
**ORPHAN DISEASE CENTER
MILLION DOLLAR BIKE RIDE
PILOT GRANT PROGRAM**

The ODC MDBR Pilot Grant Program provides a one-year grant to support research related to a rare disease represented in the 2019 Million Dollar Bike Ride. Number of awards and dollar amounts vary per disease based on fundraising totals by each disease team.

Eligibility

All individuals holding a faculty-level appointment at an academic institution or a senior scientific position at a non-profit institution or foundation are eligible to respond to this RFA.

Letter of Interest Instructions:

Please visit our [website](#) to submit your Letter of Interest (LOI), which can also be found [here](#). This one-page LOI is due no later than **Monday, September 23, 2019 by 8pm (EST)**.

Full Application Instructions and Review Procedure

NOTE: Full Application is by invitation only after review of Pre-Application

Proposal Due Date: **Thursday, October 24, 2019 no later than 8pm (EST)**

Full application documents are to be uploaded on our [website](#), by invitation only.

FORMAT for documents:

Font and Page Margins: Use Arial typeface, a black font color, and a font size of 11 points. A symbol font may be used to insert Greek letters or special characters. Use 0.5 inch margins (top, bottom, left, and right) for all pages, including continuation pages. Print must be clear and legible; all text should be single-spaced.

Header: There should be a header at the top right on all pages of the PDF indicating the full name of the PI (e.g., **PI: Smith, John D.**).

For your convenience, a continuation page template is included at the end of the application document.

File names: ALL files to be uploaded should start with the LAST NAME of the PI followed by the brief name of the document. Examples: SMITH CV, SMITH Cover Page, SMITH Budget. **If files are not labeled properly, you will be asked to resubmit the PDFs before your application can be considered.**

CONTENT to be uploaded:

- Cover Page/Checklist/Institutional Signature Page [PDF].**
- NIH-style Biosketch with Other Support of PI and key personnel (5 pages max). [PDF]**
The PI must include accurate and complete information regarding all other sources of grant support (current and pending), including title, abstract, annual and total amount of grant, inclusive funding period, and percent effort.

□ Detailed Budget and Justification. [combined into one PDF]

Complete Excel budget sheet (to be provided). Describe justifications in a Word document. Award will be for one year. Proposed funding period: February 1, 2020 – January 31, 2021. Total Budget depends on disease RFA:

Disease	Total Funds	# of Awards	Award Total
APBD	\$105,017	2	\$52,509
A-T	\$56,418	1	\$56,418
BPAN	\$61,245	1	\$61,245
CADASIL	\$81,951	1	\$81,951
Castleman	\$51,358	1	\$51,358
CDKL5	\$55,898	1	\$55,898
CHI	\$72,014	1	\$72,014
Choroideremia	\$61,079	1	\$61,079
CF	\$54,718	1	\$54,718
CMD	\$91,176 or \$45,588	1 or 2	\$91,176 or \$45,588
CMT	\$60,330	1	\$60,330
CRB1	\$80,354	2	\$40,177
DC	\$62,664	1	\$62,664
FD/MAS	\$84,325 or \$42,163	1 or 2	\$84,325 or \$42,163
FOP	\$80,415	2	\$40,208
GLA/GSD	\$62,861	1	\$62,861
Glut 1DS	\$46,858	1	\$46,858
IBM	\$102,430	1	\$102,430
LAM	\$72,704	1	\$72,704
ML4	\$78,538	1	\$78,538
MPS	\$64,063	1	\$64,063
MPS Gene Spotlight	\$61,589	1	\$61,589
MSUD	\$88,073	2	\$44,037
NEHI	\$60,989	1	\$60,989
NPC	\$61,637	1	\$61,637
NUBPL	\$61,134	1	\$61,134
Pitt Hopkins	\$68,709	1	\$68,709
RASopathies	\$59,220	1	\$59,220
SETBP1	\$67,943	1	\$67,943
Snyder-Robinson	\$69,318	1	\$69,318
STXBP1	\$139,176	2	\$69,588

Institutions may opt to take up to 10% IDCs from their award totals. Awarded amounts will not exceed Award Totals listed above.

Allowable direct costs

- Salary for PI
- Salary/stipend and related benefits for graduate student/postdoctoral fellow/technical support
- Travel (up to \$1500)
- Laboratory supplies and other research expenses
- IDCs of 10% are included in the total award amount

Unallowable costs

- Consultant costs
- Tuition
- Professional membership dues
- Equipment >\$5,000
- General office supplies, institutional administrative charges (e.g., telephone, other electronic communication, IT network, etc.)
- Pre-award charges
- Any other expenses not directly related to the project

- **Research Plan** (5 pages max) and **Bibliography** (1 page max). **[combined into one PDF]** Include the following sections: Specific Aims, Background and Significance, Preliminary Studies/Data, Research Design and Methods. Research plan should address the following questions: 1) Do you require access to reagents, cell lines, animal models, IRB/ethical board approvals, and/or equipment necessary to complete work? If so, please describe your plan to gain access within the time-frame of this grant period. 2) Have you identified qualified personnel to complete this project within the grant period? If not, please provide your plan to do so. Text citations should use a numbered format. Include all author names in the reference list.

All previous MDBR grant awardees must include a statement of outcomes including publications, patents and additional funding granted as a result of data generated from those grants. Specific aims must be different from those in previous applications.

- **Appendix [combined into one PDF]** Limited to 5 pages of supplemental information pertaining to proposal or preliminary data only; a maximum of 3 relevant reprints are also acceptable. Include IRB and/or IACUC approval letters if relevant.

Project Disclosures and No Cost Extensions (NCE):

- NCEs will be granted at the discretion of the ODC.
- Awardees will be limited to 1 NCE request for their award.
- Maximum NCE time awarded will be 6 months.
- NCEs will be granted after a formal request through [this form](#) found on the ODC website prior to the NCE deadline with adequate justification.
- If granted a NCE, you are still required to submit an interim scientific report 6 months into the duration of the original award period, regardless of your new project end date.
- In your letter of interest, you will be required to certify that you have identified qualified personnel to complete this project within the grant period **PRIOR** to the start date of the award. If you have not, you will be required to provide your plan to engage said personnel. Only under extenuating circumstances will personnel issues be considered for NCE requests.
- In your letter of interest, you will also be required to state whether or not you require access to reagents, cell lines, animal models, IRB/ethical board approvals, and/or equipment necessary to complete your work. If so, you will be required to describe your plan to gain access within the time-frame of this grant period.

Research Focus Areas for Pilot Grants:

1) Adult Polyglucosan Body Disease (APBD): Two \$52,509 grants are available to initiate or advance research of a treatment or a cure for this glycogen storage disease. These grants are made possible by the Tour de Friends bike team with the APBD Research Foundation.

2) Ataxia-Telangiectasia (A-T): One \$56,418 grant, made possible by Team Derek's Dreams and the A-T Children's Project, is available to test therapeutic approaches to the neurodegeneration and motor control problems faced by children who have Ataxia-Telangiectasia. Grant applications may propose early, preclinical studies such as the validation of proteins that could be potential therapeutic targets, the development of gene therapy vectors that could carry the large ATM gene, gene editing strategies that could correct ATM mutations, or the elucidation and modulation of neurocircuitry disrupted in A-T. Proposed projects must,

however, be novel and have a clear path for translation to a therapy. Please note that, although *Atm*^{-/-} mice may be used to evaluate the efficacy of gene therapy in correcting the expression of the ATM protein, attempting to use *Atm*^{-/-} mice to evaluate the correction of a neurological phenotype will not be funded. In addition, the generation of iPS cell lines derived from A-T patient cells and the disruption of the ATM gene in normal or carrier cells have previously been done and will not be funded.

3) BPAN -- A Neurodegeneration with Brain Iron Accumulation Disorder: BPAN - A Neurodegeneration with Brain Iron Accumulation Disorder: One pilot grant for \$61,245 is available for clinical and translational research studies related to the detection, diagnosis, or treatment of this rare, X-linked disorder caused by mutations in *WDR45*. BPAN typically is recognized in early childhood with delayed development and seizures. In adulthood, people with BPAN develop rapidly progressive parkinsonism. At the present time, symptoms may be treated but there are no cures.

Grants are expected to generate essential resources for the scientific community, advance knowledge about BPAN disease processes, and produce preliminary data to enable national and international funding to carry the work forward. Examples of priority topic areas include developing disease models that complement existing models, identifying biomarkers, delineating the molecular cascade that leads to early cellular changes, developing rational therapeutics, establishing outcome measures to be used in clinical trials, and developing other essential resources to substantially prepare the BPAN community for clinical trials. Natural history studies must have a component that includes participation in the International NBIA Patient Registry & Biobank. These grants are made possible by Team NBIA Disorders and BPAN families with the NBIA Disorders Association.

4) Castleman Disease: A \$51,358 pilot grant is available to perform further investigation and functional characterizations of candidate pathological genomic aberration(s) identified in unicentric Castleman disease (UCD) or HHV-8-negative/"idiopathic" multicentric Castleman disease (iMCD), such as *PDGFRb*. Proposals should seek to validate identified candidate genomic aberrations through functional assays to clearly demonstrate an effect of the identified aberration. We expect the investigator's application to provide information on the genomic aberration identified, functional studies to demonstrate the effect of the aberration and hypothesized mechanisms for how the aberration leads to UCD or iMCD pathogenesis. Proposing pharmacologic studies to revert the phenotype is a plus. Investigators who have preliminary data and/or a proven track record of performing in vitro or in vivo functional investigation of genomic defects in related disorders should apply. If preliminary data suggests that the aberration is acquired, proposals should also include studies to identify the harboring cell population. Applications with significant preliminary data demonstrating that the genomic aberration was discovered in patient(s) that fit the criteria for iMCD diagnosis, a strong rationale for causation and readily testable experimental systems will be favored. All grant applications will be considered confidential. The Castleman Disease Collaborative Network (CDCN) will support the project through sample procurement, as needed, and can provide its expertise and guidance to facilitate functional assay development. For a complete listing of CDCN studies, visit: <https://www.cdcn.org/research-pipeline>

5) CDKL5: One \$55,898 pilot grant available in the following priority areas:

- Research dedicated to furthering the understanding of CDKL5 function to inform the development of targeted, novel therapies.
- Transformative research to enhance our understanding of the cellular, molecular, genetic and systems-level mechanisms contributing to the pathogenesis of CDKL5

Deficiency Disorder (CDD), facilitating the continued investigation of disease-modifying strategies.

- Research aimed at improving CDD disease models (e.g., cell-based, tissue-based, or animal models) in an effort to assess the potential efficacy of therapeutic interventions against phenotypic deficits in the CDD patient population.

6) CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy): One \$81,951 grant available. CADASIL is the leading genetic cause of stroke and vascular dementia and is linked to cysteine-altering mutations in NOTCH3. The precise mechanisms driving vascular dysfunction in CADASIL are not clear. Moreover, clinical markers that can be used to assess treatment efficacy are sparse. Seeking applications for research that will advance the understanding of mechanisms of the disease or clinical phenotyping that will facilitate future treatment trials (e.g. identification of biomarkers or clinical predictors). Disease model initiatives and drug repurposing projects also of interest. Both basic laboratory and clinical projects will be considered. This grant is made possible by Team CADASIL and cureCADASIL Association.

7) Charcot Marie Tooth: The purpose of this request for proposal (RFP) is to support studies that advance knowledge of the treatment of mobility related challenges in children and youth with Charcot-Marie-Tooth disease through objective evaluation of treatment outcomes on walking function in conjunction with the study of the natural history of walking. With the support of efficient and innovative natural history and treatment outcomes studies, the Hereditary Neuropathy Foundation and the University of Pennsylvania Orphan Disease Center expect to address critical knowledge gaps and inform current and future treatments that impact walking ability and community participation. These gaps include very limited understanding of treatment outcomes in terms of walking abilities at both the joint level and community based participation in children (as well as adults). There is also very limited understanding of the natural history of walking function and community participation which is critical in order to develop and understand pending new treatments, especially in children.

Study methodology that seeks to understand walking function in terms of both the joint level as well as community participation as described under the International Classification of Function (ICF) will be given preference. To achieve these goals, objective assessment of walking function must be accomplished through using comprehensive motion analysis and measurement of community participation through activity tracking devices.

This RFA will support up to \$60,330 in funding over the course of 12 months with a 6 month no cost extension that should include both pre and post treatment assessments and a cross-sectional database by age to allow improved understanding of disease progression.

8) Choroideremia (CHM): One \$61,079 grant is available to initiate or advance research towards a treatment or cure for Choroideremia (CHM). CHM is an X-linked retinal disease causing progressing loss of vision and eventual blindness. Applications will be considered for research including gene therapy, CRISPR, stem cell therapy, or other methods that will potentially halt the progression of CHM and/or restore retinal functioning. This grant is made possible by Team CHM and the Choroideremia Research Foundation.

9) Congenital Hyperinsulinism (CHI): One \$72,014 grant available for an innovative, pre-clinical or clinical study that has the potential to lead to: (1) faster and more accurate diagnoses of congenital hyperinsulinism (HI); (2) better HI treatment; (3) a cure for HI; or (4) quality of life improvement for those affected by HI. This grant is made possible by Team Raring to Go for CHI, and Congenital Hyperinsulinism International.

10) Congenital Muscular Dystrophy (CMD): Two \$45,588 grants or one \$91,176 grant will be awarded depending on the merit, feasibility, and budget justification (please indicate solicited budget level on your LOI). The purpose of this RFA is to promote discovery of underlying disease mechanisms and pre-clinical development of potential therapies for Collagen VI-Congenital Muscular Dystrophy, as well as the clinical translation of those efforts.

Areas of interest include, but are not limited to, understanding the cause of disease, unraveling pathways involved in disease, identifying novel drug targets or gene therapies, and testing new strategies to treat disease or any of its incapacitating consequences (e.g., contractures). In addition, applications may propose to create or improve disease models (e.g., animal models, patient-derived cell models), bio markers or functional outcome measures to assess therapeutic impact. This grant is made possible by Team Cure CMD.

11) CRB1 degenerative retinal disorder: Two \$40,177 grants are available for work toward treatments for CRB1 retinal disease. Applications including gene therapy, CRISPR, cell therapy or other methods that will halt the progression of CRB1 retinal disease and ultimately restore retinal function will be considered. CRB1 retinal disease is a rare disease causing Leber's Congenital Amaurosis (LCA), Retinitis Pigmentosa (RP) or Cone Rod Dystrophy. Children with CRB1 are blind or visually impaired from a very early age (at birth in LCA) and most are Braille readers and white cane users. This grant is made possible by Team Bike4Sight and the Curing Retinal Blindness Foundation.

12) Fibrous dysplasia/McCune-Albright syndrome (FD/MAS) is a rare disease caused by somatic mutations in GNAS. The mutation results in constitutive activation of the signaling protein Gs α and downstream cAMP signaling. Skeletal manifestations include bone pain, fractures, deformity and osteomalacia/rickets.

Any study that focuses on the pathogenesis of FD/MAS or clinical investigative studies to address any of the unmet needs in FD/MAS patients and their management will be considered. Research priorities for the Fibrous Dysplasia Foundation (FDF) include: studies that characterize mouse models; studies to understand the mechanism and/or treatment of FD-related bone pain; development/testing of therapeutics, especially those targeting Gs α , PKA or Wnt signaling pathways; studies of the molecular etiology, especially the role of RANKL, IL6, cAMP and FGF23. Projects that feature collaborations across multiple institutions are encouraged.

Either a single grant of up to \$84,325 or two grants of \$42,163 will be awarded, depending on the merits of the applications received. The grants are made possible by Team FD and the FDF. First-time applicants are encouraged. Previous FDF and MDBR grant awardees must describe progress and publications and other funding awarded as a result of data generated from those grants and must describe how the new proposal is distinct from previous one(s).

Reagents and research tools, including animal models that are generated or studied using support from FDF and MDBR must be freely accessible and/or deposited in a public repository. Members of labs that have previously received support from FDF or MDBR but that have not complied with this guidance are not eligible to apply for new grants.

13) Fibrodysplasia Ossificans Progressiva (FOP): Two grantees will each be awarded \$40,208 to advance Fibrodysplasia Ossificans Progressiva (FOP) research. FOP is a rare genetic disorder that causes bone to form in muscles, tendons, ligaments and other connective tissues. Bridges of extra bone develop across joints, progressively restricting movement and

forming a second skeleton that imprisons the body in bone. These grants are made possible by Team #cureFOP and the International Fibrodysplasia Ossificans Progressiva Association. Proposals for funding should be focused on one of the following two research areas:

- Research that seeks to identify biomarkers, including novel imaging techniques, capable of measuring and predicting early FOP disease progression and/or treatment response;
- Research that investigates and further elucidates the immunologic mechanisms in FOP.

Awardees of the research funding may have access to the IFOPA's FOP Mouse Model (IFOPA will support the cost of animal models with the exception of shipping) or available samples from the IFOPA Biobank, if needed. Please contact the IFOPA at grants@ifopa.org for further details on these resources.

14) Generalized Lymphatic Anomaly (GLA; a.k.a. lymphangiomatosis) and Gorham-Stout Disease (GSD): One \$62,861 grant is available for basic science and/or clinical research on GSD, GLA or kaposiform lymphangiomatosis (KLA). Areas of interest include, but are not limited to, genetic analysis, biomarker identification, cell line creation and characterization, and imaging. These grants are made possible by Team LGDA (Lymphangiomatosis & Gorham's Disease Alliance) and Team LMI (Lymphatic Malformation Institute).

15) Glucose Transporter Type 1 Deficiency Syndrome (Glut 1DS): Glucose Transporter Type 1 Deficiency Syndrome is a rare genetic metabolic disorder characterized by deficiency of a protein that is required for glucose to cross the blood-brain barrier.

One \$46,858 pilot grant is available and will be awarded to research that has the potential to lead to a cure, better treatment options, or quality of life improvement for those affected by Glut1DS. Potential topics of interest may include but are not limited to: gene therapy, blood brain barrier, translational studies, clinical studies, alternative treatment theory, new collaboration linking to other diseases, or disease mechanisms relevant to Glut 1DS. Preference may be given to new and novel concepts. This grant is made possible by the generous support by friends of Team Miles for Millie.

16) Inclusion Body Myositis (IBM): One \$102,430 grant is available for inclusion body myositis (IBM) research. IBM is a rare muscle disease characterized by inflammation, degeneration, and mitochondrial pathology.

Proposals for funding should be focused on investigating potential treatments which may slow, stabilize, or reverse the progression of muscle weakness that characterizes IBM.

Examples may include, but are not limited to:

- Identification of candidate drugs
- Early development of therapeutic compounds that are designed to be treatments for IBM
- Investigation of already existing drugs for repurposing as possible IBM treatments
- Investigation of compounds, such as Creatine and Vitamin B3 complex, that may improve mitochondrial function in people with IBM.
- Exercise as Therapy

This grant is made possible by Cure IBM.

17) Lymphangiomyomatosis (LAM): One \$72,704 pilot grant available focusing on translational proposals with strong likelihood of future federal funding, that use LAM samples, animal models or patient data, and which have the potential to favorably impact human health will be given priority. Examples of desirable topic areas include identification of molecular targets, biomarker development, and biomarker driven small pilot trials. These grants are made

possible by Team LAM Foundation Easy Breathers and the LAM Foundation.

18) Maple Syrup Urine Disease: Two \$44,037 grants are available for work towards improved treatment and/or a cure of MSUD, a life-threatening disease characterized by an inability to metabolize branched-chain amino acids. Our intent is to award one grant for a gene therapy project and one grant for a non-gene therapy approach to treatment. These grants are made possible by the MSUD Family Support Group.

19) Mucopolidosis Type IV (ML4): One \$78,538 grant is available. Mucopolidosis Type IV is caused by a single-gene mutation in p19 which encodes for MCLON1. Most patients experience total loss of this transmembrane protein resulting in severe psycho-motor delays, neurodegeneration, and blindness. We offer this grant to investigators conducting research on all aspects of disease with particular preference for projects focusing on gene therapy, natural history, biomarkers, or functional outcome measures. This grant is made possible by TeamCureML4, Pedal4Paul, Cycle4Scott, Dream4Danielle, AlonFamilyFund and other supporters.

20) Mucopolysaccharidoses (MPS): Mucopolysaccharidoses represent a broad array of diseases due to enzyme defects that lead to abnormal metabolic storage products and multi-organ pathologies. We are seeking applications directed to treating the central nervous system manifestations, and secondary metabolic manifestations from MPS including cardiac, lung, and bone issues. One grant of \$64,063 is made possible by Team MPS and the National MPS Society.

21) Mucopolysaccharidosis (MPS I) Gene Spotlight: a \$61,589 pilot grant is available for proposals focused on translational or clinical research to treat MPS I Scheie or MPSI Hurler-Scheie that have a strong likelihood of future federal funding or where the grant amount can be matched. MPS I S/HS results from reduced enzymatic activity of alpha-L-iduronidase that leads to abnormal metabolic storage products and multi-organ pathologies. We are seeking proposals for oral or parenteral drugs that will slow the progression of central nervous system (CNS) manifestations of this disease or new methods for measuring CNS disease progression, including identification of novel disease-related structural or biochemical changes. This grant is made possible by Gene Spotlight, Inc.

22) Neuroendocrine Cell Hyperplasia of Infancy (NEHI): One \$60,989 pilot grant is available for research initiating or advancing the understanding of NEHI. Areas of interest include, but are not limited to, increasing understanding of pathology (including Genetics), advancements towards accelerated diagnosis, increasing quality of life through treatments or cures. This grant is made possible by NEHI Research Foundation.

23) Niemann Pick Type C (NPC): One \$61,637 grant available. Consideration will be given to research projects developing new therapies for NPC as well as those designed to complement therapies presently in the pipeline (upon confirming no redundancies exist i.e. multiple dosing studies on pipeline drugs.) Consideration will further be given to gene therapy proposals. Research exploring psychiatric issues impacting quality of life through the lifespan of the patient population and research projects that improve our understanding of the biology, pathogenesis and disease state and have a direct impact on translation of new treatments to patients is encouraged. Studies looking to understand variants in the population to formulate targeted supportive care and therapy are welcome. This grant is made possible by Team NPC.

24) Nonsense Mutations in Cystic Fibrosis: One \$54,718 grant available. Cystic fibrosis is a genetic condition affecting the lungs and digestive system. The grant will be awarded to advance research and understanding of a treatment or cure that would impact people carrying a

nonsense mutation. The research should include, but not be limited to, the R1158X gene mutation. This grant is made possible by Team Movin' for Mallory: Cure Cystic Fibrosis! and the Movin' for Mallory organization.

25) NUBPL: One \$61,134 grant available for research related to treatments or cures for the form of mitochondrial disease caused by mutations to the NUBPL gene. This grant can advance research or projects already in progress, or be used to initiate new research or studies. Examples of priority topic areas include developing, advancing, or continuing disease models, identifying potential therapeutics whether they consist of drugs, vitamins, diets, or supplements that are currently in the market or the development of novel molecules, studying the effectiveness of therapies currently in use for mitochondrial disease in this form of the disease (including components of what is known as the “Mitochondrial Cocktail”), establishing outcome measures to be used in clinical trials, and developing other essential resources to substantially prepare the NUBPL community for clinical trials. These grants are made possible by the NUBPL Foundation, Inc.

26) Pitt Hopkins Syndrome (PTHS): One \$68,709 pilot grant available. Pitt Hopkins Syndrome is due to a deficiency in the TCF4 gene and is characterized by severe intellectual disability and developmental delay. Other symptoms include episodic hyperventilation and/or breath-holding (55%-60%), recurrent seizures/epilepsy (40%-50%), gastrointestinal issues, and distinctive facial features. The Pitt Hopkins Research Foundation would like to focus this research on finding therapeutics and a cure for this debilitating syndrome and are not interested in natural history studies at this time. These grants are made possible by Team Pitt Hopkins Pedalers with the Pitt Hopkins Research Foundation.

27) RASopathies: One \$59,220 pilot grant available. RASopathies are a group of genetic conditions caused by mutations in genes on the Ras-MAPK pathway. These conditions, including Noonan syndrome/Noonan-related conditions (NS), cardio-facio-cutaneous syndrome (CFC), Costello syndrome (CS), and Neurofibromatosis type 1 (NF1) share many clinical features, such as developmental delay, gastrointestinal difficulties, skeletal abnormalities, hematologic abnormalities, and growth delay.

28) SETBP1 Disorder: One \$67,943 grant will be awarded. The purpose of this RFA is to promote discovery of underlying disease mechanisms and pre-clinical development of potential therapies for SETBP1 disorder, which is caused by SETBP1 haploinsufficiency. Areas of interest include, but are not limited to, understanding molecular pathways or cellular mechanisms involved in disease, analyzing the changes in gene expression associated with SETBP1 genetic alteration, identifying novel therapeutic compounds, drug targets or gene therapies, and testing new strategies to treat SETBP1 disease. In addition, applications may propose to create or leverage existing disease models (e.g., in vitro systems, animal models, patient-derived cell models) to assess therapeutic impact. This grant is made possible by Team SETBP1 Strong and SETBP1 Society

29) Snyder-Robinson Syndrome (SRS): is a genetic condition resulting in the dysfunction of Spermine Synthase (SMS). This enzyme conversion is the last step in the polyamine pathway. Polyamines are ubiquitous and SRS is a rare condition involving a polyamine inborn error of metabolism. Clinical features include intellectual disability, seizures, developmental delay, and osteoporosis with fractures in the absence of trauma, along with defects in other organ systems. There is a wide range of severity among individuals with SRS.

One \$69,318 grant is available for SRS. Research focus areas include new studies into understanding pathophysiology or mechanisms by which SRS causes disease, as well as corresponding treatment options. There is particular interest in the following areas: creating a non-radioactive assay for SMS; molecular and behavioral phenotype analysis of SRS mouse

models available through Jackson Laboratories; further development and testing of AAV9 to deliver a normal copy of SMS to cells of patients; biomarker or “omic” analysis. We strongly encourage the use of our existing platform for collaboration of data as well as fellow research scientists as it relates to SRS. These funds have been made available by Team SRS.

30) STXBP1 Encephalopathy: Two \$69,588 grants are available to advance research into the development of new therapies for STXBP1 disorders. Projects addressing any stage of therapeutic development will be considered, spanning both clinical and basic science applications. Particular areas of interest include:

1. Functional characterization of patient-derived iPSC-neurons harboring STXBP1 mutations as a model system to study STXBP1 disorders and test novel therapies.
2. Evaluation of gene therapeutic approaches to correct STXBP1 haploinsufficiency.
3. Drug repurposing efforts to treat STXBP1 disorders.
4. Development of novel therapeutic approaches.

These grants are made possible by Lulu’s Crew/Team STXBP1.

31) Telomere Biology Disorders, including Dyskeratosis Congenita: One \$62,664 grant available to investigators conducting basic or clinical research on all aspects of Dyskeratosis Congenita / Telomere Biology Disorders. Dyskeratosis Congenita is a progressive, genetic condition caused by defects in telomeres, the protective caps at the ends of chromosomes. Impaired telomere maintenance in Dyskeratosis Congenita/Telomere Biology Disorders results in problems throughout the body, notably including blood, liver, and lung disease, and cancer. Proposals that seek to advance understanding of the genetics, biology, pathophysiology, disease manifestations, treatment, including late effects of stem cell transplant, natural history and/or outcomes of telomere diseases will be considered. This grant is made possible by Team Telomere.

Grant Review Procedure:

- 1) Grants will be reviewed for scientific content and relevance to the goals of the RFA.
- 2) Full applications proceed through a two-step review process. The first step includes external review and rating with an assessment of the strengths and weaknesses of each application based on the defined review criteria described below. During the second step, funding recommendations are determined based on an assessment of the reviewer scores and written comments. Final decision of funding will be made by Center Leadership.
- 3) Proposal Content and Review Criteria: The following criteria will be utilized in proposal review.
 - **Project Proposal** - Is the proposed project of high scientific quality? Is the budget fully justified and reasonable in relation to the proposed project?
 - **Background** - Is the fundamental objective of the study and hypothesis to be addressed clearly defined?
 - **Scientific Approach** - Will the proposed specific aims answer the study hypothesis? Will the scientific approach effectively test and answer each specific aim? Are the study goals supported by existing data?
 - **Clinical Impact** - Is the answer to the study hypothesis important to our ability to treat or reduce rare disorders/disease incidence and/or mortality? Will the proposed research lead to substantial advances and/or contribute to large leaps of understanding or knowledge that will contribute to reductions in disease incidence and/or mortality within the decade?
 - **Research Significance** - Does the study address an important question that is not likely to be addressed without this funding? Does the proposed study offer a unique opportunity to explore an important issue and/or employ a novel approach to this disease research? Will the study outcomes advance our knowledge of this disease and/or contribute to changes in the focus of future research questions or the way we

conduct research on this issue?

- **Investigator Qualifications** – Does the investigator hold a track record of outstanding accomplishment as evidenced by peer-reviewed publications and funding awards? Does the investigator have access to the resources and environment necessary to complete the study as outlined?

Fund Disbursement:

Funds will be issued through a cost reimbursement mechanism executed by purchase order from the University of Pennsylvania. Details of invoicing schedules and reporting requirements will be made available upon award. For additional information, please contact Samantha Charleston at scharle@upenn.edu or 215-573-6822.