the CTSI-CN support this overall mission through an integrated network of components and programs. These resources are organized to optimize success achieving our five strategic priorities: enhancing the research infrastructure; promoting investigator education, training and career development; accelerating discovery across the T1 interface; building community partnerships; and expanding value-added partnerships. The CTSI-CN connects the research community and provides investigators with access to: a broad array of resources and services; training for the next generation of researchers and research teams; and community partners to develop/
very across the T1 interface; building community
erships; and expanding value-added partnerships.
the resources of the CTSI-CN can be accessed
g through a system of senior staff guides and a web-
d access portal (PIBEAR).

New Faculty

Monika Goyal, MD, is a pediatric emergency medicine physician and health services researcher who joined Children’s National from The Children’s Hospital of Philadelphia. Her research focuses on adolescent sexual health within the emergency department setting. She was recently awarded a K23 career development award from NICHD to design and implement a standardized and confidential computerized sexual health screening tool to improve sexually transmitted infection (STI) screening in the emergency department.

Catherine Gillespie, MD, is an epidemiologist who joined Children’s National from the University of Washington at Seattle. Her previous research has included studies of newly-recognized sexually transmitted pathogens and chronic disease surveillance. She is providing clinical support on Dr. Tuchman’s new clinical trial on children with organic acidemias in perammonemia crises, as well as biostatistical support for clinical and translational studies.

Selected Publications

- Lewin A, Mitchell SJ, Burrell L, Beers LS, Duggan A. Patterns and predictors of involvement among...


The Sheikh Zayed Institute for Pediatric Surgical Innovation

VISION STATEMENT: Launched in September 2009, the Sheikh Zayed Institute for Pediatric Surgical Innovation at Children's National Medical Center redefines what is possible in surgery for children by combining research and clinical expertise into one, collaborative team. The Institute develops knowledge, tools, and procedures that benefit children in the Washington, DC, region, across the country, and around the world.

The Institute's primary focus is to learn from today's surgeries, and conduct innovative research based on that knowledge to improve pediatric care.
FACULTY

Kevin Cleary, PhD
Laurie Conklin, MD
Rohan Fernandes, PhD
Julia Finkel, MD
Angela Fletcher, PsyD
Rohan Fernandes, PhD
Eric P. Hoffman, PhD
Monica Hubal, PhD
Timothy Kane, MD
Axel Krieger, PhD
Marius George Linguraru, PhD
Evan Nadler, MD
Kurt D. Newman, MD
Craig Peters, MD
Diego Preciado, MD
Zenaide Quezado, MD
Sasa Radoja, PhD, MEd
Sarah Rebstock, MD, PhD
Cynthia R. Ronzio, PhD
Nabile M. Safdar, MD
Anthony Sandler, MD
Karun Sharma, MD, PhD
Raj Shekhar, PhD
Raymond Sze, MD
Zohreh Tatari-Calderone, PhD, MBBS, MBA
Stanislav Vukmanovic, MD, PhD
Ziv Yaniv, PhD
Innovation and Knowledge Sharing

- Distinguished faculty have published more than 232 peer-reviewed research studies in academic journals since 2009
- Institute investigators served as invited presenters at major medical and scientific conferences around the world, including Germany, India, the United Arab Emirates, and Saudi Arabia
- Sponsored weekly Innovation Rounds lecture series

Clinical Care

- The institute funded the addition of a da Vinci Surgical System as well as a training model to the Children's National Medical Center Joseph E. Robert, Jr., Center for Surgical Care, which launched the robotic surgery program at Children's and has opened the door for further pediatric robotic surgery research through the Bioengineering Initiative.
- In collaboration with the Joseph E. Robert, Jr., Center for Surgical Care, the institute completed the construction of a state-of-the-art operating room with adjacent MR compatibility using a 1.5T Philips magnet. This will facilitate the launch of the first pediatric clinical trial application of high intensity focused ultrasound (HIFU).
- The Pain Medicine team began seeing patients on a part-time basis as the construction for the first-of-its-kind Pain Medicine Clinic is under way and scheduled to open in 2013.

Creative Connections

Academic collaborations with area universities and research institutions including:
- American University Kogod School of Business
- Arizona State University School of Engineering
- George Washington University School of Medicine and Health Sciences
- George Washington University School of Business
- Georgetown University Medical Center
- Johns Hopkins Applied Physics Lab
- National Institutes of Health
- Tainjin University (China) School of Mechanical Engineering
- University of Maryland A. James Clark School of Engineering
- Industry partnerships to develop innovative pediatric tools
- American GNC Corporation
- Design Resource Group
- EndoEvolution
- Hyundai Heavy Industries
- Infoscitex Corporation
- Interface Media Group
- Intuitive Surgical, Inc.
- MDA Corporation
- Philips
- ReveraGen Biopharma, Inc.
- Samyang Optics, Ltd.
- Samsung

Infrastructure

Institute added several new major pieces of equipment to fuel surgery innovation, including:
- Jet 3 dimensional rapid prototyping machine, which allows investigators to print prototype parts from a medical scan. This printer will allow the institute to offer the ability to print high definition three dimensional models as a core service for clinicians to use in planning procedures and treatments.
- cBio RS, a so-called third generation genetic sequencer, that completes sequences faster and with more precision than ever before.
- Two KUKA Seven Degree of Freedom robot arms that are being used to develop better anastomosis and other surgical techniques.
- Two da Vinci Surgical Systems, one in use in the operating room and the other in the institute itself for education, training, and product development.
- Microscopy: state of the art microscopes, including first in the country spinning disk live cell and live animal scope.
President’s Initiatives

C. W. Kim, MD, CM, PhD
Axel Krieger, PhD
Simon Leonard, PhD

Evolved business paradigm for scholastic activity
Evolved clinical paradigm for pediatric care

Scientific Highlights
Display of congenital heart defects
D Printing
Krieger, PhD
Olivieri, MD

Diagnosis and management of structural heart disease is largely driven by two-dimensional (2D) methods. Nearly every type of heart defect with a spectrum of severity, and structure ties to function. Currently, cardiologists and vascular surgeons rely on mental conversion of echocardiography data into a three-dimensional (3D) understanding of the spatial relationships of intracardiac structures. However, current medical robotic technology does not address all the needs unique to pediatric surgery. Therefore, Drs. Kim, Leonard, and Krieger are developing and evaluating a novel robotic system with supervised autonomy for minimally invasive anastomosis in pediatric surgery in collaboration with the Canadian technology and robotics company MDA. This Smart Tissue Anastomosis Robot (STAR) consists of a robotic positioning platform, smart end effectors, and a shared control operating system, which will enable precise, accurate, and efficient closure of any hollow organ including vessels, bowel, and wounds. STAR provides the surgeon with the ability to select the anastomosis site, access path, and critical structures. STAR then performs the anastomosis under the surgeon’s supervision, optimally reaching small spaces with a miniature multi-jointed tool and precisely placing surgical clips for anastomosis. This new paradigm of supervised autonomy will incorporate expert surgeons’ movements and decision algorithms into robotic movement and thus expand the surgeon’s capacity and capability, making future surgical procedures more effective with improved safety.

Device for transcatheter surgical repair of esophageal atresia
Peter C. W. Kim, MD, PhD
Axel Krieger, PhD

Esophageal atresia, where one portion of a child’s esophagus does not naturally connect to the other, occurs in one out of every 4,000 live births. Drs. Kim and Krieger are creating a Natural Orifice Anastomosis Device (NOAD) for minimally invasive surgical repair of esophageal atresia. The NOAD is a robotic tool that can access and connect the two esophageal lumens. A provisional patent has been filed and several prototype designs are underway at this time for a device that is compatible with a pediatric endoscope.

Development of a Smart Tissue Anastomosis Robot (STAR) for pediatric surgery
Peter C. W. Kim, MD, PhD
Axel Krieger, PhD
Simon Leonard, PhD

The Smart Tissue Anastomosis Robot (STAR) performs surgical anastomosis under the surgeon’s supervision, optimally reaching small spaces with a miniature multi-jointed tool and precisely placing surgical clips for anastomosis.
ge-guided non-invasive therapeutic energy (NITE) program
Peter C. W. Kim, MD, PhD
Jeffrey Dome, MD, PhD (Chief of Oncology)
Arun Sharma, MD, PhD
Raymond Sze, MD (Chief of Diagnostic Imagery and Radiology)

Children's National, in collaboration with the National Institutes of Health, is completing construction of a new operating room that includes intraoperative magnetic resonance (MR) imaging. The capabilities of the new operating suite will allow for three primary activities: creation of a state-of-the-art "Brain Lab" that will provide neurosurgeons with accurate up to the minute images of a patient's surgical site with greater precision and clarity than ever before; the addition of time functional spectroscopy during surgical procedures; and the launch of the first pediatric clinical trial of high intensity focused ultrasound (HIFU) as a n-invasive method to treat inoperable tumors in children. In 2012 and 2013, the team will collaborate with the National Institutes of Health to establish the safety, efficacy and clinical potential of HIFU for treating children through a mix of both pre-clinical and phase I clinical trials.

Minimally invasive cardiac pacemaker implantation
■ Peter C. W. Kim, MD, PhD
■ Charles Berul, MD (Chief of Cardiology)
■ Axel Krieger, PhD

Drs. Kim, Berul, and Krieger have developed a multidisciplinary pilot study that demonstrates a novel minimally invasive approach to left ventricular epicardial pacemaker implantation. Using a porcine model to simulate a human infant, the team maps how a pediatric cardiologist and surgeon may, under direct thoroscopic visualization, access the pericardial space and then fixate an epicardial pacemaker lead upon the left ventricular free wall epicardium and pace the ventricle. If successful, the implantation method will be applied in a human clinical trial for infants and small children.

Goals
- Customization in pre-surgical planning and post surgical evaluation: Integrating simulation technology and phenomics to provide advanced analytic tools for understanding the anatomy and pathology of the patient
- Enhanced tissue/cell visualization during surgery: Apply augmented vision to provide surgeons with the ability to see internal structures in real time during surgery through continuously updated and refreshed digital images
- Minimally and noninvasive surgical techniques: Pursue the established and new minimally to noninvasive approaches in pediatric surgery to reduce pain and shorten recovery time for patients

Scientific Highlights
Improving surgical visualization and tools is a longstanding clinical need that will make surgeries more precise, lead to fewer complications, improve a surgeon's efficiency, and thus shorten the length of surgeries, while also allowing surgeons to perform more complex open surgeries using minimally invasive techniques. The Bioengineering team seeks to harness the latest imaging and robotics equipment to uncover new ways for surgeons to better see their surgical field.

Bioengineering
■ Kevin Cleary, PhD
■ Rohan Fernandes, PhD
■ Timothy Kane, MD
■ Marius Linguraru, PhD
■ Craig Peters, MD
■ Nabile Safdar, MD
■ Raj Shekhar, PhD
■ Karun Sharma, MD, PhD
■ Ziv Yaniv, PhD

Costomy creation utilizing high-intensity focused ultrasound for bladder outlet obstruction
■ Axel Krieger, PhD
■ Amy Burns, MD
■ Jaeye Kim
■ Aaron Martin, MD
■ Craig Peters, MD

Burns, Krieger, Kim, Martin, and Peters are developing a novel preclinical application of high-intensity focused ultrasound for the creation of a costomy for children with bladder outlet obstruction is a common congenital defect that can cause serious damage to a child even before he or she is born. The team proposes that the application of HIFU to create an opening in the bladder could create a non-invasive procedure conducted in utero. The preclinical proof of concept trial is currently underway.
The stereoscopic AR system being used to image a phantom.

- "navigation" refers to the use of a tracking system to determine the position of surgical instruments relative to the anatomy and displaying relevant information on a computer monitor. Endoscopic procedures from the major manufacturers are similar and involve controls based on simple flexion of the tip of the endoscope, rotational control, and in and out longitudinal movement. These three movements are performed by the operator at the head of the bed and are all distinct in their character, making intuitive control difficult to learn and maintain.

Engineering of Tianjin University in China, proposed a new paradigm for making navigation simpler for endoscopic procedures by developing an “add-on” package to provide mechanical control and navigation capability. The team developed a prototype system for such navigated ureteroscopy. The preliminary tests have showed the feasibility of this control concept using kidney phantoms.

Surgery continues to evolve toward minimizing the invasiveness of the procedure. Single incision laparoscopic surgery (SILS) is a rapidly developing field that may represent the future of laparoscopic procedures.
Goals

- Utilize immunity in defining the pathogenesis of disease and applying the science of immunology to discover novel therapeutic strategies and targets, as well as disease markers for novel diagnostic purposes.
- Appropriately exploit immune mechanisms that could enable a more directed and targeted therapeutic approach that is less invasive and less toxic.
- Understand and apply immunologic principles to solid tumors and inflammatory diseases of surgical interest.

Project Highlights

The immunology initiative focuses on the interface of the immune system and disease. This initiative will use immunity in defining the pathogenesis of disease and applying the science of immunology to discover novel therapeutic strategies and targets, as well as disease markers for novel diagnostic purposes.

Immunology

- Anthony Sandler, MD
- Stanislav Vukmanovic, PhD
- Sasa Radoja, PhD
- Zohreh Tatari-Calderone, PhD

- Down syndrome early detection: Automated facial recognition from photography
  - Marius Linguraru, PhD
  - Marshall Summar, MD, PhD
  - Kenneth Rosenbaum, MD
  - Qian Zhao, PhD
  - Dina Zand, MD
  - Raymond Sze, MD

- Tumor cell migration essentially scarless if the incision is hidden in the umbilicus. Along these lines, the concept of natural orifice transluminal endoscopic surgery (NOTES) has been introduced clinically. While TES has its limitations with current instruments, it has been proposed that NOTES could be facilitated with the introduction of robotics technology. The team, together with American GNC Corporation in the Department of Engineering at Arizona University, is developing a system concept and structure for a robotic NOTES system. Several components have been developed to date. This system was tested in a preclinical swine model, using a multi-DOF passive module. Additionally, the robot was attached to a 7-DOF Kuka lightweight robot to demonstrate that the robot could maintain a constant force against an abdominal phantom.

- Mari-Functional nanoconstructs for pediatric brain stem glioma diagnosis and therapy
  - Rohan Fernandes, PhD

  Pediatric brain stem glioma (BSG) is an aggressive tumor of the brain stem. The prognosis of patients diagnosed with BSG is typically poor, with a median survival rate of 20 months. The research group of Rohan Fernandes is involved in the synthesis of tri-functional nanoparticles that can be used for diagnosis and therapy (theranostics) of pediatric brain stem glioma. The nanoconstruct consists of a particle platform that can be optically visualized (attached fluorescent molecules) and detected by I. The nanoconstruct has targeting groups, which enable it to selectively target biomarkers expressed on cancer cells. Another functionality is the ability of the nanostate to carry therapeutic cargo to targeted cancer cells. The team is investigating methods to deliver the nanoconstructs selectively to the targeted site, facilitating visualization and therapy.

The cancer research program has four primary objectives:

- Understand how tumors evade immunity (tumor cloaking)
- Develop effective and safe approaches to adoptively transfer activated immune cells for tumor destruction (adoptive cellular therapy)
- Expand tumor vaccination strategies for protection against tumor recurrence (tumor vaccine therapy)
The complimentary effects of novel tumor therapies with tumor immunity (tumor on and immunity) program weaves immunity with cancer for the of discovering novel immune therapies in and four sub-programs are inter-linked. Tumor is the ability of the cancer to evade the system and treatment despite unique and al proteins (tumor antigens) expressed on cells. This immune suppressive and immune phenomenon renders any immune response the tumor inadequate. Adoptive cellular is geared to specifically target cancer with cells containing potent lytic (effector) sms, but the failure to induce long-termity with this approach is a limitation that low for tumor recurrence. Tumor vaccines designed to specifically induce long-term against the tumor and prevent recurrence e when the primary tumor load is destroyed. novel ablative therapies are a powerful means of the primary tumor, but cells that are gaged in the ablation will survive and recur. abination of immune activation with ablation potential to not only completely destroy the tumor load, but to also induce immunity hose cells not destroyed by the ablation. ernary disease program focuses on early s of certain inflammatory conditions and ing genetic factors underlying normal and promoting immunity in infants, children descents. By initiating treatment sooner for ary diseases, we can effectively minimize of many complications associated with these ns. To achieve this, our research is focused earlier diagnosis and improved recognition of perditis. We are exploring the microbiome.

The team leads a clinical study on the genetics of immunity in response to vaccines as well as immune mechanisms controlling the development of necrotizing enterocolitis (NEC), a serious intestinal illness common in premature newborns. The immune systems of infants and children under five years of age are not as effective as those of adults. The goal of these genetic studies is to identify molecular markers as well as targets specific to an individual for therapeutic interventions.

Pain Medicine

- Julia Finkel, MD
- Angela Fletcher, PsyD
- Zenaide Quezado, MD
- Sarah Rebstock, MD, PhD
- Cynthia Ronzio, PhD

Goals

- Develop the alpha prototype and commence clinical trials for the human algometer
- Generate the composite cortical pain response index based on signal processing from analysis of human algometer clinical trials
- Establish the laboratory infrastructure for the conduct of preclinical trials of novel analgesics for sickle cell pain
- Build the complex pediatric pain medicine clinic at Children's National
- Start clinical trials to determine the value of digital media technology for the diagnosis and therapy of complex pain syndromes
- Develop the infrastructure to start the development of new analgesic compounds to treat sickle cell disease

Scientific Highlights

Although pain is still the most common reason why patients seek healthcare, the mechanisms of transmission and perception of pain are incompletely understood. Understanding of the neurophysiologic mechanisms by which noxious and non-noxious stimuli are perceived, and how different treatment modalities affect patients differently, are imperative for the development of new drugs and techniques to treat pain.

Diagnostics

Human algometer objective pain assessment system

- Julia Finkel, MD
- Zenaide Quezado, MD

Assessment of pain in children and infants is subjective in nature. Drs. Finkel and Quezado are developing a method and an instrument to objectively assess pain in pediatric patients. This approach represents the integration of neurospecific electrical sensory stimuli and near infra-red spectroscopy signals that establish an automated stimulus/response. The response provides an objective measure of pain perception intensity, an objective measure of analgesic impact, a diagnostic characterization of pain, (e.g., neuropathic, hyperalgesia (heightened sensitivity to pain) etc.), and with repeated measures of analgesic impact can determine the onset of tolerance or opioid induced hyperalgesia. The approach allows the team to separate the affective/emotional component of pain response from actual nociception in both verbal and non-verbal patients. The algometer started phase I clinical trials in fall 2012.
method to enable the efficient preclinical study of novel therapies to treat pain. This method will enable efficient screening of novel pain therapies as well as the collection of preclinical data aiming at facilitating the process of bringing the novel therapies to clinical use.

**Therapeutics**

**Development of NO-opioids**

- Julia Finkel, MD
- Zenaide Quezado, MD

This series of investigations involves synthesizing several candidate opioids containing nitric oxide (NO) donating moieties for the purpose of mitigating tolerance and opioid induced hyperalgesia as well as preventing withdrawal. A successful compound would transform this class of drug by preventing iatrogenic morbidities and abuse and the addition of a non-steroid or NSAID (non steroidal anti-inflammatory drug) anti-inflammatory profile would make it a “super analgesic.” Drs. Finkel and Quezado synthesize candidate NO-morphine and NO-fentanyl for testing in murine models; test NO-opioids vs. parent compounds using mouse nociception assays; test NO-opioids in murine models of opioid tolerance; and test NO-opioid candidates in murine models of inflammation.

**Pharmacogenetics of Analgesia**

**Resiniferatoxin**

- Zenaide Quezado, MD

Dr. Quezado studied, in animal models, the effects of two different medications, resiniferatoxin and capsazepine, that are known to impact TRPV1, an ion receptor channel that signals sharp, painful stimuli to the brain, and triggers a pain response. These drugs block the activation of the TRPV1 channels and ultimately destroys the nerves that have the receptor. The team discovered that resiniferatoxin causes a chemical reaction that also negatively impacts the body’s reaction to bacterial infections by altering cytokine and chemokine expression, signaling molecules which are key to the natural immune response to bacteria.

**Arginine supplementation as a strategy for pain control in sickle cell disease (SCD)**

- Zenaide Quezado, MD
- Louis Almeida, MD, PhD
- Julia Finkel, MD

NO is a powerful vasodilator that is exclusively synthesized from the amino acid arginine. Diet arginine supplementation is a safe and effective method to increase plasma arginine and NO levels, which may mitigate acute pain crises often experienced by SCD patients. The team investigates the effects of arginine supplementation in pain levels using a mouse model of SCD (“BERK” model). In the near future, this approach can be combined with other strategies (for example, supplementation of antioxidants or BH4) that could have synergistic effects to alleviate SCD.

**Tetrahydrobiopterin (BH4) supplemented diet in sickle cell mice**

- Zenaide Quezado, MD
- Nicholas Spornick
- Julia Finkel, MD

It is well documented that patients with sickle cell disease (SCD) have reduced NO bioavailability simultaneously with vaso-occlusive events that lead to pain episodes. Low levels of NO in sickle cell disease are related to increased levels of free hemoglobin due to hemoglobinopathy. The team hypothesized that supplementation of tetrahydrobiopterin (BH4) could increase NO bioavailability. They tested this hypothesis using a murine model of SCD and found that BH4 supplementation significantly reduced pain scores and increased NO levels. This strategy may provide a novel approach to pain management in sickle cell disease.
Improve endothelial function in humans with cell disease. The team hypothesized that increasing levels of BH4 by stimulating increased NO at the synthesis pathway, rather than further downstream, will improve murine models. The study administers BH4 to a mouse model of SCD and follows the pain, plasma NO levels, pro-inflammatory gene expression and behavioral tests, both before and after treatment with BH4.

Motion and thermoregulation in a model of Infantile Neuronal Ceroid Lipofuscinosis (INCL)

Quezado, Khaibullina, and Finkel studied the role of protein tyrosine phosphatase (PTP1) in INCL in cell biology. This study could help identify targets for therapy of INCL and other lysosomal diseases for which effective therapy is lacking. Previous research showed that INCL and sickle cell disease have altered nociception compared to wild type counterparts. The team determined that behavioral changes associated with these altered pain phenotypes will improve our understanding of the biology of the human disease counterparts.

Psychological Impacts of Pain

Study of behavior abnormalities associated with altered nociception in animal models of human diseases.

- Zenaide Quezado, MD
- Li Wang, MD, PhD
- Julia Finkel, MD

This project examines the impact of genetic manipulation that result in animal models of human diseases. The studies evaluate the effect of several genetic mutations, including sickle cell disease, infantile neuronal lipofuscinosis (INCL), and autism, on behavior parameters including learning capabilities and mood changes associated with existing changes in nociception. Previous research showed that INCL and sickle cell models have altered nociception compared to wild type counterparts. Now, the team is determining the behavioral changes associated with these altered pain phenotypes. Characterizing these behavioral phenotypes will improve our understanding of the biology of the human disease counterparts.

Pain, sleep, and depression in women and children

- Cynthia Ronzio, PhD

Dr. Ronzio completed a study designed to develop a clearer understanding of the role of socioeconomic status (SES) in maternal depression among African American women. The study evaluated whether multiple dimensions of SES could be independently associated with maternal depression, and determined if psychosocial characteristics mediate relationships between SES and maternal depression, to explicitly link social processes to financial resources with psychological ones. This is one of the few studies of maternal depression in a middle ear epithelial metaplasia and inappropriate over-expression of mucins in otitis media cell models.

Systems Biology

- Eric Hoffman, PhD
- Monica Hubal, PhD
- Evan Nadler, MD
- Diego Preciado, MD, PhD
- Laurie Conklin, MD

Goals

- Establish fee-for-service clinical biomarkers service based upon state-of-art mass spec assays
- Demonstrate that a novel drug, VBP15, is effective for improving wound healing
- Identify peripheral microRNA biomarkers of disease response to corticosteroids and infliximab in pediatric Crohn’s disease
- Develop an animal model of eosinophilic esophagitis to test a newly developed gadolinium-antibody construct
- Establish patient-enabling mobile app programs for tracking ostomy output and evaluating rashes
- Interrogate how pathologically relevant infectious stimuli result in a cascade of inflammatory mediator up-regulation which in turn leads to middle ear epithelial metaplasia and inappropriate over-expression of mucins in otitis media cell models

links between contextual variables and intrapersonal characteristics. In collaboration with Drs. Ed Huntley and Maureen Monaghan (Clinical and Community Research), Dr. Ronzio completed analysis of pilot data on sleep quality in postpartum women and its association with the quality of mother-infant interaction. This is the first study to empirically evaluate the consequences of sleep quality within the family system.
understand the mechanisms of action of propranolol in infantile hemangioma therapy, specifically by further elucidating its effects on MP-9 expression and activity.

Identify genetic variants driving outcome variability following weight loss surgery in adults and adolescents.

Define molecular mechanisms underlying ethnic differences in cardiometabolic disease development.

Demonstrate that increased adiposity potentiates inflammation by altering subcutaneous fat signaling.

**Scientific Highlights**

- **Genetic basis of surgical weight-loss outcomes**
  - Evan Nadler, MD
  - Monica Hubal, PhD

The childhood obesity epidemic has reached the point where one in four high-school children are overweight or obese, and weight loss surgery for adolescents has dramatically increased in frequency. The two most commonly utilized forms of surgery are gastric bypass (a malabsorptive and restrictive procedure) and gastric banding (restrictive alone). While bands may be the more attractive choice for adolescents due to their enhanced safety profile, there is a great deal of variability in the response to gastric banding. Some patients fail banding (i.e. do not lose significant excess body weight), and this failure is thought to be largely due to patient behavior. However, given the high heritability of body composition traits, it is quite plausible that particular genetic predispositions render some patients less able to lose weight with restriction alone; necessitating a malabsorptive component to achieve significant weight loss in these individuals. Our overall hypothesis is that specific genetic patterns can predict outcomes following bariatric surgery, especially in adolescents who generally have fewer or less severe co-morbid conditions.

**Genomics**

- Eric P. Hoffman, PhD
- Joseph Devaney, PhD
- Susan Knoblach, PhD

The Sheikh Zayed Institute has collaborated with the Center for Genetic Medicine Research to obtain three next-generation sequencing units (Illumina, Pacific Biosciences, and Ion Torrent). Emulsion PCR is now routinely offered to investigators at Children’s National and elsewhere.

**Proteomic networks of MUC5B infectious/inflammatory induction in Otitis Media**

- Diego Preciado, MD, PhD

Dr. Preciado received the institute’s first NIH R01 to study the proteomic contributors to otitis media (OM). Otitis media, also known as chronic ear infection, is one of the most common conditions of early childhood. Due to the high incidence of OM in children, the surgical placement of a tympanostomy tube to treat OM is the most common pediatric surgical procedure requiring anesthesia in the United States. Previous studies by Dr. Preciado and Dr. Mary Rose, in the Center for Genetic Medicine Research, have shown that the molecular profile of the ear (the amount and types of specific proteins in and around the inside of the ear) changes significantly when a child has an ear infection. The research team found that specific proteins within the ear appear to cause the secretion of a type of mucus (MUC5B) similar to the mucus in a child’s airway. The study is a joint project between Children’s Sheikh Zayed Institute, the Center for Genetic Medicine Research, and the Clinical and Translational Science Institute at Children’s National.

**Innovation and Education**

- Floortje Blindenbach-Driessen, PhD
- Martha Houle, PhD
- Craig A. Peters, MD

**Goals**

- Inspire a diverse group of students and trainees to explore and enter into careers related to surgical medicine.
Early career surgeons, engineers, epidemiologists and related healthcare providers in principles of biomedical innovation were learners in real-life innovation projects in context of clinical care. A culture of innovation at all levels of a large teaching pediatric hospital introduces learners to the concepts, vision, and excitement of medical innovation internationally.

**Highlights**

Dr. Peter Kim, the institute’s Vice President, elevated Innovation and Education to the fifth initiative of focus for the Sheikh Zayed Institute. While the goals of education and advancement are constant throughout all four original initiatives (pain medicine, bioengineering, epidemiology, and systems biology), Dr. Kim believes that by elevating the profile of the important programs and Education helps shift the current culture of pediatric healthcare to something uniquely different.

The institute welcomed its first class of Student Interns, a two-month program for students in school, college, and graduate and medical school. The first class of eight interns worked on a project with an assigned research mentor from the institute, enjoyed opportunities to shadow clinical faculty, and completed a focused coursework in the fundamentals of medical theory and practice.

The institute also welcomed its first class of Joseph E. Jr., Fellows in Pediatric Surgical Innovation, a new hybrid research and clinical fellowship track for innovation-minded early career professionals in the biomedical sciences. The four Robert Fellows who are completing their fellowship this year will develop four full business plans around their chosen projects.

Five provisional applications for patents were filed by the Office of Innovation Development on behalf of Dr. Peter Kim and others in the faculty of the Bioengineering group as well as Robert Fellows. Varying in focus from new minimally invasive surgical tools to infant training methods, every indication appears that FY13 will see many new projects successfully complete the steps necessary for patent applications.

One of the more advanced institute projects was the development of the human algometer capable of the objective measurement of pain, by Drs. Julia Finkel and Zenaide Quezado. With the patent filed in early 2011, much of FY12 was spent finalizing the first prototype. The prototype was delivered in summer 2012, and the first clinical trials in humans began shortly thereafter to validate the functionality and safety of the prototype.

Finally, the institute organized cross-department meetings with representatives from the Food and Drug Administration pediatric groups and contributed educational components to National Institutes of Health-sponsored grant applications. The institute anticipates further expansion of these programs and collaborations as well as new initiatives in FY13.

This year marked great strides in converting the innovation potential of the Sheikh Zayed Institute into reality, with tremendous opportunity for even greater successes in the coming year.

- Mahdi Azizian, PhD, a post-doctoral engineer with expertise in image-guided surgery
- Alana Beres, MD, a general surgeon with expertise in minimally invasive techniques
- Amy Burns, MD, a urology fellow
- Katherine Davenport, MD, a general surgeon with an engineering background

This year’s Robert Fellows chose one promising technology innovation around which to develop a full business plan. The Robert Fellows, working with Dr. Raj Shekhar of the Sheikh Zayed Institute, created a promising approach to placement of PICC lines that also monitors changes in PICC line position that can lead to unwanted side effects. Using both novel and existing technologies, this approach will be considered for a provisional application for patent as it moves into the proof-of-concept stage under Dr. Shekhar’s supervision. The creation of the business plan was a critical step in the evaluation of the merits of investing resources in the project.

To serve the Children’s National community at large, the institute launched two initiatives. First, a weekly series of talks and workshops, called Innovation Rounds. While some speakers come from regional and national organizations and universities, most are invited from among the institute’s and Children’s National faculty and staff, with the goal of promoting their innovative work and encouraging internal partnerships. In spring 2012, topics included “Issues in Telehealth,” “Medical Robotics: Fact and Fiction,” and “Next Generation Sequencing Tools for Systems Biology.” Second, the Innovation Curriculum, created primarily for the Robert Fellows, was opened to all interested institute and Children’s National faculty and staff. There were as many as 15 participants at sessions ranging from brainstorming and team-building for all the employees of the institute.


New Faculty

Evanh Fernandes, PhD, conducts research in fabrication. He builds synthetic micro- and nanostructures for delivering therapeutics to precise locations within the body using modalities for targeting markers expressed at the treatment site.

Angela Fletcher, PsyD, specializes in the assessment and treatment of children suffering from complex pain and their families.

Axel Krieger, PhD, has unique expertise in magnetic resonance (MR) compatible robotics, integrated tool design, and image guidance for minimally invasive surgeries.

Vratis Linguraru, PhD, works within the engineering Initiative, to develop tools for computer-aided diagnosis, minimally-invasive interventions, and multi-organ modeling of anatomy and physiology in children.

ego Preciado, MD, PhD, is a pediatric otorhinolaryngologist who conducts research in the genetic and proteomic makeup of the ear, and how it is impacted when the ear develops an infection.

Sarah Rebstock, MD, is a fellowship trained pediatric anesthesiologist who oversees the multi-disciplinary Complex Pediatric Pain Medicine outpatient Clinic, which treats children with complex pain.

Oshre Tatari-Calderone, PhD, MBA, specializes in cancer and immunology research related to red blood cells and is currently part of a translational research study for sickle cell disease that investigates the role of RhoG gene polymorphism in alloimmunization after red blood cell transfusion in African American patients.

Selected Publications

Bioengineering


Immunology

- Davenport KP, Blanco FC, Sandler AD. Pediatric Malignancies, Neuroblastoma, Wilms Tumor, Hepatoblastoma, Rhabdomyosarcoma, and Immunology.

Pain Medicine


Muscle & Biology


Academic Affairs

VISION STATEMENT: The vision of Academic Affairs is to ensure that Children’s National is a leader in pediatric academic medicine. To promote academic success, we foster career development through education, training and mentorship programs, enhance the presence of women and minorities in leadership positions, and encourage faculty engagement in discipline specific organizations leading to national and international leadership positions and recognition.

Academic Affairs works with CRI and hospital leadership, faculty, and administration to support the advancement of Children’s National as a leader in Pediatric Academic Medicine. To accomplish our vision, we provide degree and non-degree certification in clinical and translational research and specialized education and training programs across disciplines and CRI centers. Our aims are:

- The appointment, promotion, and retention of excellent clinical and translational faculty
- Providing junior faculty opportunities for furthering their careers
- Ensuring faculty are skilled in being mentored and mentoring others
- Collecting and analyzing faculty data in support of academic advancement

Naomi L. C. Luban, MD  
Chief, Division of Laboratory Medicine  
Director, Transfusion Medicine/The Edward J. Miller Donor Center  
Component Director, Clinical and Translational Science-CN,  
Vice Chair of Academic Affairs  
Professor of Pediatrics and Pathology, The George Washington University School of Medicine and Health Sciences

Arlene Gendron  
Program Manager, Appointments, Promotions and Tenure  
Office of the Chief Academic Officer

Patricia Minor  
Staff Assistant, Lab Medicine
Academic Affairs

Appointment, Promotion, and Tenure (APT)

An institution-wide overhaul of the faculty onboarding process was initiated this year utilizing a methodology. APT provided valuable input to a paperless, online process of candidate onboarding. That process has been further refined so that faculty can now apply online prior to arrival. A faculty member and chief can track the progress of the application electronically.

Tenure Committee “White Paper” recommendations were fully implemented this past year. Tenure on tenure track must now include a detailed letter from the CRI Director/Division chief detailing funding, protected time allotment, salary, space/resources, mentoring plan and a letter for independence. Tenure track faculty in year 4 of appointment were and will be reviewed for their ability to remain on track. Faculty members at the associate professor level with tenure is now eligible for an annual stipend of $10,000 per year for salary and educational needs.

Tenure and tenure applications were reviewed by the APT committee for nine faculty; two were approved with tenure and seven were promoted to associate professor. Three additional faculty were pre-reviewed for future tenure status and action plans developed with their mentors for future success. This process of pre-review will continue indefinitely. This coming year, the Academic Affairs website will be fully revamped and

Research Education, Training, and Career Development

- Naomi Luban, MD
- Rachel Moon, MD
- Lisa Schwartz, MS, EdD (George Washington University for CTSI-CN)
- Joseph Bocchino, EdD (George Washington University for CTSI-CN)

Research education and training is available to a wide range of CRI and Children’s National faculty and staff including high school and college students, research coordinators, GWUSOM and visiting medical and doctoral students, faculty and staff. Training programs include a six-hour summer lecture series for high school, college, and medical students participating in research within CRI. More than 140 students participated in bench and clinical research and the lecture series this summer. A non-degree, online Introduction to the Principles and Practice
Clinical Research was utilized by 28 faculty and Responsible Conduct of Research training utilizing the interactive video “The Lab” created by the Office of Research Integrity, moderated by its Director Dr. Elizabeth Holmes, was attended by more than 100 CRI staff. This year, CRI was well represented at the US Science and Education Festival. With the National Children’s Museum, Sheikh Zayed Institute, and Dr. Laura Tosi’s Bone Health Initiative, our Science Educational Partnership Award (SEPA), “Being Me”, touched more than 9,000 children and families who learned about obesity, bullying, healthy eating, asthma and bone health; they practiced their surgical skills and inflated healthy and “sick” pig lungs.

Through CTSI-CN, 14 students began the second year of a two-year Masters in Clinical and Translational Research (MsCTR) and 22 began their first year as the second cohort. Among these students are our seven KL2 scholars. Our annual spring K Scholar Retreat hosted 32 K scholars. Our educational initiatives also extend to elementary school students. This year, CRI was well represented at the US Science and Education Festival. With the National Children’s Museum, Sheikh Zayed Institute, and Dr. Laura Tosi’s Bone Health Initiative, our Science Educational Partnership Award (SEPA), “Being Me”, touched more than 9,000 children and families who learned about obesity, bullying, healthy eating, asthma and bone health; they practiced their surgical skills and inflated healthy and “sick” pig lungs.

Other research education training occurred through the two-year fellows curriculum run through the Office of Education and the Clinical Research Training Program for research associates, nurses and other staff.

Master Mentor Group (MMG)

- Dorothy Bulas, MD (Radiology/CAPE)
- Anamaris Colberg-Poley, PhD (Center for Genetic Medicine Research)
- Robert Freishtat, MD, MPH (EM/Center for Genetic Medicine Research)
- Jeffrey Dome, MD, PhD (Hematology-Oncology/Center for Cancer and Immunology Research)
- Julia Finkel, MD (Anesthesiology/Sheikh Zayed Institute)

For summer positions. This summer, 27 GWUSOM medical students took advantage of this opportunity, 25 of whom received Gill or Health Services stipends. Our educational initiatives also extend to elementary school students. This year, CRI was well represented at the US Science and Education Festival. With the National Children’s Museum, Sheikh Zayed Institute, and Dr. Laura Tosi’s Bone Health Initiative, our Science Educational Partnership Award (SEPA), “Being Me”, touched more than 9,000 children and families who learned about obesity, bullying, healthy eating, asthma and bone health; they practiced their surgical skills and inflated healthy and “sick” pig lungs.
Clinical Research Directors (CRDs)

Following several meetings of CRI directors with senior hospital leadership focused on strategic and collaborative research initiatives, we instituted the Divisional Clinical Research Directors (CRD) group. The vision of the CRDs is to encourage an ethos of...
translation and clinical research in the diagnosis, treatment and health outcomes of the patients we care and to further develop pediatric physician specialists. A group of 13 experienced investigators develop a training program for the remaining 28 designated divisional representatives; we will focus on remediation of failed R, K, and CTSI-pilot awards, publish a structured grant presentation plan and workshops among other activities. Several MMG members are part of the CRD pilot group.

Promoting Faculty

The second annual Academic Accomplishment recognition was incorporated into Research and Education Week activities. Research and Education incorporated two Grand Rounds by Dr. Bobander on education and by Dr. Susan Shurin, Director of NHLBI/NIH, on research advances in pediatrics. Honorific awards, 68 new or competitive renewal competitive awards, 14 CTSI-pilot awards, multiple national committee memberships, and the award of five new master degrees to faculty were recognized. Three individuals selected by their peers were recognized for their contributions to mentorship in clinical (Ben Teach), translational (Anthony Sandler) and national (Anne Greene) research. Three faculty members elected to the Society for Pediatric Research/American Pediatric Society.

Focused on leadership training for women and minorities this year with a series of four dinner sessions through CREATE on time management, mentorship, academic advancement and portfolio building. In addition to internal faculty, Dr. R. Grigsby, DSW, Senior Director, Leadership & Talent Development, AAMC, presented on "Talking..." Hospital of Michigan, provided additional training in communication and academic leadership modeling during WATCH Grand Rounds—her title: Changes in Academic Pediatrics to Support the Professional Workforce supplied a valuable focus on how institutions need to adapt to change.

The AAMC Group on Women in Medicine and Science (GWIMS), Early Career Women Faculty Professional Development Seminar accepted three of our up and coming junior faculty from Cardiology (Anitha John), Emergency Medicine (Sabah Iqbal), and the Hospitalist Division (Neha Shah). They will be responsible for new leadership training programming planned for 2011–12.

We increased the Division Chief’s meetings with Drs. Batshaw, Luban and Ottolini from quarterly to monthly to ensure that in-person communication, current educational and academic opportunities and regular dialogue augments electronic notifications.

Selected Publications

The Office of Medical Education

THE OFFICE OF MEDICAL EDUCATION

is responsible for providing an organized educational program for residents and fellows, under the guidance and supervision of the Graduate Medical Education Committee (GMEC). The goal is to facilitate the ethical, professional, and personal developmental of residents and fellows, while ensuring safe and appropriate care for patients.

The Graduate Medical Education office oversees the following programs:

- ACGME Fellowship Programs

In addition, Children’s Office of Continuing Medical Education (CME) assists the institution in carrying out its mission by supporting and assisting faculty to develop and produce formal continuing medical education activities. These activities provide physicians and other pediatric healthcare professionals with the knowledge and skills necessary to enhance their practice of medicine and improve healthcare outcomes through a continuing learning process.

ADMINISTRATORS

Channell Freeman, Sr.
Administrative Assistant for the Pediatric Residency Program

Dewesh Agrawal, MD
Director, Pediatric Residency Program

Terry Kind MD, MPH
Associate Professor of Pediatrics, Director of Pediatric Medical Student Education

Joyce Campbell BSN, MS
CIC Senior Quality Manager

Jacklyn Fuller, MS, GME
Manager

Janet Barbour
Pediatric Residency Program Coordinator

Wilhelmina Bradford
Medical Student Education Administrator

Kyle Shah, MHA, GME
Program Coordinator

Lisa Mercado-Foster
Staff Assistant
The following new programs were formally approved by the DC Board of Medicine:

- Plastic Surgery
- Fetal Medicine
- Bone Marrow Transplant

...through the Electronic Residency Application Service (ERAS), including applications from 55 percent of all fourth year U.S. medical students applying in pediatrics. Highlights from the 2012 Match include the most members of Alpha Omega Alpha honor society, the highest average Step 1 and 2 scores, the most interns with doctorate degrees, and the most under-represented minorities for any of our residency classes on record.

Children's pediatric residency program has expanded during the past few years and now trains a total of 114 residents. The program has seven tracks: Categorical, Community Health, Primary Care, Child Neurology, Genetics, Neurodevelopmental Disabilities, and Intensive Research Pathway. After completion of training, our graduates go on to be...
In community pediatrics, public health, and family care, matching at top fellowships at Children's National and at other elite institutions across the country.

**Academic Productivity**

An innovative program called REACH (Reach, Education and Advocacy in Child Health), our pediatric residents have the ability to submit a research proposal to receive time in a longitudinal fashion over two years to accomplish a scholarly project. For academic years 2011–2012, pediatric residents authored publications from their REACH projects. In addition, 25 projects were presented at major international conferences, and residents were awarded $17,000 in grants to support their projects, winning two prestigious AAP CATCH (Community Advocacy through Child Health) grants. Dr. Ryan will now be leading the REACH program in her new role as Director of Resident Research.

**Pediatric Residency Program at Children's National Innovation**

Children's National and the Pediatric Residency Program at Children's National is proud to announce the unveiling of our On-Line Learning Community, created by Associate Residency Program Directors Dr. Davis and Dr. Edward Sepe, it is an extensive and innovative virtual learning tool originally launched on November 4, 2011. The On-Line Learning Community is a combination of file sharing, media, and other tools like wikis and blogs, which will help residents and faculty organize learning on busy residency. Residents now have a centralized access to all of their educational tools and resources, which in the past were fragmented not only across the program but also faculty and hospital computers.

Range of stored literature. Each resident rotation has an easy-to-use webpage to illustrate goals, rotation requirements, readings, and interactive learning and discussions. Our On-Line Learning Community also has the qualities of a social and professional networking website. Residents and faculty form individual profiles, share their research and have a forum for innovative ideas.

**Children's Academy of Pediatric Educators (CAPE)**

- Ellie Hamburger, MD

Under the leadership of Mary Ottolini, MD, MPH, and Ellie Hamburger, MD, Children's National instituted CAPE in 2010. This group is comprised of 26 clinician educators, representing 14 pediatric disciplines, selected based on their dedication to teaching excellence and educational scholarship. The Academy provides these educational leaders with administrative, design, and research support, as well as a community with whom to exchange and refine innovative initiatives. CAPE has reached beyond its members to host noon meetings for all faculty that focus on medical education innovation. Since CAPE's inception, members have made significant medical education contributions locally, nationally, and internationally. There were 45 collaborative projects among members.

**Productivity: Dissemination**

- Grants: 6 ($6 million)
- National and International Presentations: 89
- Peer-reviewed abstracts: 34
- Published papers: 27

**Productivity: Educational Innovations Produced**

- New Learning Resources (books, guides, etc.): 7
- Incorporation of new modalities into teaching strategies: simulation, social media, electronic health record: 4

In its third year, CAPE members are providing leadership for all divisions in design and delivery of faculty development sessions and in the implementation of a new assessment system for trainees that focuses on outcomes of training. Known as the Milestone project, this system has been mandated by the Accreditation Council for Graduate Medical Education.

**Medical Student Education**

- Terry Kind, MD, MPH

Terry Kind, MD, MPH, Director of Pediatric Medical Student Education, represents Children's National on the New Curriculum Committee at the George Washington University School of Medicine and Health Sciences (SMHS), with a charge to redesign years one through four, strengthening and further integrating the basic and clinical sciences with an overall focus on patient care.

The clinical educational experiences in pediatrics continue to receive strong reviews from students, and there is a strong interest in this field, with about 25 students each year choosing pediatrics as a career. We continue to have about 180 SMHS students annually completing their third year pediatric core clerkship here at Children's on inpatient and outpatient units and at Holy Cross Hospital. In addition, we had 66 visiting fourth year medical students and 47 SMHS fourth year students completing senior electives last academic year (2011–12) at Children's National, under the leadership of Dr. Ryan.
pediatric Acting Internships at Children's National in the 2011–12 academic year. Dr. DeWolfe also led another successful Pediatric Capstone course in 2012 with 26 students.

Children's National faculty served as mentors for approximately 40 senior SMHS medical students in the past two years, in addition to serving as peer mentors for all 20-25 students applying for pediatric and pediatric combined residency programs. Mentorship resulted in several local and national presentations, publications and a successful pediatric capstone course.

Also continue to have about 48 Howard University students annually completing their third year pediatric patient clerkship here at Children's National under the leadership of Drs. Gabrina Dixon and Terry Kind.

The medical education pediatric career advice blog http://PediatricCareer.org has had more than 20,000 page views since launch in 2011. Guests are welcome; please email ideas/submissions to PediatricCareer@childrensnational.org.

**Education Day**

Children's Academy of Pediatric Educators (CAPE) hosted “Education Day” on Wednesday, April 18th as part of Research and Education Day. Education Day featured Robert Englander, MPH, Senior Director of Competency-Based Learning at the American Association of Medical Colleges as the keynote speaker for the Greenberg Medical Education Grand Rounds entitled: A Systems-Vision for Medical Education in the 21st Century, led by CAPE members such as: Virtual Reality and Simulation: A Primer in Uses and Application in Teaching at CNMC, Implementing Online Curricula: Why or Why Not, and How to Get Started, Diagnostic Decision Support: web based technology for practice and education, and Online Teaching & Learning Opportunities at CNMC: How to Get Started, Participate in, or Create Your Own Online Community.

The Board of Visitors Simulation Program at Children's National Medical Center

- Randal Burd, MD
- Janice LePlatte, MS, RN-BC
- Susan Stanley, MSN, RN, Director of Nursing Systems

The Board of Visitors (BOV) Simulation program is celebrating the first year under management of a collaborative team of nurses and physicians. With a generous grant from the Children's National Board of Visitors, the simulation program is directed by Randal Burd, MD, Chief Trauma Surgery, and Susan Stanley, MSN, RN, Director of Nursing Systems. The program is managed by Janice LePlatte, MS, RN-BC, with simulation technician Matthew Schoenherr, BS, EMT. Over the past year, the BOV simulation center facilitated more than 165 sessions and 1,500 clinicians have experienced simulation education using sophisticated high fidelity manikins and task trainers.

The appropriate use of simulation in a professional education program allows participants to hone their clinical skills without danger of harming the patient during the learning process. The BOV simulation center at Children's National provides a safe, non-threatening environment for our clinicians to practice procedures and emergency situations using scenarios.

In addition to highly sophisticated pediatric manikins, equipment and task trainers are available for practicing specific procedures which may include, but are not limited to:
- Intubation
- Chest tube insertion
- PICC line dressing change
- Intraoesseous (IO) access
- Tracheostomy and wound care
- Resuscitation
- Lumbar puncture

The “patient” electronic medical record documentation can be integrated into a scenario to fully simulate an inpatient event. The simulation team is collaborating with Ambulatory Services to develop an emergency preparedness program to be presented in 44 clinics including the Regional Outpatient Centers within Children's National. Several research projects are under way with medicine and nursing using simulation education.

The simulation team has participated in several community advocacy activities such as an outreach venture with Mary Washington Hospital (MWH) in Fredericksburg, Va., in which the BOV Simulation Program provided simulation sessions to assist MWH staff in responding to pediatric emergencies. In addition, the simulation team has provided consultative services in the operation of the high and medium fidelity manikins to Trinity University, Howard University, and the District of Columbia Fire and Emergency Medical Services.
Selected Publications


Grants

SELECTED NIH GRANTS AND OTHER AWARDS

Center for Cancer & Immunology Research
ANGELO. Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN). NIH.
MANI. Clinical and Translational Science Institute at Children's National-RKS-Core. NIH.
DISCH. Role of gangliosides in tumor progression. NIH.
ICHNER. Development of an in vivo screening technology for cancer vaccine immunogens. NIH.
ICHNER. HIV Microbicides and the Vaginal microbome. NIH.
ICHNER. Identification of Antigens for Anti-HIV badly Neutralizing Responses. NIH.
ICHNER. Metagenomic Evaluation of the Oral flora of Pediatric HIV Patients. NIH.
ICHNER. Contract for the International and domestic Pediatric and Maternal HIV Studies. NIH.

Center for Genetic Medicine Research
TASHAW. Gene Therapy for Urea Cycle Disorders-Object 2. NIH.
UMAN. Propranolol vs Prednisolone for Infant Angiomas-A Clinical and Molecular Study. NIH CHD.
HAN. Molecular Pathophysiology of FSHD Muscular Dystrophy via Genome-wide approaches. NIH NIAMS.
IAAN. CINRG Infrastructure for Clinical Trials in Duchenne Dystrophy. DOD.
IAAN. Clinically Meaningful Outcomes for Duchenne Dystrophy. NIH.

Center for Neuroscience Research
BERL. Cognitive Impairment Moderated by Working Memory in Pediatric Partial Epilepsy. NIH.
CORBIN. Development of the Basal Telencephalic Limbic System. NIH.
DuPLESSIS. Quantitation of Insult and Injury to the Preterm Brain. NIH.
GALLO. Intellectual and Developmental Disabilities Research Centers (IDDRC) at Children's Research Institute. NIH.
GALLO. Postdoctoral Training in Developmental Disabilities Research. NIH.
GALLO. A Common Glial-Neuronal Progenitor in Postnatal Brain. NIH.
JONAS. Protection of Developing White Matter during Cardiac Surgery. NIH.

Connor. Pre-clinical Toxicology for Exon Skipping. DOD USAMRAA.
FREISHTAT. Vitamin D, Steroids, and Asthma in African American Youth. NIH NIMHD.
FRICKE. BioEffects of Ultra-High MRI Gradient Slew Rates. NIH NINDS.
HATHOUT. Biomarker discovery and validation in a Duchenne dystrophy natural history. NIH NIAMS.
HILL. DICERT and the Pleuropulmonary Blastoma Family Cancer Syndrome. NIH NCI.
HOFFMAN. Center of Research Translation of Systemic Exon-skipping in Muscular Dystrophy - PROJECT I. NIH NIAMS.
HOFFMAN. Improved Diagnostic of the Muscular Dystrophies. NIH NINDS.
HOFFMAN. NCRR-DC Core Molecular and Functional Outcome Measures in Rehabilitation Medicine-Pilot Project. NIH NIAMS.
JONAS. Protection of Developing White Matter during Cardiac Surgery. NIH.
TUCHMAN. N-acetylglutamate Synthase: Structure, Function & Defects. NIH NIDDK.
TUCHMAN. The Molecular Bases of Inherited Urea Cycle Disorders and Ureagenesis Regulation. NIH NIDDK.
VANDIVER. Nuclease Immune Mediated Brain & Lupus-like conditions: Natural history, Pathophysiology, Diagnostic and Therapeutic Modalities with Application to other disorders of Autoimmunity. European Union.
WANG. Systems Biology of Glucocorticoids in Muscle Disease. DOD.
WU. An in vitro Model of Glandular Hyperplasia in Pediatric Chronic Rhinosinusitis. NIH NCRR.
Selected NIH Grants and Other Awards

DI. Enhanced EGF Receptor Signaling in White Matter Injury in Perinatal Hypoxia.

ROPOULOS. Advanced Pediatric Brain Imaging Research and Training Program. DOD.

White Matter Injury in Perinatal Hypoxia.

Novel Ubiquitin Dependent Pathways Regulating Neural Tube Closure and Placentation.

DI. Elucidation and rescue of amygdala abnormalities in the Fmr1 mutant mouse model of X Syndrome. Autism Speaks.

The basis of epilepsy in the mouse model of lissencephaly. Epilepsy Foundation.

ARD. Early Onset Epilepsy Consortium.

Epileptic Epilepsy Research Foundation.

FINKEL. A Randomized, Placebo Controlled, Multi-Center Study of the Efficacy, Pharmacokinetics (PK) and Pharmacodynamics (PD) of Intravenous (IV) Acetaminophen for the Treatment of Acute Pain in Pediatric Patients. Cadence.


FINKEL. Open-Label Evaluation of the Pharmacokinetic Profile and Safety of Tapentadol Oral Solution for the treatment of Postsurgical pain in Children and Adolescents Aged From 6 to Less Than 18 Years. Janssen Research & Development, LLC.

CLEARY. Actively Compliant Parallel End-effector Mechanism for Medical Interventions. DOD.

CLEARY: Robotic System for Natural Orifice Transluminal Endoscopic Surgery. DOD.


BEATON. Developing a Pathway to Diagnosing Early Rheumatic Heart Disease. KL2.

CARTER. Relating Documentation to Clinical Workflow in Pediatric Trauma Resuscitation. KL2.


Zayed Institute for Pediatric Medical Innovation

FINKEL. A Randomized, Placebo Controlled, Multi-Center Study of the Efficacy, Pharmacokinetics (PK) and Pharmacodynamics (PD) of Intravenous (IV) Acetaminophen for the Treatment of Acute Pain in Pediatric Patients. Cadence.


CLEARY. Actively Compliant Parallel End-effector Mechanism for Medical Interventions. DOD.

CLEARY: Robotic System for Natural Orifice Transluminal Endoscopic Surgery. DOD.


Academic Affairs

BEATON. Developing a Pathway to Diagnosing Early Rheumatic Heart Disease. KL2.

CARTER. Relating Documentation to Clinical Workflow in Pediatric Trauma Resuscitation. KL2.


### 2012 (Most Recent Activity Listed)

#### ENTOR(S) TITLE AFFILIATION U.S.NO. DATE

<table>
<thead>
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<th>Title</th>
<th>Affiliation</th>
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<td>Antibody Based Method for Isolating TH1 and TH2 Helper Lymphocytes from Human Peripheral Blood</td>
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<td>A Methodology for the Regional Analysis of Electronic Health Record Data Using Geographic Information Systems and Statistical Data Mining</td>
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CHILDREN’S NATIONAL MEDICAL CENTER, located in Washington, DC, is a proven leader in the development of innovative new treatments for childhood illness and injury. Children’s has been serving the nation’s children since 1870. Children's National is proudly ranked among the best pediatric hospitals in America by U.S. News & World Report and the Leapfrog Group. Children’s also has been recognized by the American Nurses Credentialing Center as a Magnet® designated hospital, the highest level of recognition for nursing excellence that a medical center can receive. Children’s Research Institute, the academic arm of Children’s National Medical Center, encompasses the translational, clinical, and community research efforts of the institution.

For more information, visit:
www.ChildrensNational.org/Research

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