2023 Neuropsychiatric Illness and Regression Fellowship

REQUEST FOR APPLICATIONS

Phelan-McDermid Syndrome Foundation/Developmental Synaptopathies Consortium

When:

RFA released: **Jan 17 2023**
Letter of intent deadline: **March 1 2023 midnight ET**
Full application deadline: **April 1 2023 midnight ET**
Announcement of award**: ~August 2023**

What:
$100,000 for one year ($90,000 direct costs, $10,000 indirect)

Fellowship description:

We are seeking highly qualified postdoctoral applicants with an MD, PhD, or MD/PhD, for the Phelan-McDermid Syndrome Foundation/Developmental Synaptopathies Consortium Young Investigator Fellowship. The ideal candidate has a clinical and/or research background in psychiatry, psychology, or neurology with a focus on neurodevelopmental disorders, and seeks to complement their expertise to become a leader in this growing field.

The fellow will help characterize neuropsychiatric phenotypes in patients with Phelan-McDermid syndrome (PMS). PMS is a rare genetic condition caused by a deletion or other structural change of the terminal region of chromosome 22 or a disease-causing sequence variant of the *SHANK3* gene: pmsf.org. PMS is commonly associated with hypotonia, intellectual disability, and delayed or absent speech.

Data is emerging that a subset of individuals with PMS experience devastating psychiatric symptoms, such as regression, bipolar disorder, and catatonia. **The goal of this fellowship is to deeply characterize these psychiatric symptoms, refine guidelines, and/or explore their biological underpinnings.**

The fellow will work within the NIH-funded Developmental Synaptopathies Consortium (DSC), a Rare Disease Clinical Research Network, under the training of leaders in the field with a pre-established infrastructure for recruiting and phenotyping large numbers of individuals with this rare disorder.

The training environment afforded by the Consortium includes access to PMS investigators, clinicians, and affected individuals, as well as interaction with other groups working on related genetic disorders - Tuberous Sclerosis Complex and PTEN Hamartoma Tumor Syndrome.

In addition, the investigator will have access to the PMS Neuropsychiatric Consult Group – a group which offers provider to provider medical advice for the treatment of people with PMS with a neuropsychiatric illness: https://pmsf.org/neuropsychiatric-consultation-group/. This group has accrued data on neuropsychiatric consults (Appendix 3).

Priority will be given to fellows motivated to utilize the rich datasets that have been generated by the Developmental Synaptopathies Consortium and the Neuropsychiatric Consult Group. Details describing the research resources available are in Appendices 2 and 3 of this document.

Areas of potential research focus include, but are not limited to, mechanistic studies of neuropsychiatric decompensation and regression in PMS, identification of preceding or co-occurring symptoms alongside neuropsychiatric episodes, clinical guidelines for assessment and care of people with PMS who experience neuropsychiatric decompensation, and outcome measure development for use in clinical trials in PMS. Applicants are encouraged to review literature and consult with their mentor on current understanding of phenotyping/characterization of neuropsychiatric illness in PMS, and to extend beyond this in their application to biological underpinnings and clinical assessment or intervention.

Eligibility:

- This opportunity is open to all early career investigators (<8 years since graduate degree) working in a relevant field (neurology, psychiatry, or psychology, and/or a focus in neurodevelopmental disorders or rare disorders). Funding is not restricted to US residents or citizens.

- Mentorship: The fellow will work closely with a Developmental Synaptopathies Consortium (DSC) mentor during the fellowship and is required to connect with a mentor ahead of time to express interest, discuss qualifications, and receive a letter of recommendation. All PMS DSC leaders and their respective sites are listed in Appendix 1. Applicants already eligible to work at one of the five PMS DSC sites, including Boston Children's Hospital, National Institute of Mental Health, Rush University Medical Center, Stanford University, and Seaver Autism Center at Icahn School of Medicine at Mount Sinai, should contact a mentor at that site. Applicants

from outside of these institutions are still eligible to apply and are required to receive a letter of recommendation from a DSC mentor at any site who the applicant feels is a good match for their proposed work. If the applicant is having trouble connecting with a mentor, please contact DSC leadership at TNC@childrens.harvard.edu for help.

Important notes:
Applications which do not have all components or are not submitted on time will be disqualified.

Applicants must submit a letter of intent by March 1, 2023 in the form of a scientific abstract (250 word limit) describing their project *prior* to full submission of their application on April 1. All applicants are invited to submit both a letter of intent and full application without review from PMSF. The letter of intent allows PMSF to find grant reviewers and gauge the volume of applications and is thus required and should only be submitted if the applicant is submitting a full application. **Early submissions of letters of intent prior to March 1st are highly encouraged.**

PMS families will take part in the final stage of the review process. Applications which are not highly relevant to families or do not have well-written lay abstracts are unlikely to be successful.

Submission process:
All required components should be sent as a combined PDF email attachment to PMSF's Scientific Director, Dr. Kate Still (kate@pmsf.org) with the subject line: [Grant title; last name of applicant; part of application]

There are four parts to each application, requiring four separate emails: (Letter of intent, full application, two separate reference emails).

Required Components:

By March 1 2023:

- **Letter of Intent** – scientific abstract describing the proposed project (<250 words)

By April 1 2023 (full application components):

- **Investigator CV or NIH-format biosketch**, either is accepted (< 5 pages)
- **Scientific abstract** (<250 words) – can be the same as letter of intent or have minor updates
- **Lay abstract** (<250 words)
    - *Important: PMS families will review applications– successful applications will have lay abstracts which fully encompass the work, including methods, and will be written in a digestible way
- **Research Strategy -** (<2 pages not including references)

    - Should include background/rationale, preliminary data (if applicable), project aims and methods
    - References should be included and do not count towards the page limit (no limit)
- **Early Career Investigator Statement** (< 1 page)
    - Explain career goals, how they will be achieved, and how Phelan-McDermid syndrome could continue to be a focus after completion of this award
- **Budget** (<1 page or spreadsheet)
    - Exact budget allocations as line items
- **Budget justification** (<1 page)
    - Short descriptions explaining budget line items
- **2 letters of support** (<1 page each) – sent to kate@pmsf.org separately by references (mentor, colleague, collaborator, etc)

Review process:

Initial review will be done to remove incomplete applications. A second review will occur based on scientific merit including reviewers from the PMSF Scientific and Medical Advisory Committees, the PMS Neuropsychiatric Consult Group, and from the wider PMS research community. Applications will be scored from 1-5 based on the following categories, and additional categories as needed:

- Investigator background
- Research strategy
- Impact of grant to PMS families
- Impact of grant to PMS research field
- Probability the grant will be technically successful
- Reasonable budget

Top-scoring applications will be sent to a third review from PMS families. Final decisions will be made in conjunction with PMSF staff and Board of Directors, and successful applicants will be notified in the summer of 2023. Applications not selected for an award will receive a summary of reviews in an anonymous fashion in the fall of 2023.

For Grant-Related Inquiries, Contact: kate@pmsf.org

Appendix 1: Developmental Synaptopathies Consortium PIs/Mentors

*PMS investigators are highlighted

Boston Children's Hospital (TSC, PTEN, and PMS):
PI – Mustafa Sahin, MD, PhD (Consortium Investigator)
EEG Lead – Chuck Nelson, PhD
MRI Lead – Simon Warfield, PhD
Biostatistician – Bo Zhang, PhD

Stanford University (TSC, PTEN, and PMS):
TSC PI – Brenda Porter, MD
PTEN PI – Antonio Hardan, MD
PMS PI – Jon Bernstein, MD

Cincinnati Children's Hospital Medical Center (TSC and PTEN):
PI – Darcy Krueger, MD, PhD (TSC Study Chair)
PI – David Ritter, MD, PhD

University of California at Los Angeles (TSC and PTEN):
TSC PI – Shafali Jeste, MD
PTEN PI – Julian Martinez, MD, PhD

University of Alabama at Birmingham (TSC):
PI – Martina Bebin, MD

University of Texas Health Science Center at Houston (TSC):
PI – Hope Northrup, MD
Lead TSC Psychologist – Deborah Pearson, PhD

Cleveland Clinic (PTEN):
PI – Charis Eng, MD, PhD (PTEN Study Chair)
Lead PTEN Psychologist – Robyn Busch, PhD

Mount Sinai School of Medicine (PMS):
PI – Alex Kolevzon, MD (PMS Study Chair)
Director of Administrative Core – Joseph Buxbaum, PhD

National Institutes of Health (PMS):
PI and Lead PMS Psychologist – Audrey Thurm, PhD

Rush University Medical Center (PMS):
PI – Elizabeth Berry-Kravis, MD, PhD
PI – Latha Soorya, PhD

Consultant:
Lead Psychologist – Celine Saulnier, PhD

Developmental Synaptopathies Consortium

RARE DISEASES CLINICAL RESEARCH NETWORK

Appendix 2: Data fields

Data Field	Group 1: Subjects	Group 2: Biological Parents/Siblings	Group 3: Healthy Controls
Demographics	X	X	X
Diagnostic History	X		
Development History (i.e. speech/language, school, early life, etc.)	X		
Medical History (i.e. Treatment, interventions, seizure, diet, etc.)	X		
Seizure History	X		
Imaging Studies	X		
mTOR Inhibitor Use	X		
Vital Signs	X		X
Physical and Neurological Exam	X		
Biological Parent Medical History	X	X	
Biological Sibling Medical History	X	X	
DNA/ RNA Sample Collection	X	X	
Prior and Concomitant Medications	X		
MRI Data Quality	X		
Protocol Deviation Form	X		
Conclusion of Study Participation	X		
Death Record	X		
Optional Blood/ Bio Sample Collection	X		
Renal Ultrasound Upload Form	X		
Mullen Scales of Learning	X		X
Stanford-Binet Intelligence Scales	X		X
DAS-II	X		
Peabody Picture Vocabulary Test – 5 (PPVT-5)	X		X
Expressive Vocabulary Test – 2 (EVT-2)	X		X
Beery Test of Visual-Motor Integration, Sixth Edition (VMI-6)	X		
Autism Diagnostic Observation Schedule-2 (ADOS-2)	X		
Wechsler Processing Speed Index Subtests – (WAIS, WISC, WPPSI)	X		
Connors Continuous Performance Test (CPT-3/K-CPT-2)	X		
Early Skill Attainment and Loss (Regression Supplement)	X		

Vineland Adaptive Behavior Scales (VABS-II & VABS-III) – Comprehensive Interview Form	X		
Autism Clinical Certainty Score	X		X
Diagnostic and Statistical Manual of Mental Disorders (DSM-5) Checklist	X		X
CARS-2	X		
Autism Diagnostics Interview Revised (ADI-R)	X		
Developmental Profile, Fourth Edition (DP-4)	X		
Child Behavior Checklist/Adult Behavior Checklist (CBCL/ABCL)	X		
Aberrant Behavior Checklist (ABC-2)	X		X
Developmental Coordination Disorder Questionnaire (DCDQ)	X		
Repetitive Behavior Scale – Revised (RBS-R)	X		
Short Sensory Profile Questionnaire (SPQ)	X		
Child/Individual & Family Quality of Life Measure (CFQL-2 or IFQL)	X		
Social Responsiveness Scale, 2nd Ed	X		X
TSC-Associated Neuropsychiatric Disorder (TAND) Checklist	X		
ORCA Ages 2+, minimally verbal or nonverbal	X		
Vineland Adaptive Behavior Scales (VABS-II & VABS-III) – Parent/Caregiver Form	PHTS and TSC only		X
Psychoeducational Profile-III	PMS ONLY		
MacArthur CDI-III	PMS ONLY		
PDD-BI	PMS ONLY		
Sensory Assessment for Neurodevelopmental Disorders (SAND)	PMS ONLY		
Early Detection Screen for Dementia	PMS ONLY		
Children's Sleep Habits Questionnaire	PMS ONLY		
Waisman Activities of Daily Living	PMS ONLY		
Vineland Adaptive Behavior Scales (VABS-II & VABS-III) – Comprehensive Interview Form	PMS ONLY		X
BRIEF	PHTS ONLY		
Stanford-Binet-5 Working Memory	PHTS ONLY		
Behavior & Stereotyped Interests Questionnaire (BSIQ)	BCH ONLY		

Appendix 3: Neuropsychiatric Consult Group – Available datasets

Data is available on >50 PMS patients with neuropsychiatric illness:

- **ECHO case consultation forms provided by consulting physicians – https://pmsf.org/wp-content/uploads/2021/01/PMS-NCG-Echo-form_updated-3.4.19.pdf**
- **Early skill attainment and loss measure (regression)**
- **Family survey – deep dive into each symptom domain**