

Kirby Center News & Updates

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Announcements

The Kirby Center formed an Equity, Diversity and Inclusion (EDI) Committee to lead the Center in its goals to embody the highest ideals of equality, diversity, and inclusion by training ourselves, strengthening bonds within our Center, aligning our efforts with those of the hospital, enriching the greater community, and recruiting individuals from underrepresented backgrounds. Please contact Sable Smith to ask questions or get involved. All are encouraged and welcome to participate!



Congratulations to **Clifford Woolf**, MB, BCh, PhD, <u>who was elected</u> to the American Academy of Arts and Sciences, an honor that signifies the high regard in which he is held by leaders in his field and AAAS members throughout the nation. Read more <u>here</u>.

The Université de Lausanne (UNIL) in Lausanne, Switzerland<u>distinguished Clifford Woolf</u>, bestowing upon him the title of Doctor Honoris Causa. Congratulations, Clifford!

The Harvard Club of Boston <u>named **Ann Poduri**</u>, MD, MPH, one of Boston's Most Influential Women of 2020. Congratulations, Ann!

Meera Modi, PhD (Sahin lab), was promoted to Principal Associate in Neurology, Harvard Medical School. Congratulations, Meera!

For the 12th year in a row, *US News & World Report* ranked as #1 the Boston Children's Hospital **Departments of Neurology and Neurosurgery.** Congratulations to everyone in the Departments for this honor, which is the direct result of our combined efforts and dedication.

2020 Service Awards: The following Kirby Center personnel achieved BCH service milestones in 2020:

- 20 Years: Tom Schwarz, PhD
- 15 Years: Padam Gharti; Judith Steen, PhD; Jianlin Wang
- 10 Years: Maorong Chen, PhD; Sameer Dhamne; Mike Do, PhD; Henry Lee, PhD; David Roberson, PhD; Kathy Rodrigues; Beth Sheidley
- 5 Years: Pietro Artoni, PhD; Himanish Basu, PhD; Mantu Bhaumik, PhD; Lynn Bruning; Jasbir Dalal, PhD; Lasse Dissing-Olesen, PhD; Xuan Huang, PhD; Ali Jannati, MD, PhD; Arthur Lee, MD, PhD; Meera Modi, PhD; Allie Muthukumar, PhD; Mariko Okuyama, MD; Rheanna Sand, Phd; Xiaofan Wang, PhD; Zicong Zhang, PhD

Research in the News

In <u>To make mini-organs grow faster, give them a squeeze</u>, *MIT News* discusses the cell compression study of **Xi He**, PhD.

Published in *Nature*, the work of **Zhigang He**, PhD, BM, and Kirby Center colleagues reveals how <u>Scar-free healing after spinal cord injury relies on specialized cells.</u>

Jeff Holt, PhD, and collaborators at the Broad Institute published a paper in *Science Translational Medicine* showing how <u>In vivo base editing restores sensory transduction and transiently improves auditory function in a mouse model of recessive deafness. This story was also covered in <u>Genetic Engineering & Biotechnology News</u> and <u>Discoveries</u>. (photo credit: <u>STM</u>)</u>



Nature published a study by **Karl Koehler**, PhD, and his lab about <u>Hair-bearing human skin generated entirely from pluripotent stem cells</u>. This story was also covered in <u>Nature "News and Views."</u>

Cure Epilepsy features Christopher McGraw, MD, PhD (Poduri), and his work on A Reverse Genetic Screen Using CRISPRi and Calcium Fluorescence to Identify Novel Seizure Resistance Genes in Zebrafish.

Rett Syndrome Awareness

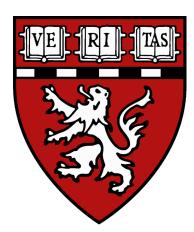
On October 17, **Michela Fagiolini**, PhD, virtually hosted several speakers for the **Rett Syndrome Scientific Symposium**, sponsored by the Kirby Center, the Translational Neuroscience Center, Harvard Medical School, and the <u>Rett Syndrome</u> <u>Association of Massachusetts</u>. The symposium celebrated ten years of <u>Blue Sky Day</u>, a day held annually in October to raise Rett Syndrome awareness. This year, Blue Sky Day was observed virtually on October 24.



Learn more:

- The <u>Community Swim Class</u> is a volunteer swim program offered by Dr. Fagiolini, in partnership with Crimson Aquatics, for individuals with Rett Syndrome.
- In Western Mass News, a Wilbraham mother discusses daughter diagnosed with Rett Syndrome

Graduate Student News



Recent Dissertation Defenses: Congratulations, PhDs!

Kayla Davis (Schwarz): Functional analysis of Miro GTPase domains in the mitochondrial motor adaptor complex.

Sivapratha Nagappan Chettiar

Postdoc News

Former Engle lab postdoc, **Mary Whitman**, MD, PhD, was promoted to Assistant Professor of Ophthalmology at HMS and is starting her own lab in the Department of Ophthalmology at BCH. Congratulations, Mary!

Qianbin Wang, PhD (Z. He), will join the UMass Amherst faculty in December. Congratulations, Qianbin!

Support for Fellows Entering the Job Market

If you are entering the market and would like assistance, please email Lynn Bruning and Mike Do well in advance of your first deadline. We will convene a committee of Kirby faculty members who are appropriate for your research. This committee will

- 1. Review a draft of your application.
- 2. Provide coaching on preliminary interviews.
- 3. Offer feedback on your job talk.
- 4. Take you through a mock chalk talk.
- 5. Provide advice on closing the deal.

When reaching out to us, please copy your advisor and ask them to give the green light for this process. We are most effective when your application, talk, and chalk talk are each (Umemori):

To keep or not to keep: The molecular mechanisms of activity-dependent synaptic refinement.

Jenelle Wallace (Stevens): Functional development of adult-born neurons in the olfactory bulb.

Himanish Basu (Schwarz): Mechanisms regulating movement and distribution of neuronal mitochondria. at the fine-tuning stage.

Note that BCH offers a related service. Please choose one to avoid overburdening our faculty. I recommend ours because it is a fine way to strengthen ties within Kirby.

This assistance is meant to be highly individualized. If you communicate your particular needs (e.g., "I am a biophysicist with neuroethological leanings for whom English is a second language"), that would help us arrange the appropriate committee.

If you have suggestions for how we can be more helpful, especially in this unusual time, please let us know.

Kirby Center Awards & Publications

Recent Awards

A consortium of **Larry Benowitz**, PhD; **Chinfei Chen**, MD, PhD; **Mike Do**, PhD; and **Tom Schwarz**, PhD, received a Kirby Innovation Award to support their project entitled, Mitochondrial Disorders and Visual Dysfunction.

Todd Anthony, PhD, received a Kirby Innovation Award for his project entitled, Neural Circuitry of Opiod Withdrawal-Induced Sleep Disruption.

 Dr. Anthony was also awarded a Harvard Medical School grant to support his project entitled, Cannabidiol modulation of neural circuits that control anxiety and sleep.

Chinfei Chen received a grant from Harvard Medical School to support her project entitled, Functional Interrogation of ASD-related mutations in Sensory-dependent Brain Development—Synaptic Circuits in the Thalamus.

Mike Do was awarded an HBI Seed Grant for his project entitled, Defining a Circadian Control System to Counter Bipolar Disorder.

Michela Fagiolini received a National Science Foundation (NSF) grant with a colleague at Northeastern University for their project entitled, Novel transparent, ultra-soft neuroelectrode arrays based on nanomeshing conventional electrode materials.

Dr. Fagiolini also received the following funding:

- Harvard Medical School New approaches to dissect neuronal circuits dynamics in ASD.
- ECRAC With the AB&P Core Celeris High Throughput ERG (electroretinography) and VEP (visual evoked potential) Testing System.
- 2020 Cellular Imaging Core STED RFA Alterations in long- vs. short-range connectivity in CDKL5 Deficiency Disorder.

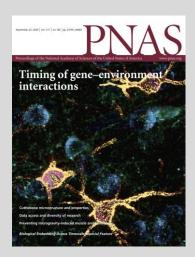
Xi He received an NIH R35 for his project entitled, Wnt Signaling and Vertebrate embryogenesis.

 Dr. He is also a 2020 Cellular Imaging Core STED RFA awardee for his project entitled, Subcellular imaging of TMEM79 using super-resolution STED microscopy.

Zhigang He was awarded an NIH/NCCIH R01 grant for his project entitled, Mechanism and Optimization of CBD-mediated analgesic effects.

 Dr. He also received funding from Axonis Therapeutics, Inc., to support his project entitled, Proof-of-concept efficacy study testing function recovery after spinal cord injury in rats after upmodulation of KCC.

Recent Featured Publications



Steen lab.

Tau PTM Profiles Identify Patient Heterogeneity and Stages of Alzheimer's Disease. Cell. December 2020.

X. He lab.

TMEM79/MATTRIN defines a pathway for Frizzled regulation and is required for Xenopus embryogenesis. Elife. September 2020.

Hensch lab.

Critical period regulation across multiple timescales. PNAS. September 2020. (photo credit: PNAS)

Lee lab.

Dense neuronal reconstruction through X-ray holographic nano-tomography. Nature Neuroscience. September 2020.

Do lab.

Optimized Signal Flow through Photoreceptors Supports the High-Acuity Vision of Primates. **Takao Hensch**, PhD, received funding from Brainq Technologies, Ltd., to support his project entitled, Targeting local neural circuits for critical period plasticity reactivation and post-traumatic neurorecovery by very-low intensity and frequency electromagnetic (Vlife) neuromodulation.

 Dr. Hensch also has a subcontract from Harvard School of Public Health on an NIH/NIEHS P42 for their project entitled, Metals and Metal Mixtures - Cognitive Aging, Remediation and Exposure Sources (MEMCARE).

Jonathan Lipton, MD, PhD, received an NIH/NHLBI R01 for his project entitled, Investigating Circadian Mechanisms of Cellular Resilience: Rhythmic Condensates, Disorder, and Stress.

 Dr. Lipton is also a 2020 Cellular Imaging Core STED RFA awardee for his project entitled, Imaging subcellular condensates of the circadian clock.

Ann Poduri received an NIH/NINDS R01 subcontract with UNC Chapel Hill for their project entitled, Identification and Molecular Characterization of Somatic Mutations in MCD

- Dr. Poduri is also the recipient of an award from Boston Children's Hospital to support her project entitled, Creating Zebrafish Models of Mosaic Neurodevelopmental Disorders.
- Together with Clifford Woolf, Dr. Poduri received a Kirby Innovation Award for their project entitled, Genetic Epilepsy - Neuronal Excitability and Drug Screening in an iPSC-derived Model.

Scott Pomeroy, MD, PhD, received an NIH U01 for his project entitled, Harnessing clinical genomic characterization to accelerate translational advances for patients with IDD.

Paul Rosenberg, MD, PhD, was awarded an NIH/NEI Administrative Supplement for his project entitled, An interneuronal signaling network governs the fate of retinal ganglion cells after optic nerve injury.

 Dr. Rosenberg and Alex Rotenberg, MD, PhD, recieved a Kirby Innovation Award for their project entitled, Can a magnet mimic ketamine?

Alex Rotenberg received an NIH/NIMH R21 grant for his project entitled, Neurophysiologic investigation of somatosensory dysfunction in Autism Spectrum Disorders.

Dr. Rotenberg also received the following funding:

- SSADH Association Developing an inducible SSADH mouse model for enzyme replacement therapy.
- ECRAC equipment funding for a Signal Integration Module for Rodent Wireless EEG Telemetry System.

Mustafa Sahin, MD, PhD, received an Autism Speaks award for his project entitled, Phenotype Library of ASD Neurons. Dr. Sahin also received the following funding:

- Biogen Interrogating Novel Targets for the treatment of Tuberous Sclerosis Complex (TSC).
- Aeovian Pharmaceuticals, Inc. Development of Novel, Highly mTORC1-Selective Inhibitors for the treatment of Tuberous Sclerosis.
- PTEN Research 1) EEG Characterization of a novel
 Pten mutant mouse model and 2) A Randomized DoubleBlind Placebo-Controlled Trial of Everolimus in Children
 and Adolescents with PTEN Mutations (Rare Disease
 Clinical Research Consortium-Developmental
 Synaptopathies Consortium).
- ECRAC equipment funding for EpiSonic Ambulatory Polysomnograms and Embletta MPR PSG System-XD.
- LouLou Foundation Phenotypic characterization of iPSCderived human neurons for CDD disease modeling.
- 2020 Cellular Imaging Core STED RFA Characterization of Connectivity Defects in Autism: using STED microscopy for dentritic spines.

Judith Steen, PhD, received a Kirby Innovation Award for her

Neuron. August 2020.

Géléoc lab.

Direct Delivery of Antisense Oligonucleotides to the Middle and Inner Ear Improves Hearing and Balance in Usher Mice. Molecular Therapy. August 2020.

Poduri lab.

The role of sodium channels in sudden unexpected death in pediatrics. Molecular Genetics & Genomic Medicine. August 2020.

Woolf lab.

Transcriptional Reprogramming of Distinct Peripheral Sensory Neuron Subtypes after Axonal Injury. Neuron. August 2020.

Rotenberg lab.

Increase in Seizure
Susceptibility After Repetitive
Concussion Results from
Oxidative Stress, ParvalbuminPositive Interneuron
Dysfunction and Biphasic
Increases in Glutamate/GABA
Ratio. Cerebral Cortex. July
2020.

Fagiolini lab.

The Stage of the Estrus Cycle Is Critical for Interpretation of Female Mouse Social Interaction Behavior. Front Behavioral Neuroscience. June 2020.

X. He lab.

Single molecule dynamics of Dishevelled at the plasma membrane and Wnt pathway activation. PNAS. June 2020.

Sahin lab.

Phenotypic Screen with TSC-Deficient Neurons Reveals Heat-Shock Machinery as a Druggable Pathway for mTORC1 and Reduced Cilia. Cell Reports. June 2020.

Hensch lab.

Single-nucleus RNA sequencing of mouse auditory cortex reveals critical period triggers and brakes. PNAS. May 2020.

Anthony lab.

Stimulus salience determines defensive behaviors elicited by aversively conditioned serial compound auditory stimuli. Elife. March 2020.

Crickmore lab.

CaMKII Measures the Passage of Time to Coordinate Behavior

project entitled, Fetal brain-immune Interactions in Congenital Viral Infection.

 Dr. Steen also received funding from the Alzheimer's Drug Discovery Foundation to support her project entitled, Profiling of Blood-based Proteolytic Fragments from Proteopathy-associated Proteins to Diagnose FTLDs and to Monitor Treatment Responses.

Hisashi Umemori, MD, PhD, received a grant from Harvard Medical School to support his project entitled, Pathway-specific effects of early-life cannabis exposure on dopamine synapse development.

 Dr. Umemori is also a 2020 Cellular Imaging Core STED RFA awardee for his project entitled, Super-resolution imaging of Protocadherin-19 at hippocampal mossy fiber synapses.

Clifford Woolf received a grant from the U.S. Department of Defense to support his project entitled, Targeting Kv2 Channels to Prevent Neuronal Apoptosis in ALS.

Dr. Woolf also received the following funding:

- Multi-PI NIH/NINDS R01 with David Ginty and Jan Drugowitsch - Spinal Cord Nociceptive Circuits that Deliver Outputs to the Brain to Initiate Pain.
- Multi-PI Blavatnik (Harvard Medical School) with Bruce Bean - Developing novel neuropathic pain therapies

and Motivational State. Neuron. January 2020.

Stevens lab.

Ocular Dominance Plasticity in Binocular Primary Visual Cortex Does Not Require C1q. Journal of Neuroscience. January 2020.

Umemori lab.

Neuronal fibroblast growth factor 22 signaling during development, but not in adults, is involved in anhedonia. Neuroreport. January 2020.

For a listing of additional recent Kirby Center publications, please visit PubMed:

- last name A-K
- last name <u>L-Z</u>

Darius Ebrahimi-Fakhari, MD (Sahin), received funding from CURE AP-4, Inc., to support two of his projects: 1) Development and Characterization of a Novel In Vivo Model of SPG47 Using CRISPR/Cas9-based ap4b1 Knockout in Zebrafish and 2) An International Registry and Natural History Study for AP-4-HSP

Shane Hegarty, PhD (Z. He), was awarded a grant from the William Randolph Hearst Foundation to support his project entitled, Characterizing role of SNRK kinase in neuronal survival and regeneration after CNS injury.

Aakanksha Jain, PhD (Woolf), received funding from the Jane Coffin Childs Memorial Foundation for Medical Research to support her project entitled, Somatosensory control of barrier tissue immunity.

Julie Jurgens, PhD (Engle) was selected for an NIH T32 grant to support her project entitled, Genetic dissection of cranial motor nerve development in zebrafish.

Arthur Lee (Engle) received the 2020 Manton Center for Orphan Disease Research Fellowship Award.

• Dr. Lee also is also the recipient of a Boston Children's Hospital grant to support his project entitled, Leveraging epigenomics for non-coding variant interpretation in orphan disease.

Samuel Marsh, PhD (Stevens), was selected to receive an NIH T32 Training Grant.

Paola Matos-Ruiz (Engle) was awarded an NIH/NEI Research Supplement to Promote Diversity in Health-Related Research.

Christopher McGraw, MD, PhD (Poduri), received a grant from Citizens United for Research in Epilepsy to support his project entitled, A reverse genetic F0 screen using CRISPRi and calcium fluorescence to identify novel seizure resistance genes in zebrafish.

Aboozar Monavarfeshani, PhD (Z. He), received an NIH F32 fellowship for his project entitled, Uncovering novel targets for retinal ganglion cell neuroprotection and axon regeneration.

Jessica Page, PhD (Z. He), received an NIH F32 fellowship for her project entitled, Somatosensory corticospinal neurons as a biomarker for mind-body pain management strategies.

Alex Ren (Woolf) won the Hoopes Prize for his project entitled, Modeling NaV1.7 Channelopathies Using Genetically-Engineered Human iPSC-Derived Sensory Neurons.

Daniel Taub, PhD (Woolf) received funding from Harvard Medical School to support his project entitled, The Role of Phytocannabinoids in the Emotional Aspects of Pain.

Kellen Winden, MD, PhD (Sahin), received an NIH/NINDS K08 for his project entitled, Molecular mechanisms of neuronal hyperactivity in Tuberous Sclerosis Complex.

Christopher Yuskaitis, MD, PhD (Sahin), received funding from the American Academy of Neurology Foundation to support his project entitled, Neuroscience is Rewarding Internship. Dr. Yuskaitis also received the following awards:

• Boston Children's Hospital - Nutrient sensing defects in DEPDC5-related epilepsy.

• Child Neurology Foundation - Targeted nutrient manipulation via the mTOR pathway as targeted epilepsy therapy.

• Hearst Fund - Determination of the critical amino acids for mTORC1 signaling in neurons.











