RLS Foundation Research Grant Program: 1997–2024

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

In 1997, the RLS Foundation established the Research Grant Program to fund seed money 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 and biotechnology and medical technology companies. Funding priorities include basic and clinical research to promote a better understanding, advance new treatments to 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 include genetics, iron regulation, neurophysiology, animal models and treatment.

Since the grant program began, the Foundation has funded over 50 research grants totaling over \$2 million. The average grant amount is \$38,129 and recipients reside both inside the United States and internationally.

The Research Grant Program Application Process

In January, the RLS Foundation announces a request for grant proposals of a 1 year-duration, with funding up to \$50,000 (including 8% for F&A costs). A renewal or extension for a proposed project may be considered, but this extension would be subject to the regular competitive approval process for year two.

Submission is a two-step process requiring both a preapplication (letter of intent) and a full application if requested.

The Foundation's Scientific and Medical Advisory Board (SMAB) reviews grant applications and selects studies for funding based on scientific merit and alignment with funding priorities. The SMAB will evaluate and rank the full proposals based on scientific merit. Overall impact, significance, approach, innovation (conceptual, technical) and individual criteria will be taken into account for funding consideration.

The RLS Foundation Board of Directors will make final award decisions in accordance with available funds, based on the evaluation provided by the SMAB and other prioritization factors as determined by the Board of Directors.

Application Requirements

Eligibility: All institutions within the United States and other countries where supervision of grant administration is possible are eligible.

Human Subject Protection: Approval by the institution's human investigation committee is necessary for all projects that involve human subjects.

Recombinant DNA Research and Animal Welfare: The RLS Foundation has adopted the regulations pertaining to these areas, as established by the US Public Health Service.

Multiple Awards: Individual investigators may receive a maximum of one RLSF grant award of any kind in a given year.

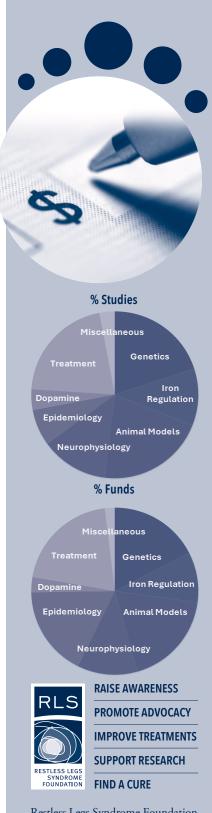
Research Grant Program Advances Progress

Over the years, RLS Foundation funded research has led to new discoveries on the pathophysiology of RLS. Numerous researchers have secured additional funding for their studies from government agencies and have published findings at conferences, in novels and peer-reviewed publications.

Notable Research Funding Results

2007: David Rye, MD, funded in part by the RLS Foundation, discovered the first gene variant (BTBD9) that contributes substantially to the risk of RLS.

2017: Sergi Ferré, MD, PhD, with research grants from the RLS Foundation, hypothesized that the reason for increased glutamate and dopamine transmission in RLS is due to a decrease in adenosine transmission; increased dopamine and glutamate transmission leads to PLMS and hyperarousal in



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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.

2017: John Winkelman, MD, PhD was awarded a grant 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.

2017: William Ondo, MD was awarded a grant for a small study using a D1-receptor specific antagonist to treat individuals with augmentation.

These studies advance our knowledge and understanding of the causes of RLS, paving 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.

Grants by Priority Area, 1997-2024

Priority Area	No.	% of Studies	Award	% of Funds
Genetics	11	20%	\$368,954	18%
Iron Regulation	6	11%	\$206,311	10%
Animal Models	12	21%	\$410,746	19%
Neurophysiology	7	13%	\$257,359	12%
Epidemiology	4	7%	\$326,356	15%
Dopamine	2	4%	\$69,600	3%
Treatment	12	21%	\$446,669	21%
Miscellaneous	2	3%	\$49,250	2%
TOTAL	56	100%	\$2,135,245	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, MD, PhD (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 MEIS1 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 (IRPs) 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,

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

Shawn Hochman, PhD (2024)

Sensory dysfunction in a diet-induced iron deficiency mouse model of RLS: Characterization and control by dopamine-sensitive spinal gating circuitry

Emory University School of Medicine, Atlanta, GA

Yuqing Li, PhD (2015)

Characterization of Meis1 heterozygous knockout mice as a model of Willis-Ekbom 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 rats: 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

Linguisting of California, Los Angeles, North

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 - Non-human primate model of PLMS

Emory University School of Medicine, Atlanta, GA

Neurophysiology

Iman Ghorayeb, MD, PhD (2024)

Functional connectivity of the interoceptive network in RLS: an anatomo-clinical prospective study

Hospital Center University De Bordeaux, Bordeaux, France

Brian Koo, MD (2024)

Cerebrospinal Fluid Melanocortin and Endorphin in Restless Legs Syndrome Related Augmentation

Yale Center for Sleep Medicine, New Haven, CT

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 Fellowship 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 and 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

Mauro Manconi, MD, PhD (2024) Epidural Spinal Cord Stimulation in Refractory or Augmented Restless Legs Syndrome Sleep and Epilepsy Center; Civic Hospital Neurocenter of Southern Switzerland, Lugano, Switzerland

Mark Boulos, MD (2023)

Using Cannabis to Treat Restless Legs Syndrome: A Safety and Feasibility Study University of Toronto, Toronto, Canada

Sergi Ferré, MD, PhD (2019)

Elucidating the mechanisms of the therapeutic effects of opioids in RLS
National Institute on Drug Abuse, Baltimore,

John Winkelman, MD, PhD (2017–2019, 2019, 2020, 2021, 2022, 2023, 2024)

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 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 advance research to find a cure.

This publication has been reviewed and approved by reviewers from the RLS Foundation Scientific and Medical Advisory Board.

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