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 of the disease, 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 44 research grants totaling nearly $1.8 million. Eighty-three percent of the grant recipients reside in the United States and the remaining seventeen percent of grant recipients are international. The average grant amount is $39,927.

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 22 papers and several book chapters.

Grants by Priority Area, 1997–2018

<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>25%</td>
<td>$368,954</td>
<td>21%</td>
</tr>
<tr>
<td>Iron Regulation</td>
<td>6</td>
<td>14%</td>
<td>$206,311</td>
<td>12%</td>
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<tr>
<td>Animal/Treatment Models</td>
<td>12</td>
<td>27%</td>
<td>$397,299</td>
<td>23%</td>
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<tr>
<td>Neurophysiology</td>
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<td>11%</td>
<td>$157,500</td>
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<td>Epidemiology</td>
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<td>9%</td>
<td>$326,356</td>
<td>19%</td>
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<tr>
<td>Dopamine</td>
<td>2</td>
<td>5%</td>
<td>$69,600</td>
<td>4%</td>
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<tr>
<td>Miscellaneous</td>
<td>4</td>
<td>9%</td>
<td>$230,782</td>
<td>13%</td>
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<tr>
<td>TOTAL</td>
<td>42</td>
<td>100%</td>
<td>$1,756,802</td>
<td>100%</td>
</tr>
</tbody>
</table>

Research study uncovers gene variant for RLS

In 2007, Dr. David Rye, funded in part by the RLS Foundation, discovered the first gene variant that contributes substantially to the risk for RLS. More recently, in 2017 Dr. Sergi Ferré, with research grants from the RLS Foundation, has hypothesized that the reason for increased glutamate and dopamine transmission in RLS is due to a decrease in adenosine (which exerts a brake on both systems) transmission. It has been known for some time that the increased dopamine and glutamate transmission leads to PLMS and hyperarousal in RLS. The researchers have also pinpointed a subtype of receptor in the brain – the dopamine D4 receptor – as a new and better target for dopamine drug development.

This influential research significantly advanced understanding of the causes of the disease, paving the way for future improvements in diagnostic methods and treatments.

To keep this great work moving forward toward a cure, please contribute to the RLS Foundation Research Grant Program at www.rls.org or call 512-366-9109.
Grant Award Recipients

Genetics

Lan Xiong, MD, PhD (2009)
Genome wide gene expression profile & iron regulation in RLS patients carrying the MEIS1 genetic 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

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); 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

Genetic linkage analysis of RLS in Irishland
Emory University School of Medicine, Atlanta, GA

Guy Rouleau, MD, PhD (1999)
Searching for genes predisposing to restless legs 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 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 deregulation of iron homeostasis in RLS
Pennsylvania State University Milton S. Hershey Medical Center, Hershey, PA

James R Connor, PhD (2003)
5-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/Treatment Models

Sergi Forner, 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

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

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 VA Hospital, Los Angeles, CA

Subhabrata Sanyal, PhD (2011)
Genetic modeling of Restless Leg 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
Emory University School of Medicine, University Park, PA

Yuan-Yang Lai, PhD (2002)
Ventriculomegaly: putative role of iron metabolism in the brain during deep sleep
University of California, Los Angeles, North Hills, CA

Felipe Espinosa, DVM, PhD (2001–2002)
Potential animal models for human RLS (ARLS)
University of Texas Southwestern Medical Center, Dallas, TX

David B. Rye, MD, PhD (2001)
Neurodegeneration 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)
Fellowship for Drs. Anuradha Freeman and Genda Kato - Non-human primate model of PLMS
Emory University School of Medicine, Atlanta, GA

Michael Polydendis (2000)
A Trail of glutapentin in RLS patients by presence/absence of small fiber neuropathy
Johns Hopkins University School of Medicine, Baltimore, MD

Epidemiology

Hochang Benjamin Lee, MD (2013)
Subclinical 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 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 legs syndrome in Kaiser Permanente
Stanford University School of Medicine, Stanford, CA

Christopher J. Farley, 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 [18F-FP-CIT] PET Scanning
North Shore University Hospital, Manhasset, NY

Miscellaneous

John Winkelmann, MD, PhD (2017)
Midcerebellum Longitudinal Pilot Observational Study of Efficacy and Tolerability of Long-term Treatment of Restless Legs Syndrome Using Opioids
Harvard Medical School/Manuscripts General Hospital, Boston, MA

William Onso, MD (2016)
Treatment of RLS augmentation with Epopipam, A D1 Specific Antagonist
Houston Methodist Neurological Institute, Houston, TX

William Padula, PhD, MS, Msc (2016)
Economic Evaluation of Restless Leg 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

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