ROSE F. KENNEDY INTELLECTUAL AND DEVELOPMENTAL DISABILITIES RESEARCH CENTER

NEWS

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From left to right: Dr. Shlomo Shinnar, Dr. Lori Isom, Dr. Steven Walkley, Dr. Aristea Galanopolou, Dr. Solomon 'Nico' Moshé, and Dr. Sophie Molholm.

IN THIS ISSUE

Rose F. Kennedy Intellectual and Developmental Disabilities Research Center

EINSTEIN
Albert Einstein College of Medicine

The 8th Annual Isabelle Rapin Conference on Communication Disorders: Tackling Epilepsy

The fall was time for the 8th Annual Isabelle Rapin Conference on Communication Disorders, a conference series created to honor the memory of Dr. Rapin, a leading authority on autism and fellow of the American Academy of Neurology. This year's conference was organized by the RFK IDDRC with the help of Drs. Aristea Galanopoulou and Solomon (Nico) Moshé of the Saul R. Korey Department of Neurology with the goal to celebrate the career of Dr. Shlomo Shinnar and his extensive contributions to epilepsy research.

Dr. Gordon Tomaselli, Dean of Albert Einstein College of Medicine and Dr. Sophie Molholm, Co-Director of the RFK IDDRC welcomed the audience and introduced the conference program, which focused on the pathogenesis and treatments of early life epilepsies. The prestigious line up of local and invited speakers included Dr. Solomon Moshé, the Charles Frost Chair in Neurosurgery and Neurology, Dr. Annapurna Poduri, professor of neurology and director of the epilepsy genetics and neurogenetics programs at Boston Children's Hospital, Dr. Mark Mehler, the Alpern Family Foundation professor and chairman of the Saul R. Korey Department of Neurology, Dr. Aristea Galanopoulou, professor of neurology and neuroscience and director of the laboratory of developmental epilepsy, and Dr. Lori Isom, the Maurice H. Seevers professor and chair of pharmacology at the University of Michigan Medical School. Conference attendees learned about early life epilepsy syndromes (Dr. Moshé), cutting edge research on mTOR pathway related mutations in developmental epilepsies (Dr. Poduri), epigenetic principles governing epileptic encephalopathies (Dr. Mehler), preclinical treatment discoveries for developmental and epileptic encephalopathies (Dr. Galanopoulou), and strategies for precision medicine in early life epilepsies (Dr. Isom).

Honoring his 40-year long career at the forefront of epilepsy research, the plenary speaker was Dr. Shlomo Shinnar, the Hyman Climenko Professor of Neuroscience Research, and professor of neurology, pediatrics, epidemiology, and population health at the Albert Einstein College of Medicine. Dr. Shinnar discussed the lessons learned from the FEBSTAT study, an NIH-funded prospective study that has provided unique insights on the natural history, biomarkers, and consequences of febrile status epilepticus in children. After his lecture, Dr. Shinnar was awarded the Isabelle Rapin Life Achievement Award.

SAVE THE DATE!

Rare Disease Day: February 28, 2023

The Rose F. Kennedy IDDRC, as it has done since 2013, will once again host Rare DIsease Day on the internationally-recognized last day of February. The theme of this year's meeting will be "Adults with Rare Disease as Advocates for Their Disorder". Individuals with Williams syndrome, Gaucher disease, Late Onset Tay-Sachs disease, and Maple Syrup Urine Disease, will be our guest speakers. This will be a hybrid meeting in LeFrak Auditorium from 2-5 pm and followed by a reception on Main Street in Forchheimer.

The Challenge of Rare Disease as Told Through the Voices of Three Moms

In 2017 the Rose F. Kennedy IDDRC leadership created a personalized medicine program called Operation IDD Gene Team (https://www.einsteinmed.edu/centers/iddrc/research-programs/idd-gene-team/) which was designed to help families in which a child had been diagnosed with a rare genetic disorder characterized by neurodevelopmental delay, IDD or related features. To date, nearly a dozen families have participated in this program and/or its closely related Rare Disease Day event sponsored annually by the RFK IDDRC. Remarkably, some of these participating families have gone on to create foundations for their child's condition and this article explores the experiences of three of them. Jessica and Mike Foglio who have a son, Ben, diagnosed with Salla disease, created the Salla Treatment And Research (S.T.A.R.) Foundation. Amy and Chris Robl whose daughter, Gabby, has a gene variant in KDM5C, created the KDM5C Advocacy, Research, Education, and Support (KARES) Foundation. And finally, Lisa and Mike Manaster whose daughter, Emily, was born with a CACNA1A variant, created the CACNA1A Foundation. What follows are answers to a series of questions we presented to each of the moms to learn about the challenges they faced as they confronted their child's diagnosis and moved toward creating a foundation.

The Manaster's visit Einstein for Rare Disease Day, February 2019. Lisa Manaster is third from the right, and daughter, Emily, is on her right; Heather Snell, also mentioned in the article is second from the right.

The Foglio's and Robl's meet during Rare Disease Day at Einstein, February 2020. Jessica Foglio is third from the left and son, Ben, is in front of her; Amy Robl is second from the right and daughter, Gabby, is on her right.

SAVE THE DATE - NEXT EVENTS

Rose F. Kennedy Center Day (RFK Day): April 21, 2023

This past year saw the establishment of a unified Rose F. Kennedy Center that integrates long standing and nationally recognized programs focused on clinical care, research and training in intellectual and developmental disabilities at Einstein-Montefiore. These include The Children's Evaluation and Rehabilitation Center (CERC), which is an interdisciplinary clinical service program for children and adults with intellectual and developmental disabilities that promotes health and well-being throughout the lifespan; the University Center for Excellence in Developmental Disabilities (UCEDD), which works to build the capacity of people with developmental disabilities by effecting systems change through advocacy, so they can participate fully in their communities; the Leadership Education in Neurodevelopmental Disabilities (LEND) program, which trains graduate level health professionals, self-advocates, and family members to assume leadership roles in their respective fields to improve health outcomes of children with disabilities; and the Intellectual and Developmental Disabilities Research Center (IDDRC), which supports basic and translational and clinical cutting-edge research and training directed at better understanding and treating IDDs. Collectively, these programs share the goal of improving the lives of individuals affected by intellectual disabilities.

To launch this unified RFK Center, we are establishing an annual symposium ("RFK Day") as an opportunity for our full community to come together, and to increase awareness of our collective efforts.

What inspired you to create a foundation for your child's condition and when did you conceive of the idea?

Jessica Foglio: *After Ben's diagnosis, Drs. Walkley and Wasserstein asked us if we would like to come to the Rose F. Kennedy Center at the Albert Einstein College of Medicine so that they could give us a slide-show presentation and explanation of what exactly was happening in Ben's body. In the months preceding this meeting Dr. Walkley had conceived of the idea of IDD Gene Teams designed to give families more of an understanding of their child's rare disease diagnosis by connecting them with scientists and researchers who knew about their disease. Their goal was to give families a sense of hope and knowledge amidst the saddest times of their lives.*

At the end of this meeting, Dr. Walkley suggested that perhaps we should consider starting a foundation for Salla Disease since there was none. Being that Ben was so young and in therapies 30 times a week (Occupational, Feeding, Speech, Physical, Play, Vision, Swim and Horse Therapy) I declined the idea immediately. However, a friend of ours, David Halperin, happened to run a foundation of his own and suggested that he would walk us through the endless paperwork that would need to be submitted in order to become a 501(c)(3), as well as all of the hoops that could lie ahead with the Internal Review Service. With this expertise, we were able to follow his guidance and S.T.A.R. Foundation was born. Six months after meeting with Dr. Walkley and Dr. Wasserstein, we called back and proposed the idea of S.T.A.R., and the rest is history.

Amy Robl: *In 2017, when our daughter was 10, we finally received a diagnosis that explained her symptoms and challenges: a mutation of the KDM5C gene. I searched online for other parents and families affected by this extremely rare syndrome but couldn't find much support. That led me to create a KDM5C support group on Facebook, which has grown to hundreds of members representing approximately 100 diagnosed individuals worldwide. An MD-PhD student, Hayden Hatch, from Albert Einstein College of Medicine who was researching KDM5C variants in Dr. Julie Secombe's laboratory, joined the group to learn more about the affected families. He subsequently invited our family to the Rose F. Kennedy IDDRC's Rare Disease Day event in late February 2020 as spokespeople for KDM5C (one of three rare diseases being featured that year). Remarkably, nearly a dozen other families in the Facebook group, including one from the U.K., joined as well. It was an incredible experience to see families, clinicians, and scientists come together in support of KDM5C research for the first time. We all felt excited and inspired to start a foundation upon meeting one another, especially after hearing of Jessica Foglio's success with starting the S.T.A.R. Foundation for her son's rare disease. We wanted to fund research, raise awareness, and support other families who were facing a diagnosis of a KDM5C variant.*

Lisa Manaster: *My daughter, Emily, made having a third child seem easy; she nursed well, slept well, rarely cried and was content to lie in her crib staring at a mobile while I was busy tending to her three and five-year-old siblings. However, it didn't take long for my world to shatter. At six months old, the pediatrician referred us to a neurologist for an "upgaze" and shivering spells. Emily had her first MRI at seven months old due to global developmental delays, and at eight months old, she had her first seizure. So much for an easy baby!*

And thus, our quest to figure out what was wrong began. We were privileged to see some of the best specialists in the country. However, in 2007, when Emily was 10, we stopped searching for answers. We knew she had epilepsy, speech and language issues, motor planning difficulties, balance and coordination issues (most doctors called her "clumsy"), nystagmus, daily headaches, and intellectual disability. We just didn't know why. In 2016, I began to think about genetics again after reading an article about the Human Genome Project. I contacted our neurologist and he offered to enroll Emily in a study on epilepsy genes. It took nine months to receive a diagnosis of a CACNA1A variant (de novo) from Whole Exome Sequencing. For me, the diagnosis brought closure. What a relief that Emily's challenges were not the result of something I did during my pregnancy (the Benedryl I once took for a rash/the tuna sandwich I ate for lunch.)

Discussing the results with a geneticist, I thought a diagnosis would mean a change in medications and life would somehow become simpler. Instead, I was told, "We don't know much about CACNA1A. Maybe there's a Facebook group you can join." And so, I did. The life of a special needs mom can be incredibly isolating. In this group, I found my tribe! The kindness and support from other parents were incredible. Yet I realized we were all struggling with the same questions around treatments and therapeutics, and no one had any answers, especially our doctors. I went into action mode. I began reading scientific papers, emailed the authors, and made connections. In March 2020, just as the pandemic was taking over the world, I jumped onto the rare disease bandwagon and launched the CACNA1A Foundation to unite our community and find a cure for this rare disease.

What were some of the major challenges you faced in starting a foundation?

Jessica Foglio: *To be honest, it has been a lovely process. I think the key to our success was being able to identify and ask the RIGHT people for help. David Halperin, as mentioned, helped us navigate the paperwork. However, what about the finances? Who would have the time to take on such a challenge? I immediately thought of my Uncle Ken. Ken Klein is a retired math teacher in Florida; a calm, highly organized, and overall easy-going man. Ken has kept us incredibly organized and fiscally responsible, and this choice for our Treasurer position could not have been a more perfect fit. My gifts lie in my ability to unite and rally families and the surrounding community. When we were first diagnosed there were no family networks to lean on. We were simply alone in our diagnosis. Using social media, I have been able to connect with families on Facebook, Twitter, and Instagram. In addition to this, I have planned events from Walks to fun Raffle/Cocktail hour parties. All proceeds, of course, go to S.T.A.R. Foundation.*

Amy Robl: *Honestly, the first and biggest challenge was the pandemic. The world shut down upon our return home from the*

2020 Rare Disease Day event at Einstein. That definitely stalled the momentum we felt when we all met in person. I started to feel like the weight of the world was on my shoulders - that the other families were looking to me to start a foundation, and for no logical reason, I thought I needed to do it all by myself. With all of life's responsibilities, including raising a child with special needs, I didn't know where to start. I was overwhelmed. As the world started opening back up, I reached out to three of the moms who had expressed an interest and shown initiative, Lara Erekson, Amanda Lowry, and Melissa McNeilly. We started meeting via zoom, and within a few months, in May 2022, we were granted 501(c)(3) status and things began moving along faster than I could have ever imagined.

Lisa Manaster: *To start, I had no idea how to run a foundation, so I began reading a book on how to form a 501(c)(3). Luckily, the rare disease community is extremely inclusive, and I reached out to other Parent Advocacy Group leaders for advice, which they readily gave. Our first challenge was putting together a scientific advisory board – getting scientists to join an organization run by mothers with no track record wasn't easy. But never underestimate the power of moms on a mission! As a parent-led group, a sense of urgency is at the forefront of everything we do and as a result, we were able to convince some of the world's experts on CACNA1A-related diseases to take a chance on us. Finding our patients and enrolling them in our natural history study is an ongoing challenge. We spend a lot of time explaining the importance of data collection. Still, it's hard to get parents/caregivers to take the time to fill out the questionnaires. Fundraising is another challenge. We can't fund research if we don't raise money. We have raised approximately $200,000 a year for the last two years from our community for research. But we need to do better. If we are going to get closer to the discovery of new treatments and cures for our kids, we need to continue to find sources of income.*

How did other affected families respond? How many have become part of your effort, and how many countries are involved so far?

Jessica Foglio: *As I navigate S.T.A.R. and hope for family involvement, I must understand that each family grieves in their diagnosis differently. Although we have been fortunate to have strong family connections, not everyone wants to be a part of the effort. My grief manifests itself in running S.T.A.R. Foundation, while other families grieve quietly and have made it clear they are not interested in our efforts. I struggle with this sometimes, especially as we have seen so much success with S.T.A.R. Foundation. How could you NOT want to be a part of the journey? But then I realize that not everyone is the same, and that is what makes our world complicated, yet beautiful. I have to learn to embrace that, and it's been difficult for me to understand. However, more families have been coming forward, mostly due to the awareness and success of S.T.A.R. Foundation. Families are finally receiving the correct diagnosis for their child. We are truly an international effort as we have ACTIVE families in Switzerland, Sweden, Finland, Norway, Saudi Arabia, Canada, Australia, Brazil, The Dominican Republic, Russia, Germany, and the United Kingdom.*

Amy Robl: *The families have been very supportive. We have expanded our board, and have several subcommittees, a scientific advisory board, and we've been collaborating with other rare disease organizations. As of now, we are US-based, but we are learning more each day about running a non-profit organization. We would very much like to expand globally, as we have families throughout the world who are affected and would like to be more involved.*

Lisa Manaster: *Engaging with the community and keeping a pulse on their needs is one of the most important things we do. We have a contact registry with 250 members, but we know many more are out there. We attend conferences, have a strong social media presence, and have developed relationships with genetic testing companies, such as GeneDx, which puts our organization's name under the resources section of positive genetic reports. However, there is still a lot of work to be done. We hosted our first in-person Family conference this past summer in Texas. People traveled from all over the US and Canada and came from Australia, South America, Europe, and the Middle East to join us. It was a magical experience for all those that attended, including the scientists, some of whom had never met a patient before. We host a monthly virtual meet-up for families. Our Board of Directors and Science Engagement Director are all parents of children with a CACNA1A variant. We are in the process of setting up a global Ambassador program staffed by parent volunteers to help us further engage the community. Finally, there is a group of families in Italy that we meet with monthly who represent our Foundation there. Patients exist all over the world, and we are working hard to find and support them!*

What are your goals for the foundation?

Jessica Foglio: *S.T.A.R. Foundation stands with the unwavering belief that no disease is too rare for viable research and treatment options. Although this is the main underpinning of our vision, we also want to embrace education to the public while building family networks and relationships along the way. So far, we have been able to beautifully intertwine the above-mentioned goals. Our Scientific Advisory Board is simply an incredible group of world-renown doctors and scientists. As mentioned, the use of social media has really helped S.T.A.R. to connect families, allowing us to have more private social media pages (for caretakers and parents only) as well as larger online forums for families, researchers, and supporters. S.T.A.R. Foundation is 100% volunteer based. No one takes a salary or a stipend. After the overhead of insurance, online platforms, and licensing, 90-92% of all money raised goes directly to our research efforts.*

Amy Robl: *We named the foundation KARES: KDM5C Advocacy, Research, Education, and Support. We had our first fundraiser on October 8-9, 2022, which was a virtual 5k. Families all over the U.S. walked, ran, and rolled, all while raising over $55,000. As a board, we are working to finalize a budget that will fund research, support families by providing tools like AAC (Augmentative and Alternative Communication) devices, and we hope to eventually hold an in-person conference for affected families. Because of our efforts, when a new family is diagnosed, they are no longer left to figure it out on their own. Their lab reports will show our organization's information, so they can learn more and connect with other families.*

Lisa Manaster: *Our mission is to find specific treatment options and a cure for CACNA1A patients by building a collaborative network of patients, families, clinicians, and scientists that will work together to raise awareness and accelerate the understanding, diagnosis, and treatment of CACNA1A-linked diseases. We believe collaboration is the key to success because we can't change the course of this rare disease without all our stakeholders working together. Specifically, our goals are three-fold – to fund translational research, raise awareness of the disease, and provide educational resources to our community. We are currently focused on becoming clinical trial ready. We've launched a biorepository, are developing iPSC lines, and are investing in mouse models that align with human variants. We have a mandate to share all our resources, making them accessible to anyone who wants to study them. Next, we have set a goal of*

getting 500 patients enrolled in our Natural History Study and into RARE-X, a collaborative platform for rare disease data sharing that now includes 25 diseases. Finally, we hope to continue to educate and support families through webinars, our Creating Connections Family Conference and by continuing to develop resources for physicians and families. We also recently hosted a Research Roundtable where a group of clinicians decided to work together to develop and publish a much-needed consensus on how to treat CACNA1A-related disorders. We are building momentum and are grateful for all those who are joining our cause. So stay tuned!

How (if at all) was the Rose F. Kennedy IDDRC helpful in your idea to create a foundation? Are there things the IDDRC could be doing to help you now that the foundation is established?

Jessica Foglio: *We wouldn't exist without the vision of the Rose F. Kennedy IDDRC. They planted the seed and the idea of a foundation – from walking our family through the early stages of our diagnosis, to gently suggesting the idea of a foundation being started, to helping us identify and recruit doctors who are fully invested in our efforts. It has been an amazing journey. However, it's not easy to rally families to continually fund this work. It's a mountain of money that we must raise to have families be a part of a Natural History Study, clinical trial readiness programs, and ACTUAL clinical trials. This doesn't even include the financial efforts put in place to create our mouse models and cell assays. So, although Einstein's IDDRC has impacted our lives with Salla Disease in a profound way, a next best effort to help foundations like ours might be to provide advice on how to best organize and run a foundation, and how to most effectively raise and distribute critical research funding.*

Amy Robl: *If it had not been for the Rose F. Kennedy IDDRC's decision to feature KDM5C in their 2020 Rare Disease Day event, I am certain this foundation would not yet have been started, let alone thriving. Words cannot express how meaningful it was for the families of such a rare disease to connect, learn from the researchers, and meet Jessica Foglio from S.T.A.R. Foundation at the Rare Disease Day event in 2020. We are also eternally grateful for Dr. Julie Secombe's willingness to participate on our Scientific Advisory Board.*

Lisa Manaster: *After receiving a diagnosis of a rare disease, one of the first things I did was reach out to all (and there were many!) of the neurologists and geneticists we had taken Emily to over the years. Most of them never responded or didn't seem that interested in our 20-year-long diagnostic journey that finally resulted in a positive finding after Whole Exome Sequencing. The exception was Dr. Bob Marion at Montefiore, who had cared for Emily in 2001 when she was 4 years old. At the time, he did not have any other patients with a CACNA1A variant. We began an email exchange in which he told me how he's always "staggered by how such a minuscule change in one's DNA (Emily has a point mutation) can have such a drastic impact on a child, their family, community, and society." His empathy was undeniable and atypical of most clinicians we'd seen over the last two decades. We stayed in touch and then six months later, I received an invitation from Dr. Walkley to meet with the IDDRC team for a tutorial on CACNA1A with the labs at Einstein that were studying ion channelopathies. It was there we met Dr. Kamran Khodakhah and his postdoctoral fellow, Dr. Heather Snell. It took another year to start the Foundation but there's no question that that initial meeting made me realize the need to raise awareness and, more importantly, funding, if we were going to make a difference for kiddos with CACNA1A genetic mutations. Fast forward another two years – The CACNA1A Foundation recently held its first Research Roundtable in New York City. It was a historic event with 37 of the world's experts on CACNA1A, ion channels, genetics, ataxia, epilepsy, hemiplegic migraine, and eye movement disorders convening for the first time. Dr. Khodakhah as well as another Einstein faculty member, Dr. Peri Kurshan, attended and we are excited to collaborate with them in our quest for new therapeutics and cures.*

What advice would you share with other parents/care givers facing the issue of a rare genetic disease in their family?

Jessica Foglio: *I call it "going dark." It's so easy for the loneliness, sadness, anger, pain, and overall devastation to set in after something like this happens to your child/family. Our own grief can easily manifest in an extra glass of wine (or 3) at the end of the night. Recognizing this was crucial for me, especially during the seclusion of the Covid-19 crisis. Finding S.T.A.R. and pouring my grief into doing something positive has helped curb these feelings. Believe me, overwhelming sadness can still come on STRONG and these dark thoughts and fears can be paralyzing. However, establishing S.T.A.R. has helped my marriage as Mike and I try and put good into our broken world through our sadness and loss. Mustering the strength to take on such an endeavor has not been easy, but worth every moment as we see our success and our foundation flourish, paving the way for future families and patients. We now have a purpose. Ben's little life has a purpose too, and that is everything.*

Amy Robl: *Never give up. When we received our daughter's diagnosis, the geneticist didn't have any information to work with, and said my best bet would be to find other families through Facebook. At first, having a diagnosis felt like a huge relief. It soon turned to despair, because of the lack of information and inability to connect with other families. After one year of very little luck finding other families, I decided to take fate into my own hands and start an online support group, which eventually led us to where we are now. I have made lifelong friends as a result. Our family is no longer alone on an island. As Dory in Finding Nemo says, "Just keep swimming."*

Lisa Manaster: *First, if your child isn't checking off the boxes concerning milestones, don't be afraid to advocate for them. As a former special educator, I know that there is nothing more valuable than early intervention. Next, find a doctor committed to helping you find an answer and advocate for genetic testing. If your insurance doesn't cover it, so many companies will do it for free today. There is no reason for the diagnostic odyssey for rare disease patients to be as long as it is. Trust your gut and fight for your kid! Most importantly, know that those feelings of guilt, loneliness, and anger are all normal! You will grieve and lie in bed at night and worry about the future. We all do this, so don't beat yourself up about it. But find a support system. Go for walks and care for yourself because you need to be at your best for your child.*

To learn more about the S.T.A.R., KARES and CACNA1A foundations, and the three genetic diseases mentioned in the article, visit these websites:

https://www.sallaresearch.org/

https://kares.foundation/

https://www.cacna1a.org/

IDD Gene Team In the News

The Rose F. Kennedy IDDRC's Operation IDD Gene Team program goes national with publication of an article by IDDRC members, Dr. Steven Walkley and Melissa Wasserstein, in the online magazine, The Conversation https://theconversation.com/when-it-comes-to-the-rarest-of-diseases-the-diagnosis-isnt-the-answer-its-just-the-starting-point-177424 and with the airing of a description of the program on National Public Radio's Academic Minute program https://academicminute.org/2022/06/steven-walkley-albert-einstein-college-of-medicine-rare-disease-when-the-diagnoses-is-not-the-answer/. For more information about this program and how it works visit https://www.einsteinmed.edu/centers/iddrc/research-programs/idd-gene-team/.

The IDDRC Welcomes New Leadership

Following the renewal of IDDRC funding in July 2022, we are pleased to welcome new leadership to our IDDRC Administrative Core. Sophie Molholm Ph.D., professor of pediatrics, neuroscience and psychiatry and behavioral sciences and formerly associate director of the Center, has now joined Steven Walkley D.V.M., Ph.D., professor of neuroscience, pathology and neurology, as co-director. Importantly, Dr. Molholm was also recently elected by her peers to serve as co-chair of the national IDDRC Network which is comprised of the directors of all 15 NICHD funded IDDRCs. The RFK IDDRC has also named two new associate directors. These are Melissa Wasserstein M.D., professor of pediatrics and genetics, and Bryen Jordan Ph.D., associate professor of Neuroscience and Psychiatry and Behavioral Sciences. In addition, we are pleased to welcome new IDDRC administrator, Julie Y. Esaki Mota.

Bryen Jordan, Ph.D.

Melissa Waserstein, M.D.

Sophie Molholm, Ph.D.

T32 FELLOWSHIP PROGRAM

Through a grant from the National Institute of Child Health and Human Development (NICHD), the Rose F. Kennedy IDDRC offers postdoctoral training to eligible candidates interested in careers in the biomedical sciences focused on the neurobiological underpinnings of neurodevelopmental disorders associated with intellectual disability and autism. We are seeking candidates whose skills, and personal and professional experience will support our commitment to diversity and excellence and the communities we serve. Candidates must be U.S. citizens or permanent residents (green card holders) and have a Ph.D., M.D., M.D./Ph.D., D.V.M. or D.V.M./Ph.D. Underrepresented minorities are strongly encouraged to apply. See https://www.einsteinmed.edu/centers/iddrc/training/ for more information.

We are pleased to Introduce our newest T32 fellows:

- Dr. Carlos Rivero Quiles joined Dr. Autry's lab in October 2022. Carlos conducted research on the impact of nandrolone on reward circuitry and the reproductive system of adolescent females during his Ph.D. studies. During his fellowship he plans to determine the impact of maternal stress on maternal care and subsequent impacts on juvenile and adolescent social/emotional behaviors and cognition. He aims to use both physiological and pharmacological stressors in the perinatal period to compare neurobiological and behavioral sequelae in the offspring.
- Dr. Annie S. Maguire joined Dr. Jordan's lab in January 2023. Annie has both a D.V.M. and a Ph.D. degree. She was previously at AVID Radiopharmaceuticals working on novel Alzheimer Disease therapeutics. Annie will play a key role in testing the contribution of oligodendrocytes and white matter pathologies to autism spectrum disorders using biochemical, neuroanatomical, and genetic approaches.

IDDRC Signature Research Project: Mechanisms of IDD in children with mutations in the transcriptional regulator lysine demethylase 5c gene, KDM5C

The Signature Research Project of our NICHD funded IDDRC brings together a multi-disciplinary team of researchers using diverse analytical tools and model systems to understand KDM5C-induced intellectual disability (ID), also known as Claes-Jensen syndrome. While mutations in the gene KDM5C, which encodes for the the transcriptional regulator lysine demethylase 5C (KDM5C) lead to disease, how KDM5C functions to mediate critical neuronal processes, and therefore the consequence of mutations for mechanisms of IDD, remains unknown.

The research team is led by Dr. Julie Secombe, who has expertise in KDM5C-mediated transcription and its relationship to ID using the animal model Drosophila melanogaster. Dr. Secombe works closely with Dr. Herb Lachman, who is using iPSCs and cerebral organoids from patients to analyze the function of KDM5C in a human neuronal context for the first time. Molecular studies using both Drosophila and iPSC-induced neurons require the bioinformatic expertise of Dr. Deyou Zheng, to delve deeply into the transcriptional deficits caused by genetic variants in KDM5C. Complementing the Drosophila and human cell studies, Dr. Bryen Jordan is testing how variants in KDM5C alter cognition by using mouse models. To fully utilize model organism and human organoid data, it is critical to understand patient phenotypes. Dr. Lisa Shulman brings this expertise to the team, as she is a developmental pediatrician who specializes in diagnosing and treating children with ASD and other developmental and learning disabilities. These studies make critical use of all four of the scientific cores funded by the RFK IDDRC to support basic and translational research (HCP, NGEN, NCEI and AP). Fundamental insights gained from these studies will provide a mechanistic understanding of why variants in KDM5C cause cognitive impairment and are expected to highlight possible avenues for therapies for affected individuals.

The ultimate goal of this research is to help individuals with Claes-Jensen syndrome and their families. Drs. Secombe and Shulman have established a relationship with families of

Families and researchers linked to KDM5C-associated intellectual disabilities pose for a group picture after attending Rare Disease Day at Einstein in Feb 2020. Twelve of these families and the research team led by Dr. Julie Secombe met at this event for the first time.

individuals with mutations in KDM5C through a Facebook support group and recently formed foundation (the KARES Foundation, see article by Three Moms in this newsletter). As seen in the accompanying photo, twelve of these families traveled from within the USA and from the UK in early 2020 to meet each other for the first time and attend Einstein IDDRC's Rare Disease Day, which featured KDM5C research.

Because the range of clinical features observed in those with genetic variants in KDM5C remain poorly described, this previous Rare Disease Day included a presentation of new data from 37 families in the Facebook group collected by Drs. Secombe and Shulman. These data have now been published (Hatch HAM, et al. Oct 2021, American Journal of Medical Genetics) and emphasize the variability in the severity of the cognitive and behavioral features seen in individuals heterozygous for variants in KDM5C. Further integration and analyses of genetic variants and clinical data from these families will greatly extend our understanding of Claes-Jensen syndrome.

CONGRATULATIONS TO OUR TRAINEES ON THEIR RECENT AWARDS!

Hayden Hatch: Marmur Award
Hayden A. M. Hatch, M.D./Ph.D. candidate, was recognized for his thesis work using Drosophila melanogaster (the fruit fly) to understand how the enzyme KDM5 functions in the brain to influence nerve development, and how genetic variants of the enzyme may lead to intellectual disability.

Ilana Vasilisa Deyneko (Vasi): top poster award
Ilana "Vasi" Deyneko, Ph.D. candidate, received the top poster award at the 13th Great Lakes Glia Meeting in Traverse City Michigan. The award was presented Tuesday October 11th and she got a $250 check!

Sarah Goebel: Diana Casper Women in Science Award
Funded Sara's attendance to the 2022 Society for Neuroscience conference in San Diego where she presented her ongoing work examining the disease mechanism of a mouse model of Fragile X Syndrome.

Heather Snell: Allen Institute Next Generation Leaders Council
Heather has been named one of six new Next Generation Leaders (NGL) by the Allen Institute, a nonprofit research organization based in Seattle. The NGLs are members of a neuroscience advisory panel made up of early-career researchers who will help advise research efforts at the Allen Institute for Brain Science, the MindScope Program, and the Allen Institute for Neural Dynamics.

THE IDDRC GOES SOCIAL

https://twitter.com/RFK_IDDRC

https://www.einsteinmed.edu/centers/iddrc/

The IDDRC is joining forces with the Association of University Centers on Disabilities (AUCD) to share our research to a broader audience. The AUCD is a network of centers working to advance policy and practice for and with individuals with developmental and other disabilities, their families, and communities. The network of centers includes University Centers for Excellence in Developmental Disabilities Education (UCEDDs), Leadership Education in Neurodevelopmental and Related Disabilities (LEND Programs), and Intellectual and Developmental Disabilities Research Centers (IDDRCs) such as ours. The AUCD's communication initiative allows us to amplify our research findings and related content via their website and/or other individual centers' social media platforms to reach both scientific and non-scientific audiences. Check out our recent contribution: AUCD - Autism research is a family affair: Steps toward increasing inclusion and diversity. Reach out to us when you have IDD relevant material for posting through our social media venues!

2022-2023 IDDRC PILOT AWARDS

Each year the IDDRC runs a competition for Pilot and Feasibility awards for both basic science and translational projects that involve intellectual and developmental disabilities (IDDs). We are happy to announce the 2022 awardees and the titles of their projects:

Shlomit Beker, Ph.D.
Autism as a Disorder of Synchronization of the Central and the Autonomic Nervous Systems

Coralie Berthoux, Ph.D.
Investigating the role of hilar mossy cells of the hippocampus in Fragile X Syndrome

Ruben Coen-Cagli, Ph.D.
Testing computational theories of visual processing in ASD with a novel integrated approach

Aristea Galanopoulou, M.D., Ph.D.
Metabolomic profile of infantile spasms

Julie Secombe, Ph.D.
Transcriptional programs regulated by the intellectual disability-associated histone demethylase KDM5C

The next competition will be announced in the summer of 2023. Check out our website for updates at **www.einsteinmed.edu/centers/iddrc/opportunities/**

RECENT FUNDING ANNOUNCEMENTS

Karen Bonuck, Ph.D. (PI)
University Center of Excellence on Developmental Disabilities
DHHS/AIDD 90DDUC0095
07/01/2022-06/30/2028

Karen Bonuck, Ph.D. (PI)
Regional Support Centers for the Children and Youth with Special Health Care Needs (CYSHCN)
NYSDOH DOH01-RTATC-2019
2019-2014

Karen Bonuck, Ph.D. (PI)
Engage & Educate: Equipping New York State's Disability Community with Science-Based Information About Vaccines.
NYSDDPC DDP01-T00021GG-1100200
2021-2023

Ruben Coen-Cagli, Ph.D. (PI)
Computational Tools for assessing mechanisms and functional relevance of divisive normalization
NIH/NIDA R01 DA056400-01A1
09/15/2022-09/14/2025

Arne Gennerich, Ph.D. (PI)
Molecular Mechanism of the Cytoplasmic Dynein-Dynactin Motor Complex
NIH/NIGMS R01 GM098469-10
08/01/2012-03/31/2023

David H. Hall, Ph.D. (PI)
Center for Caenorhabditis Elegans Anatomy
NIH/OG R24 OD010943-25
02/01/1998-07/31/2022

Peri Kurshan, Ph.D. (PI)
Cell-intrinsic mechanisms of presynaptic assembly
NIH/NINDS R01 NS123645-01A1
08/01/2022-07/31/2023

Herbert M. Lachman, M.D. (PI)
Molecular analysis of glutamatergic neurons derived from iPSCs containing PPM1D truncating mutations found in Jansen de Vries Syndrome
NIH 1R21MH131740-01
01/01/2023-12/31/2024

Rachel Amy Ross, Ph.D. (PI)
Investigation of appetitive and aversive inputs to MC4R-expressing neurons of the infralimbic cortex: relevance to anorexia nervosa
Brain and Behavior Research Foundation, Young Investigator Award
2022-2023

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.

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Interested in becoming an RFK IDDRC member? Contact Julie Mota at julie.mota@einsteinmed.edu or visit www.einsteinmed.edu/centers/iddrc/who-we-are/members/become-investigator/

Make a Gift to the Rose F. Kennedy Intellectual and Developmental Disabilities Research Center

www.einsteinmed.edu/centers/iddrc/giving