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NEWS

Rose F. Kennedy Intellectual and Developmental Disabilities Research Center

Living with Lysosomal Disease

In a break with the past, Einstein's 2015 celebration of Rare Disease Day focused not on the idea of rare disease generally but instead highlighted the lives of individuals living with a distinct group of 60 syndromes known as lysosomal storage disorders (LSDs). This focus was chosen as a way of celebrating this year as the 50th anniversary of the discovery of the cause of these diseases—by Dr. H. G. Hers at the University of Louvain in Belgium, and as a means of spotlighting contributions that scientists and doctors at Einstein's Rose F. Kennedy Intellectual and Developmental Disabilities Research Center (IDDRC) have made with regard to LSDs, and in particular with regard to Niemann-Pick type C and Tay-Sachs.

On March 2, in the Michael F. Price Center for Genetic and Translational Medicine/Harold and Muriel Block Research Pavilion, the RFK IDDRC Rare Disease Day program opened with brief introductory remarks by center director Steven U. Walkley, D.V.M., Ph.D., that were followed by two compelling panel discussions, the first of which was made up of individuals living with a range of LSDs, from Gaucher to Maroteaux-Lamy (MPS VI). During this discussion, Robert W. Marion, M.D. '79, former director of the genetics division in pediatrics and of the Children's Evaluation and Rehabilitation Center (CERC), along with Frederick J. Kaskel, M.D., Ph.D., division chief of pediatric nephrology and vice chair for affiliate and network relations in pediatrics, moderated by asking each individual to share her unique clinical story with the audience. The panelists were Suzanne Krupskas (representing Gaucher disease), Alena Galan (MPS VI),

(continued on page 2)



Jill Wood and Jonah Weishaar



MESSAGE FROM THE DIRECTOR

STEVEN U. WALKLEY, D.V.M., PH.D.

Director, Rose F. Kennedy Intellectual and Developmental Disabilities Research Center
Professor, Dominick P. Purpura Department of Neuroscience
Professor, Department of Pathology
Professor, Saul R. Korey Department of Neurology

Rare Disease Day has come to be celebrated annually worldwide—as a day to reflect on individuals with rare diseases apart from their disorders, but also as a day to bring into focus what these diseases are and how research can facilitate their understanding and treatment. Just under 1 percent of the estimated 7,000 rare diseases affect the “recycling center” of cells known as the lysosomal system. Remarkably, while these diseases—Tay-Sachs, Niemann-Pick, Gaucher, Pompe and others—have been known clinically for well over a century, only 50 years ago this year was their cause discovered to be centered on an abnormal lysosomal system.

Given this anniversary and the long history of lysosomal disease research at Einstein and at Montefiore, Einstein’s University Hospital and academic medical center (beginning with Dr. Saul Korey and his colleagues), we chose this group of disorders for our 2015 Rare Disease Day focus. (See adjoining article.) In recent years, enormous strides have been made in understanding the close connections between lysosomes and less-rare diseases. Alzheimer’s, for example, has shown evidence of a dysfunctional lysosomal system, and even the Ebola virus has been found to rely on a specific lysosomal protein to escape the lysosome and infect cells. Increasingly, therapies are being developed for lysosomal disorders, lending hope that one day all individuals diagnosed with one of these conditions will indeed lead full and productive lives.

Living with Lysosomal Disease *(continued from page 1)*

Gail Graf (Fabry disease) and Laura Kruppenacker (cystinosis). The second panel was made up of parents—Jill Wood (parent of MPS IIIC child Jonah Weishaar, www.jonahsjustbegun.org) and Phil and Andrea Marella (parents of Niemann-Pick type C child, www.danasangels.org) who have, as a result of their experiences, become advocates dedicated to improving the lives of not only their children but of other patients and their families by garnering political and financial support.

The panel discussions were followed by a reception in the Leo Forchheimer Medical Science Building featuring a singing performance by 17-year-old Ms. Galan, and an art and photography exhibition consisting of selections from Levi Gershkowitz’ “Living in the Light”™



From left: Frederick J. Kaskel, M.D., Ph.D.; Judy L. Aschner, M.D.; Steven U. Walkley, D.V.M., Ph.D.; Alena Galan; Levi Gershkowitz; and Robert W. Marion, M.D.

project, a photographic compilation of individuals with LSDs, and selections from Genzyme Corporation’s “Expressions of Hope,” a collection of artworks by members of the LSD community.



ON THE WEB: For the full article, please visit www.einstein.yu.edu/centers/iddrc/highlights.aspx

THIRD ISABELLE RAPIN CONFERENCE ON COMMUNICATION DISORDERS: RETT SYNDROME



From left: Dr. Walkley; Huda Zoghbi, M.D.; Michael D. Brenowitz, Ph.D.; and Allen M. Spiegel, M.D., the Marilyn and Stanley M. Katz Dean at Einstein.

On Dec. 10, 2014, the RFK IDDC hosted its annual Isabelle Rapin Conference on Communication Disorders and, as in years past, the event involved a fully engaged audience of Einstein researchers, Montefiore doctors, students and allied health professionals. Each year the conference has focused on a different neurodevelopmental disorder with an atypical communication presentation, and this year Rett syndrome (RTT) was chosen.

The conference featured talks by some of today’s most eminent researchers and clinicians specializing in the study and treatment of RTT, in particular, Huda Zoghbi, M.D., of Baylor College of Medicine, who has done seminal work on the molecular basis of Rett syndrome, and Michael Green, M.D., Ph.D., of the University of Massachusetts, who gave a detailed and compelling elucidation of his success in X-reactivation, a strategy that could potentially revolutionize treatment options for RTT patients. Aleksandra Djukic, M.D., Ph.D.; John J. Foxe, Ph.D.; Michael D. Brenowitz, Ph.D.; and Aristeia S. Galanopoulou, M.D., Ph.D., provided the audience with current Einstein-Montefiore contributions to the research. Additionally, Monica Coenraads, co-founder and executive director of the Rett Syndrome Research Trust (RSRT) and parent of an afflicted child, provided a touching snapshot of what life is like for the RTT individuals and their families, and of the work the RSRT has done to promote research.

In the afternoon, clinical sessions covering topics ranging from bone health and scoliosis management to syndrome-related gastrointestinal issues and communication strategies were presented by Suzanne Abraham, Ph.D.; Chhavi Agarwal, M.D.; Anthony Loizides, M.D.; and Vishal Sarwahi, M.D.

ON THE WEB: See more at www.einstein.yu.edu/centers/iddrc/highlights.aspx

featured investigator

SOPHIE MOLHOLM, PH.D.



Associate Professor, Department of Pediatrics
Associate Professor, Dominick P. Purpura
Department of Neuroscience
Muriel and Harold Block Faculty Scholar in
Mental Illness, Department of Pediatrics

In July, **Dr. Sophie Molholm** was named director of the Sheryl and Daniel R. Tishman Cognitive Neurophysiology Laboratory (CNL) and associate director of the RFK IDDRC. Dr. Molholm will take over for John J. Foxe, Ph.D., who was recently named chair of the department of neurobiology at the University of Rochester School of Medicine and Dentistry. Dr. Molholm is also associate professor of pediatrics, associate professor in the Dominick P. Purpura Department of Neuroscience, the Muriel and Harold Block Faculty Scholar in Mental Illness and director of the RFK IDDRC's Human Clinical Phenotyping Core.

Dr. Molholm, a member of the Einstein research community since 2010, is a leader in the field of multisensory integration,

particularly as it relates to autism, and has authored or co-authored more than 70 peer-reviewed research studies, review articles, commentaries and book chapters. Her recent National Institutes of Health-funded research projects have established links among deficits in multisensory integration, potential biomarkers and autism spectrum disorders (ASDs). Future projects will aim to test the efficacy of behavioral interventions in ameliorating some common ASD symptoms. Said Dr. Walkley, "With a collaborative spirit and wide-ranging research interests, Sophie has proven an invaluable member of the IDDRC. We all look forward to her expanded role here."

Allen M. Spiegel, M.D., the Marilyn and Stanley M. Katz Dean at Einstein, added that "her excellence in research and leadership in the field make her the perfect choice to take the reins of the Tishman CNL and help lead the IDDRC."



ON THE WEB: For the full article, please visit www.einstein.yu.edu/r/molholm2015

IDDRC legacy series



THEODORE A. KASTNER, M.D.



Associate Professor of Clinical Pediatrics,
Department of Pediatrics
Ruth L. Gottesman Chair in Developmental
Pediatrics
Chief, Division of Developmental Medicine,
Department of Pediatrics
Director, Children's Evaluation and
Rehabilitation Center

In April, Albert Einstein College of Medicine and Montefiore Health System named **Dr. Theodore A. Kastner** the director of CERC, which for almost 60 years has provided community-based care to children with intellectual and developmental disabilities (IDDs) and their families. Dr. Kastner, who earned his M.D. from the University of Connecticut School of Medicine in 1981, has the distinction of having received his pediatric training at Jacobi, and completed a fellowship in developmental pediatrics at the Kennedy Center in CERC. After leaving CERC, Dr. Kastner worked as a developmental pediatrician, growing a large and successful practice. Since 1995 he has served as president of the Developmental Disabilities Health Alliance, Inc. (DDHA), in New Jersey, which is the largest single provider of healthcare and managed-care services to those with IDDs in the state. Through both his practice and his relationship with the DDHA, Dr. Kastner's career has been marked by a drive to develop innovative approaches in providing healthcare services to children with IDDs and their families.

Recently, Dr. Kastner was responsible for bringing to Einstein and Montefiore a \$2.4 million grant provided by the New York State Balancing Incentive Program Innovation Fund. The New York State Department of Health established this fund to expand and improve access to community-based services for people with disabilities. The fund will allow Einstein and the DDHA, along with the Community Resource Center for the Developmentally Disabled, Inc., to establish three centers that can provide home health services (integrated care, including primary care, mental health services, behavioral support and all-around case management) to IDD patients and their families. Over the years Dr. Kastner has proven himself a leader in creating more-efficient and cost-effective systems of clinical care for those with IDDs and their families—and he continues to do so. Dr. Kastner said, "It is a particular honor to return to the Bronx and lead CERC during its integration with Montefiore."



ON THE WEB: For more information, please visit www.einstein.yu.edu/r/kastner2015
www.einstein.yu.edu/r/cercgrant2015

awards and grants

CONGRATULATIONS!

Steven U. Walkley, D.V.M., Ph.D., was chosen as the University of Wisconsin's 2015 Harry Waisman Memorial Lecturer. He presented "Lysosomal Disease at Half Century: A New Era Emerges" on Jan. 23 at the John D. Wiley Conference Center. See more at www.einstein.yu.edu/centers/iddrc/highlights.aspx.

John M. Greally, M.B.B.Ch., Ph.D., received Einstein's seventh annual Faculty Mentoring Award along with Paul R. Marantz, M.D., M.P.H. (clinical sciences). See more at www.einstein.yu.edu/r/mentors2015.

2015 RFK IDDRC PILOT AND FEASIBILITY AWARDS

Joan W. Berman, Ph.D. (1/1/15–12/31/16)
Is increased surface CCR2 on mature monocytes from perinatally HIV infected and perinatally HIV exposed children a biomarker of neurocognitive impairment?

Robert A. Coleman, Ph.D. (1/1/15–12/31/16)
Dynamic live cell single molecule imaging of MeCP mutants linked to neurological disorders

Mamta Fuloria, M.B.B.S. (1/1/15–12/31/16)
Biomarkers to predict neurodevelopmental outcomes in very preterm infants

Jeannine Gerhardt, Ph.D. (1/1/15–12/31/16)
Elucidation of the mechanism of trinucleotide repeat instability in cells derived from Fragile X patient

Tingwei Guo, Ph.D. (1/1/15–12/31/16)
Genetic causes of intellectual disability in 22q11.2 DS patients

Herbert M. Lachman, M.D. (1/1/15–12/31/16)
Primary microglial dysfunction in a subset of ASD

Jose L. Pena, M.D., Ph.D. (1/1/15–12/31/16)
Learning during an early sensitive period in chickens

David C. Spray, Ph.D. (1/1/15–12/31/16)
MeCP2, gap junctions and glia

RECENT GRANTS

Michael D. Brenowitz, Ph.D.
Rettsyndrome.org
1/1/15–12/31/15
A biophysical basis for cellular and developmental regulation by MeCP2

Aristea S. Galanopoulou, M.D., Ph.D.
NIH/NINDS 1R01NS091170-01A1
7/1/15–6/30/20
GABA-inflammation interplay in infantile spasms

David H. Hall, Ph.D.
NIH 5R24OD010943
9/1/14–3/31/18
Center for C. elegans Anatomy

Eric Hollander, M.D.
Foundation of Prader-Willi Research
6/1/15–5/31/17
Oxytocin vs. placebo for the treatment of ASD features and hyperphagia in children and adolescents with Prader-Willi syndrome

Herbert M. Lachman, M.D.
NIH R01MH099427
8/14–8/18
Monoallelic expression in neurons derived from induced pluripotent stem cells

Sophie Molholm, Ph.D.
NIH/NICHD R01HD082814
9/1/15–8/31/19
Sensory integration therapy in autism: Mechanisms and effectiveness

Bernice E. Morrow, Ph.D.
Fondation Leduqc
8/1/15–7/31/20
22q11DS: Novel approaches to understand cardiopharyngeal pathogenesis

David C. Spray, Ph.D.
NIH/NINDS
7/1/15–6/30/20
The astrocyte nexus: Cx43 protein interactions

UPCOMING EVENTS

The Fourth Annual Isabelle Rapin Conference on Communication Disorders, featuring discussion of 22q11.2 deletion syndrome, is scheduled for Thursday, Dec. 3, 2015, in the LeFrak Auditorium.

Please visit the website to view details of upcoming RFK IDDRC-sponsored events: www.einstein.yu.edu/centers/iddrc/seminars-workshops/.

IN THE MEDIA

Lisa H. Shulman, M.D., RFK IDDRC member and director of Infant and Toddler Services and the Rehabilitation, Evaluation and Learning for Autistic Infants and Toddlers program at CERC, presented the results of a recent study at the Pediatric Academic Societies' annual meeting in San Diego, finding that 7 percent of toddlers diagnosed with ASDs no longer met the diagnostic criteria several years later. (April 26, 2015.) See more at www.einstein.yu.edu/r/afterasd2015.

The *New York Times* featured an article in late March about **John M. Greally, M.B.B.Ch., Ph.D.**, and Daniel Kohn, a Brooklyn-based painter and conceptual artist who has been working with Einstein's genetic researchers. "The problem today is that biological data are often abstracted into the digital domain," Dr. Greally said, "and we need some way to capture the gestalt, to develop an instinct for what's important." (March 27, 2015.) See more at www.einstein.yu.edu/r/greallynyt2015.

NEW RFK IDDRC MEMBERS

Robert A. Coleman, Ph.D. (Anatomy and Structural Biology)

Mamta Fuloria, M.B.B.S. (Pediatrics)

Jeannine Gerhardt, Ph.D. (Cell Biology)

William A. Gomes, M.D., Ph.D. (Radiology)

Tingwei Guo, Ph.D. (Genetics)

Theodore A. Kastner, M.D. (Pediatrics)

To become a member, please visit www.einstein.yu.edu/centers/iddrc/members/become-investigator.aspx

ALBERT EINSTEIN ROSE F. KENNEDY IDDRC

Our mission: to improve the lives of children with intellectual and developmental disabilities through research and clinical outreach. The center actively supports and encourages collaboration among bench scientists and clinicians.

ADMINISTRATION

Director
Steven U. Walkley, D.V.M., Ph.D.

Associate Director
John J. Foxe, Ph.D.

Administrator
Lisa Guillory, M.A.

EXECUTIVE COMMITTEE MEMBERS

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Francine H. Einstein, M.D.
Robert W. Marion, M.D.
Sophie Molholm, Ph.D.
Bernice E. Morrow, Ph.D.
Vytautas Verselis, Ph.D.

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