

# RLS Foundation Research Grant Program: 1997–2021

The RLS Foundation Research Grant Program supports basic and clinical research on restless legs syndrome (RLS).

In 1997, the RLS Foundation established the Research Grant Program to fund small research grants (\$25,000–\$35,000) to stimulate and provide data for larger grants at federal agencies such as the National Institutes of Health, Department of Defense, biotechnology and medical technology companies. Funding priorities include basic and clinical research to promote a better understanding, advance new treatments and find a cure for RLS. The Research Grant Program invites innovative approaches, interdisciplinary studies and support of promising postdoctoral candidates.

The primary areas of funding have been genetics, epidemiology, iron regulation, neurophysiology and animal models/treatment. The Foundation's Scientific and Medical Advisory Board reviews grant applications and selects studies for funding based on scientific merit and alignment with funding priorities.

Since the grant program began, the Foundation has funded 48 research grants totaling over \$1.8 million. Eighty-five percent of the grant recipients reside in the United States and the remaining 15% of grant recipients are international. The average grant amount is \$38,569.

Ten of the recipients secured additional funding for their studies from government agencies, for total grant award dollars of over \$10 million. Recipients have published findings in over 25 papers and several book chapters.

#### Research Grant Program Makes Headway

In 2007, Dr. David Rye, funded in part by the RLS Foundation, discovered the first gene variant (BTBD9) that contributes substantially to the risk for RLS. In 2017 Dr. Sergi Ferré, with research grants from the RLS Foundation, hypothesized that the reason for increased glutamate

#### Grants by Priority Area, 1997–2021

and dopamine transmission in RLS is due to a decrease in adenosine transmission; increased dopamine and glutamate transmission leads to PLMS and hyperarousal in RLS. Dr. Ferré's team have also pinpointed a subtype of receptor in the brain – the dopamine D4 receptor – as a new target for dopamine drug development.

Dr. John Winkelman was awarded a grant in 2017 to develop the RLS Opioid Registry to evaluate the longterm safety and effectiveness of opioids for treatment of refractory RLS. This study will yield important data that will help to establish treatment parameters and future research.

These studies advance our knowledge and understanding of the causes of RLS and paves the way to improved diagnostic methods and more effective treatments.

To keep our researcher's work moving forward toward a cure, please make your tax deductible contribution to the RLS Foundation at **www.rls.org** or call 512-366-9109.



Priority Area	Number	Percent of Studies	Award	Percent of Funds
Genetics	11	23%	\$368,954	20%
Iron Regulation	6	13%	\$206,311	11%
Animal Models	11	23%	\$364,450	20%
Neurophysiology	5	10%	\$157,500	8%
Epidemiology	4	8%	\$326,356	17%
Dopamine	2	4%	\$69,600	4%
Treatment	7	15%	\$308,879	17%
Miscellaneous	2	4%	\$49,250	3%
TOTAL	48	100%	\$1,851,300	100%

## **Grant Award Recipients**

#### Genetics

Lan Xiong, MD, PhD (2009) Genome wide gene expression profile & iron regulation in RLS patients carrying the MEIS1 genetic risk variant McGill University, Montreal, Canada

Guy Rouleau, MD, PhD (2008) Defining the risk variants within the MEIS1, BTBD9,

MAP2K5/LBXCOR1 genomic regions in RLS patients Human Research Centre, Notre Dame Hospital, Montreal, Canada

Juliane Winkelmann, MD (2008) Worldwide genome-wide association study for RLS: WW-GWA-RLS Institute of Human Genetics GSF National Research Center, Munich, Germany

David B. Rye, MD, PhD (2006, 2007, 2008) RLS genome study - USA/ICELAND Emory University School of Medicine, Atlanta, GA

Juliane Winkelmann, MD (2005) EU-RLS-GENE – Three loci for RLS on chromosome 12q (RLS-1); 14q (RLS-2); and 9p (RLS-3) mapping study Institute of Human Genetics GSF National Research Center, Munich, Germany

Lan Xiong (2003) Dissecting Genes Involved in Restless Legs Syndrome in French-Canadian Population with Elevated Prevalence McGill University, Montreal, Canada

David B. Rye, MD, PhD (2002, 2004) Genetic linkage analysis of RLS in Iceland Emory University School of Medicine, Atlanta, GA

Guy Rouleau, MD, PhD (1999) Searching for genes predisposing to restless leg syndrome in the French-Canadian population Montreal General Hospital Research Institute, Montreal, Canada

### Iron Regulation

Padmavathi Ponnuru, PhD (2011) A role for MEISI in brain iron deficiency in Restless Legs Syndrome Drexel University College of Medicine, Philadelphia, PA

**Stephanie Miller Patton, PhD (2006)** *The contributory role that iron-sulfur cluster proteins play in RLS* Pennsylvania State University College of Medicine, Hershey, PA

Stephanie Miller Patton, PhD (2005) The contribution of iron regulatory proteins (IRP3) to the dysregulation of iron hemeostasis in RLS Pennsylvania State University Milton S. Hershey Medical Center, Hershey, PA

James R Connor, PhD (2003) Is Defective Transferrin Receptor Expression in the brain the underlying cause of RLS? Pennsylvania State University Milton S. Hershey Medical Center, Hershey, PA

James R. Connor, PhD (2001) Elucidating mechanisms for regulation of iron acquisition by the brain Pennsylvania State University, University Park, PA

Judith Owens, MD, MPH (1999–2000) Restless leg and periodic limb movements in children with iron deficiency anemia and elevated lead Brown University School of Medicine, Providence, RI

## **Animal Models**

Yuqing Li, PhD (2015) Characterization of Meis1 heterozygous knockout mice as a model of Willis-Ekborn Disease University of Florida, Gainesville, FL

#### Sergi Ferré, MD, PhD (2014, 2015)

Measuring corticostriatal neurotransmission in iron-deficient rats as a model for screening of drugs potentially useful in WED-RLS National Institute on Drug Abuse, Baltimore, MD

Yuan-Yang Lai, PhD (2012)

Effect of histamine H3 receptor antagonism on PLM in iron-deficient nats: an animal model of RLS and its treatment University of California Los Angeles and Sepulveda Research Corporation, Los Angeles, CA

Subhabrata Sanyal, PhD (2011) Genetic modeling of Restless Legs Syndrome in Drosophila Emory University School of Medicine, Atlanta, GA

Seiji Nishino MD, PhD (2004) PLMS in hypocretin-deficient narcoleptic dogs Stanford Center for Narcolepsy Research, Palo Alto, CA

Byron C. Jones, PhD (2004) Proposal to create mouse colony to identify candidate genes related to RLS

Pennsylvania State University, University Park, PA Yuan-Yang Lai, PhD (2002)

Ventral mesopontine junction mediated muscle activity during sleep

University of California, Los Angeles, North Hills, CA Felipe Espinosa, DVM, PhD (2001–2002)

Potential mouse model for human-RLS (hRLS) University of Texas Southwestern Medical Center, Dallas, TX

David B. Rye, MD, PhD (2001) Neural substrates of and pharmacologic interventions for restless legs syndrome and paroxysmal limb movements during sleep Emory University School of Medicine, Atlanta, GA

David B. Rye, MD, PhD (2000) Fellowship for Drs. Amanda Freeman and Glenda Keating - Nonhuman primate model of PLMS Emory University School of Medicine, Atlanta, GA

## Neurophysiology

Stephanie Miller Patton, PhD (2012) The role that the nitric oxide pathway plays in regulating vasodilation of the legs in Restless Legs Syndrome Pennsylvania State University College of Medicine, Hershey, PA

Stephanie Miller Patton, PhD (2009) The role that the hypoxia response pathway & neuronal nitric oxide synthase (nNOS) plays in the mechanism of RLS Pennsylvania State University College of Medicine, Hershey, PA

Douglas E. Wright, PhD (2006) Contributions of Abnormal Sensory Input from Muscle in RLS University of Kansas Medical Center, Kansas City, KS

Karin Stiasny-Kolster, MD (2004) Quantitative sensory testing (QST) in RLS Department of Neurology, Marburg, Germany

William Bara-Jimenez, MD (1997–1999) Restless Legs Syndrome Foundation Fellouship National Institute of Neurological Disorders and Stroke, Bethesda, MD

## Epidemiology

Hochang Benjamin Lee, MD (2013) Subcortical white matter hyperintensities on brain magnetic resonance imaging: a comparison between early-onset and late-onset RLS subjects Yale University, New Haven, CT

#### Jeffrey Durmer, MD, PhD (2005)

*Identification of restless legs syndrome in children* Emory University School of Medicine, Atlanta, GA

Lorene M. Nelson, PhD, and Stephen V. Van Den Eeden, PhD (2004)

Pilot study of restless legs syndrome in Kaiser Permanente Stanford University School of Medicine, Stanford, CA Kaiser Permanente Division of Research, Oakland, CA

Christopher J. Earley, MD, PhD (2001)

*Epidemiological study of an elderly twin cohort* Johns Hopkins University Bayview Medical Center, Baltimore, MD

## Dopamine

Shawn Hochman, PhD (2003) Spinal Dopamine Dysfunction and Restless Legs Syndrome Emory University School of Medicine, Atlanta, GA

#### David Eidelberg, MD (2002)

A quantitative whole-brain imaging study of the dopamine transporter in the RLS using FP-betaCIT PET Scanning North Shore University Hospital, Manhasset, NY

## Treatment

Sergi Ferré, MD, PhD (2019) Elucidating the mechanisms of the therapeutic effects of opioids in RLS National Institute on Drug Abuse, Baltimore, MD

John Winkelman, MD, PhD (2017–2019, 2019, 2020, 2021) Multicenter Longitudinal Pilot Observational Study of Efficacy and Tolerability of Long-term Treatment of Restless Legs Syndrome Using Opioids (RLS Opiod Registry) Harvard Medical School/Massachusetts General Hospital, Boston, MA

William Ondo, MD (2016) Treatment of RLS augmentation with Ecopipam, A D1 Specific Antagonist

Houston Methodist Neurological Institute, Houston, TX

Michael Polydefkis, MD (2000) A Trial of gabapentin in RLS stratifying patients by presencelabsence of small fiber neuropathy Johns Hopkins University School of Medicine, Baltimore, MD

### **Miscellaneous**

#### William Padula, PhD, MS, Msc (2016)

*Economic Evaluation of Restless Legs Syndrome (RLS)* Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

William G. Ondo, MD (2000) Assistance with the Harvard Brain Tissue Resource Center Baylor College of Medicine, Houston, TX

The RLS Foundation does not endorse or sponsor any products or services.



The RLS Foundation is dedicated to improving the lives of the men, women and children who live with this often devastating disease. Our mission is to increase awareness, improve treatments and through research, find a cure for restless legs syndrome.

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