

## Rose F. Kennedy Intellectual and Developmental Disabilities Research Center

### Birth of Hope for People with Intellectual Disabilities: 50 Years and Counting

*"Although we have attacked on the broad front the problems of mental illness, although we have made great strides in the battle against disease, we as a nation have for too long postponed an intensive search for solutions to the problems of the mentally retarded.\* That failure should be corrected."*

– President John F. Kennedy  
October 11, 1961



Rose (fourth from right) and Robert Kennedy (third from right) at the groundbreaking of the Rose F. Kennedy Center in November 1966.

A week after President Kennedy spoke these words at a news conference, Eunice Kennedy Shriver hosted a meeting of the 27-member President's Panel on Mental Retardation at the White House. The panel, headed by Dr. Leonard Mayo, was charged with delivering—within a year—a report on what the nation should do to address the problem raised by the president.

The panel quickly broke into two factions, one headed by Dr. Seymour Kety and other scientists who emphasized the importance of basic research, the second by Dr. Anne Ritter and other behavioral/social scientists who advocated for high-quality clinical care. In 1962, after a year of debate, the President's Panel delivered

its report. It recommended development of research facilities (called Mental Retardation Research Centers or MRRCs) to advance understanding of the causes of the condition, and university-affiliated facilities (UAFs) to address the need for excellent clinical care for those affected.

At around the same time, an article appeared in the *Saturday Evening Post* in which Eunice Kennedy Shriver revealed for the first time that her sister, Rose Marie Kennedy, had intellectual

disability. People soon realized that the president's October 1961 news conference had held personal meaning; one of his siblings was affected. In October 1963, just three weeks before he was assassinated, President Kennedy signed into law PL88-164, which established 12 MRRCs and 18 UAFs.

The MRRCs were to be funded by a newly established section of the National Institutes of Health (NIH),

*(continued on page 2)*

\*At the time these words were spoken "mental retardation" was the accepted term for the condition we now know as "intellectual disability."

## Birth of Hope for the Intellectually Disabled *(continued from page 1)*

known as the National Institute of Child Health and Human Development (NICHD), which had been created as a result of lobbying efforts made by Eunice Kennedy Shriver and others on behalf of the Kennedy family. Following widespread recognition of the pejorative nature of the term 'mental retardation,' the NICHD changed the name of the MRRC's to Intellectual and Developmental Disabilities Research Centers (IDDRCs).

A key advisor to the Kennedys during this period was Dr. Robert Cooke, a prominent pediatrician at Johns Hopkins who himself had two children with intellectual disability. A colleague of Dr. Cooke's in Baltimore was another pediatrician, Harry Gordon, who in 1962 was recruited to Albert Einstein College of Medicine. Once here, Dr. Gordon, undoubtedly through the influence of Dr. Cooke, set out to bring one of the coveted 12 MRRCs to Einstein.

His effort was successful, and in 1966,

Rose and Robert Kennedy attended groundbreaking ceremonies for the construction of a new center, which would bear the name of the president's mother.

As Rose Kennedy said during this momentous event, "Fifty years ago when I was seeking help for my own daughter who was retarded, there was no place to turn. I was bewildered, frustrated and heartbroken to learn how little was known and how little could be done...I hope my name, as a mother of a retarded child, may bring faith and hope and confidence to other mothers, as they realize the perseverance and zeal, the self-sacrifice and devotion, of scientists and doctors working here."

Over the past half century, we have come to better understand the causes of intellectual disability and ways to treat it. The Rose F. Kennedy Center has been at the forefront of many of these developments; in 1974, the center also gave rise to one of the first departments of

neuroscience in the country, under the leadership of Dr. Dominick Purpura, who succeeded Dr. Gordon as the center's director.

To celebrate these successes, and in anticipation of future advances in intellectual disability research and treatment, we are holding a 50th anniversary symposium for the Rose F. Kennedy IDDRC on November 2, 2017. Please mark your calendars for this important event.

– Steven U. Walkley, director, the Rose F. Kennedy Intellectual and Developmental Disabilities Research Center (RFK IDDRC)

### SAVE THE DATE!

RFK IDDRC will celebrate its  
50TH ANNIVERSARY on  
Thursday, November 2, 2017!

Mark your calendars; details to follow!

## THE FIFTH ANNUAL ISABELLE RAPIN CONFERENCE: TUBEROUS SCLEROSIS

On November 8, 2016, the Rose F. Kennedy Intellectual and Developmental Disabilities Research Center (RFK IDDRC) hosted its fifth annual Isabelle Rapin Conference, named for the late professor emerita of the Saul R. Korey Department of Neurology and the department of pediatrics. Each year, the conference focuses on a genetically based neurodevelopmental disorder, or a group of such disorders, that is of particular interest to the clinical and research community at Einstein-Montefiore.

This year, the focus was tuberous sclerosis (TS), a rare, multisystemic genetic disease that causes the growth of benign tumors all over the body, including, in some cases, in the brain and other vital organs. Like many genetic disorders, TS is highly variable, with some patients exhibiting many more signs and symptoms than others. The complexity of TS requires the kind of multidisciplinary approach that has become a hallmark of the Einstein-Montefiore system; clinicians actively and comprehensively treat people with the disease at the Neurocutaneous Center at the Children's Hospital at Montefiore (CHAM) in the Bronx ([www.cham.org/programs-centers/neurocutaneous-center](http://www.cham.org/programs-centers/neurocutaneous-center)).

The November conference included a number of notable speakers, among them Elizabeth A. Thiele, M.D., Ph.D., director of the Pediatric Epilepsy Program at the Herscot Center for Tuberous Sclerosis Complex at Massachusetts General Hospital and professor of neurology at Harvard Medical School; Dr. Steven L. Roberds,

chief scientific officer of the Tuberous Sclerosis Alliance; Peter Crino, M.D., Ph.D., professor and chair of neurology at the University of Maryland School of Medicine; and Michael Wong, M.D., Ph.D., the Allen P. and Josephine B. Green professor of pediatric neurology at the Washington University School of Medicine.

From Einstein-Montefiore, the event featured Fatema Malbari, M.D., director of the Montefiore Neurocutaneous Center, and Adam S. Levy, M.D., director of pediatric neuro-oncology at CHAM.

The IDDRC-sponsored event also included a presentation by Luisa Vidal, a TS family caregiver, who offered a personal view of the disorder. For more details, go to [www.einstein.yu.edu/docs/centers/iddrc/Rapin-2016-Program.pdf](http://www.einstein.yu.edu/docs/centers/iddrc/Rapin-2016-Program.pdf); for video, see [www.einstein.yu.edu/centers/iddrc/seminars-workshops/](http://www.einstein.yu.edu/centers/iddrc/seminars-workshops/).



Back row, left to right: Steven U. Walkley, director of the IDDRC; Melissa P. Wasserstein; Peter Crino; Michael Wong; and Solomon L. Moshe. Front row, left to right: Adam S. Levy; Fatema Malbari; Isabelle Rapin; Luisa Vidal, a relative of a tuberous sclerosis patient; Elizabeth A. Thiele; Steven L. Roberds; Sophie Molholm, associate director of the IDDRC; and Aristeia S. Galanopoulou.

We are saddened to report that on May 24, 2017, Isabelle Rapin, M.D., professor emerita in the Saul R. Korey Department of Neurology and of pediatrics at Einstein and a neurologist at Montefiore, passed away following a brief illness. She was 89.





## R. SUZANNE ZUKIN, Ph.D.



**Professor**, Dominick P. Purpura Department of Neuroscience  
**F. M. Kirby Chair in Neural Repair and Protection**  
**Director**, Neuropsychopharmacology Center

One of the most notable researchers at Albert Einstein College of Medicine—and within the Rose F. Kennedy Intellectual and Developmental Disabilities Research Center (RFK IDDRC)

—is Dr. R. Suzanne Zukin, who came to Einstein in 1977 immediately following a postdoctoral fellowship in the laboratory of Dr. Daniel Koshland at the University of California at Berkeley. Prior to joining Dr. Koshland's lab, Dr. Zukin had already distinguished herself by having earned a bachelor's degree, *cum laude*, from Bryn Mawr College in chemistry, and by having received her Ph.D., with distinction, from the Johns Hopkins University School of Medicine. However, it was while in Dr. Koshland's lab at Berkeley that Dr. Zukin began her distinguished career of discovery and found that bacteria such as salmonella, use chemoreceptors to detect metal ions such as  $Mg^{2+}$ .

Within two years of having established her lab at Einstein, Dr. Zukin published her seminal paper on the phencyclidine receptor (1979), a paper that became a citation classic in 1982. By 1987, Dr. Zukin was a full professor in the department of neuroscience and director of the Neuropsychopharmacology Center at Einstein. In 1997, she made her landmark discovery that  $Ca^{2+}$ -permeable AMPA receptors are expressed in response to neuronal activity and insults and play a critical role in neuronal injury and neuronal death, and in 2003, her group showed that the mechanism underlying the switch in AMPAR phenotype at insulted hippocampal synapses from  $Ca^{2+}$ -impermeable to  $Ca^{2+}$ -permeable involves REST-dependent epigenetic remodeling. It is now well established that

$Ca^{2+}$ -permeable AMPA receptors are important in synaptic plasticity, the response to stress and a myriad of brain disorders, including stroke, global ischemia, epilepsy, spinal cord injury, cocaine addiction and withdrawal, ALS and alcoholism. In 2008, Dr. Zukin became the first F. M. Kirby Chair in Neural Repair and Protection, and in 2012 she published another seminal finding: that the gene-silencing transcription factor REST orchestrates epigenetic remodeling and drives the switch in synaptic NMDA receptors during brain development. This is significant in that it represents the first demonstration that REST is expressed in differentiated neurons under physiological conditions and is critical to the fine-tuning of genes involved in synaptic plasticity. Dr. Zukin's work on synaptic NMDA, AMPA receptor properties, mTOR signaling and synaptic efficacy in response to external cues, via epigenetic mechanisms, is far-reaching and was critical in uncovering the mechanisms that underlie autism, fragile X syndrome, schizophrenia, stroke and addictions.

Among her many awards and honors, in 1983 Dr. Zukin was inducted into the American College of Neuropsychopharmacology, and was elected a lifetime fellow in 2013. In 2009, she was a recipient of the McKnight Neuroscience of Brain Disorders Award, and in 2014, she was given the NARSAD Distinguished Investigator Award. She has been the beneficiary of numerous NIH and foundation grants, most recently *Rest-Activated Program of Gene Expression in Ischemia* (5R01 NS046742) and *Epigenetic Remodeling of NMDA Receptors* (5R01 HD083828-01A1), and she is the author of over 185 peer-reviewed papers in eminent journals and over 40 book chapters.



**ON THE WEB:** For more about Dr. Zukin and the work her lab is doing, visit

[www.einstein.yu.edu/faculty/6725/r-suzanne-zukin/](http://www.einstein.yu.edu/faculty/6725/r-suzanne-zukin/)

## "LIVING IN THE LIGHT™": INTERNATIONAL RARE DISEASE DAY 2017 WITH LEVI GERSHKOWITZ

On February 28, 2017, the RFK IDDRC hosted Einstein's fifth annual Rare Disease Day celebration. The event featured photojournalist/ethnographer Levi Gershkowitz, founder of *Living in the Light*, a nonprofit advocacy initiative that uses photography and personal narratives to educate the public about the difficulties and challenges faced by those affected by rare diseases.

For the past five years, *Living in the Light* has attempted to convey the unspoken thoughts and feelings of people with rare diseases in hopes that the two-dimensional view, which usually shows people only as patients and focuses solely on their diseases, can be expanded to include full portraits of each unique human being. The event also featured presentations by parent advocates, and a separate poster session in the Forchheimer Building, on Main Street, highlighting rare diseases Einstein-Montefiore researchers are currently studying. For additional information, visit [www.einstein.yu.edu/centers/iddrc/seminars-workshops/](http://www.einstein.yu.edu/centers/iddrc/seminars-workshops/).



Levi Gershkowitz, *Living in the Light* founder and photographer, standing next to one of his "storyboards" in the Price Center/Block Research Pavilion lobby.

# awards and grants

## 2017 RFK IDDRC PILOT AND FEASIBILITY AWARDS

**Scott Emmons, Ph.D.** – *Binding Studies of Neural Cell Adhesion Proteins*

**Anna Francesconi, Ph.D.** – *Exploring nAChR Function in Fragile X Syndrome*

**Bryen Jordan, Ph.D.** – *Converging Mechanisms in Autism Spectrum Disorder*

**Bernice Morrow, Ph.D.** – *Whole Exome Sequence Analysis of ID in Patients with 22q11.2DS*

**Lars Ross, Ph.D.** – *Cerebellar Hypoplasia and Saccadic Adaptation in Autism Spectrum Disorder*

**Suzanne Zukin, Ph.D.** – *Autophagy as a New Therapeutic Target for Cognitive Defects in Fragile X Syndrome*

## RECENT NIH GRANTS

**Hannes Buelow, Ph.D. (PI)**  
NIH/NINDS 1R01NS096672-01A1  
09/01/2016–05/31/2021  
*Genetic Analyses of Dendrite Development in Caenorhabditis elegans*

**Scott W. Emmons, Ph.D. (PI)**  
NIH/NIMH 1R01MH112689-01  
02/15/2017–11/30/2021  
*Neural Cell Adhesion Genes in Synaptic Specificity*

**Aristea Galanapoulou, M.D., Ph.D. (PI), and Solomon Moshe, M.D. (PI)**  
NIH/NINDS 1U54 NS1000064-01  
01/15/2017–11/30/2021  
*The Epilepsy Bioinformatics Study for Anti-Epileptogenic Therapy (Epibios4RX) Project 2*

**Steven Walkley, D.V.M., Ph.D., and Sophie Molholm, Ph.D.**  
U54 HD090260-01  
09/01/2016–08/31/2021  
*Support for the Rose F. Kennedy IDD Research Center*

**R. Suzanne Zukin, Ph.D. (PI)**  
NIH/NICHD 1R01 HD083828-01A1  
09/08/2016–06/30/2021  
*Epigenetic Remodeling of NMDA Receptors*

## CONGRATULATIONS!

**Dr. Aristea Galanapoulou** received the 2017 Saul R. Korey Prize for Translational Medicine and Science at Albert Einstein College of Medicine.

**Dr. Karen Bonuck** received a grant from the American Sleep Medicine Foundation for *Expanding Surveillance of Sleep Problems and Risk Factors for Speech-Language Impairment in Young Children*.

**Dr. Eric Hollander**, *Cannabidiol (CBDV) vs. Placebo in Children with Autism Spectrum Disorder (ASD)*, was awarded \$1,267,800 over four years by the Department of Defense office of Congressionally Directed Medical Research Programs. This phase 2, double-blind, randomized, placebo-controlled study will investigate CBDV as a treatment for the core symptoms of ASD.

**Dr. Theodore Kastner**, RFK IDDRC member and director of Children's Evaluation and Rehabilitation Center, was awarded a \$3.5 million, five-year grant, *Interdisciplinary Leadership Training in Neurodevelopmental and Related Disabilities (T73 MC00027)*, to support the Rose F. Kennedy Leadership Education in Neurodevelopmental and Related Disabilities program.

**Drs. Kastner & Bonuck** also received a renewal for the University Center for Excellence in Developmental Disabilities (UCEDD) for \$2,735,000 over the next 5 years.

## NEW RFK MEMBERS

The RFK IDDRC welcomed **J. Tiago Gonçalves, Ph.D.**, into its membership last fall. Dr. Gonçalves is an assistant professor in the Dominick P. Purpura Department of Neuroscience and in the Stem Cell Institute. To read more about Dr. Gonçalves' lab, see [www.einstein.yu.edu/r/tiago](http://www.einstein.yu.edu/r/tiago).

To become an RFK IDDRC member, please email Dr. Steven U. Walkley at [steve.walkley@einstein.yu.edu](mailto:steve.walkley@einstein.yu.edu) or visit [www.einstein.yu.edu/r/invest](http://www.einstein.yu.edu/r/invest).

## NOTEWORTHY PUBLICATIONS

**Dr. Noboru Hiroi** recently published three manuscripts on cognitive deficits in 22q11.2 mouse models: "A Self-Generated Environmental Factor as a Potential Contributor to Atypical Early Social Communication in Autism" (*Neuropsychopharmacology*, December 2016); "Human COMT Over-Expression Confers a Heightened Susceptibility to Dyskinesia in Mice" (*Neurobiology of Disease*, June 2017); and "Cry, Baby, Cry: Expression of Distress as a Biomarker and Modulator in Autism Spectrum Disorder" (*International Journal of Neuropsychopharmacology*, February 2017).

**Dr. David H. Hall** published "C. elegans Neurons Jettison Protein Aggregates and Mitochondria under Neurotoxic Stress" in the February 8, 2017, edition of *Nature*. For more information, see [www.einstein.yu.edu/r/brain](http://www.einstein.yu.edu/r/brain).

## HIGHLIGHTS

On November 7, 2016, the Rett Syndrome Center hosted a fundraising event at Capitale in New York City. With over 400 in attendance, \$550,000 was raised for the Children's Hospital at Montefiore and the Rett Syndrome Research Trust. Congratulations to **Dr. Aleksandra Djukic** and to all involved!

On May 21, 2017, Einstein and Montefiore hosted their annual 22q Day at the Zoo event. For more information about 22q at Montefiore, go to [www.einstein.yu.edu/r/delete](http://www.einstein.yu.edu/r/delete).

On September 14, 2017, Einstein-Montefiore will be opening its first 22q11.2DS clinic at the Hutchinson Metro Center, one of the new Montefiore outpatient locations. The center is the first 22q11.2DS multidisciplinary center in New York. For more information, please contact Erica Kessler at [erica.kessler@einstein.yu.edu](mailto:erica.kessler@einstein.yu.edu).

## IN THE MEDIA

The *Atlantic* interviewed Dr. Eric Hollander about his study suggesting a link between autism and addiction (March 21, 2017). For more, visit [www.einstein.yu.edu/r/autism2017](http://www.einstein.yu.edu/r/autism2017).

## 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**  
Sophie Molholm, Ph.D.

**Administrator**  
Lisa Guillory, M.A.

**Administrative Assistant**  
Frances Andrade

### EXECUTIVE COMMITTEE MEMBERS

Aleksandra Djukic, M.D., Ph.D.

Craig Branch, Ph.D.

Bernice E. Morrow, Ph.D.

Vytautas Verselis, Ph.D.

Melissa P. Wasserstein, M.D.

### To support the work of the RFK IDDRC, contact:

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