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 47 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 $39,000.

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 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.

**Grants by Priority Area, 1997–2020**

<table>
<thead>
<tr>
<th>Priority Area</th>
<th>Number</th>
<th>Percent of Studies</th>
<th>Award</th>
<th>Percent of Funds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetics</td>
<td>11</td>
<td>23%</td>
<td>$368,954</td>
<td>20%</td>
</tr>
<tr>
<td>Iron Regulation</td>
<td>6</td>
<td>13%</td>
<td>$206,311</td>
<td>11%</td>
</tr>
<tr>
<td>Animal Models</td>
<td>11</td>
<td>23%</td>
<td>$364,450</td>
<td>20%</td>
</tr>
<tr>
<td>Neurophysiology</td>
<td>5</td>
<td>11%</td>
<td>$157,500</td>
<td>9%</td>
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<tr>
<td>Epidemiology</td>
<td>4</td>
<td>9%</td>
<td>$326,356</td>
<td>18%</td>
</tr>
<tr>
<td>Dopamine</td>
<td>2</td>
<td>4%</td>
<td>$69,600</td>
<td>4%</td>
</tr>
<tr>
<td>Treatment</td>
<td>6</td>
<td>13%</td>
<td>$290,879</td>
<td>16%</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>2</td>
<td>4%</td>
<td>$49,250</td>
<td>3%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>47</td>
<td>100%</td>
<td>$1,833,300</td>
<td>100%</td>
</tr>
</tbody>
</table>
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/LBX1COR1 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

RLS genome study - USA/CELAND
Emory University School of Medicine, Atlanta, GA

Juliane Winkelmann, MD (2005)
EU-RLS-GENE - Three loci for RLS on chromosome 12q (RLS-1); 1q4 (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 Leg Syndrome in French-Canadian Population with Elevated Prevalence
McGill University, Montreal, Canada

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

Padmasvasti Pomprat, PhD (2011)
A role for MEIS1 in brain iron deficiency in Restless Leg 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 hemostasis 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

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-ElION Disease
University of Florida, Gainesville, FL

Sergi Ferré, MD, PhD (2014, 2015)
Measuring centromeric recombination 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

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

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

Byron C. Jones, PhD (2004)
Proposal to create mouse colonies to identify candidate genes related to RLS
Pennsylvania State University, University Park, PA

Yuan-Yang Lai, PhD (2002)
Vertebral osteoporosis: juxtasomatic muscle activity during sleep
University of California, Los Angeles, North Hills, CA

Felipe Espinosa, DVM, PhD (2001–2002)
Potential mouse model for Ironman-RLS (IRLS)
University of Texas Southwestern Medical Center, Dallas, TX

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

David B. Rye, MD, PhD (2000)
Follow up for Drs. Amanda Freeman and Glenda Keating - Novel human 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 Leg Syndrome
Pennsylvania State University College of Medicine, Hershey, PA

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

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

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

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 Dummer, MD, PhD (2005)
Identification of restless leg 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 leg 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 elderlyascohort
Johns Hopkins University Bayview Medical Center, Baltimore, MD

Dopamine

Shawn Hochman, PhD (2003)
Spinal Dopamine Dysfunctions 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 F18-beta-CIT 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 Winkelmann, MD, PhD (2017–2019, 2019, 2020)
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 Extispam, A D1 Specific Antagonist
Houston Methodist Neurological Institute, Houston, TX

Michael Polydefkos, MD (2000)
A trial of gabapentin in RLS of patients by presymptomatics of small fiber neuropathy
Johns Hopkins University School of Medicine, Baltimore, MD

Miscellaneous

William Pedula, 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.