The Collaborative Center for X-Linked Dystonia-Parkinsonism

2021 Request for Proposals

Purpose

The Collaborative Center for X-Linked Dystonia-Parkinsonism (CCXDP) supports an international consortium of scientists, clinicians, and patient advocates working together to advance research and treatments for X-Linked Dystonia-Parkinsonism (XDP), a debilitating neurodegenerative disease caused by a transposable element. CCXDP is now seeking applications for its 2021 Research Funding Program. Three grant mechanisms are offered:

- Investigator Awards: 2 years, up to $250,000/year in direct costs
- Exploratory Pilot Grants: 1 year, up to $100,000 in direct costs
- Postdoctoral fellowships: 2 years, $75,000/year in direct costs

In addition to the amounts listed above, awards will provide 10% indirect costs to recipient institutions.

Background

XDP is a neurodegenerative disorder endemic to the Philippines. CCXDP-funded research studies have shown that XDP is most likely caused by a disease-specific SINE-VNTR-Alu (SVA)-type retrotransposon insertion in an intron of the human *TAF1* gene. The SVA contains a hexameric sequence $(CCCTCT)_n$, the length of which is polymorphic among patients and inversely correlated to age of disease onset. The insertion results in aberrant *TAF1* mRNA splicing and partial intron retention which decreases levels of the full-length transcript. The neuropathology of XDP has not yet been fully defined, but previous studies have reported a progressive loss of striatal medium spiny neurons in the brains of individuals with XDP.

Available Resources

CCXDP has generated biospecimens and reagents which are available for research studies, including:

- DNA from XDP patients and unaffected relatives
- Fibroblasts, lymphoblasts, and induced pluripotent stem cells (iPSCs) from XDP patients and unaffected relatives
- Post-mortem human brain tissue from XDP patients
- Novel TAF1 antibodies

For a complete list of available resources and details about acquiring reagents, please see:
https://www.massgeneral.org/neurology/xdp-center/resources/

Research Objectives for the 2021 Funding Program

CCXDP welcomes applications from investigators in all disciplines proposing bold and rigorous approaches to the study of XDP. We encourage proposals involving collaborative studies, which can include investigators at different institutions, as well as ones which leverage existing resources. Areas of particular interest include, but are not limited to:

- Screening projects that develop models and/or assays to seek compounds that modulate XDP-related phenotypes, with particular emphasis on opportunities for drug repurposing
- Development and application of novel XDP model systems, including strategies for (a) studying SVA knock-in and/or TAF1 knockout in animals; and (b) creating 2D and 3D culture models using XDP-specific induced pluripotent stem cells
- Studies of post-mortem brain tissue to elucidate potential disease mechanisms
- Development of novel CRISPR-based genome editing strategies for therapeutic manipulation of the disease-specific SVA insertion
- Neuroimaging to probe markers of disease progression in XDP individuals
- Studies of the XDP-specific SVA element, including potential regulation by host cell factors and effects on chromatin, RNA transcription, and/or DNA replication dynamics
- Comparative analyses to identify cellular mechanisms that may be shared by XDP and other neurodegenerative diseases

Application Timeline

September 20, 2021:	Letters of intent due by 5 pm. Abstracts of proposed research may be emailed to aalessi@partners.org.
October 27, 2021:	Full applications due by 5 pm to aalessi@partners.org.
February, 2022:	Funding decisions announced.
May, 2022:	Anticipated project start dates.

Application Instructions

Complete application instructions and forms are attached to this announcement and available via our website: https://www.massgeneral.org/neurology/xdp-center/research/rfp

A list of previously funded projects is available here: https://www.massgeneral.org/neurology/xdp-center/research/ccxdp-funded-projects

For additional information, contact:

Dr. Amy Alessi, CCXDP Program Director, at **aalessi@partners.org**

The Collaborative Center for X-Linked Dystonia-Parkinsonism Application Instructions and Checklist

Please submit a letter of intent with proposed grant title and short project description to Program Director, Dr. Amy Alessi, aalessi@partners.org by **September 20th, 2021**. Completed grant applications are due 5pm EST **on October 27th, 2021.** Application materials in PDF and Word formats are also available here: https://www.massgeneral.org/neurology/xdp-center/research/rfp

EXPLORATORY PILOT - 1 year, up to $100,000 in direct costs

- Completed application form.
- Title and abstract of 300 words or less.
- Research plan of up to 3 pages (No less than 0.5 inch margins, 11 point font, times new roman) including specific aims, background, preliminary data (if applicable), methods, and expected outcomes. References do not count toward page count.
- Budget not exceeding $100,000 direct costs for a one year project (see attached form). Please include any data analysis costs in budget. Please note: subcontracting of CCXDP awards to third parties is not permitted. If two or more institutions are included in the application, separate subcontracts will be executed. Please prepare separate budgets for each location in USD. Indirect costs must not exceed 10%.
- Budget must include $2,500-3,000 for one in-person CCXDP meeting in 2023.
- Biosketch of Principal Investigator(s) (NIH format, 5 page maximum for each investigator)
- If grant is a resubmission, a one page introduction to revision is allowable.
- Milestones, deliverables and projected timeline and, if applicable, a resource sharing plan. Please refer to CCXDP Intellectual Property Policy regarding sharing expectations (sections 2.10-2.13).
- If proposed study involves human subjects: Applicant must demonstrate all appropriate institutional approvals and completion of Human Subjects Research (HSR) training for all study staff. Access to HSR training will be provided, if needed.
- If proposed study will utilize human derived tissue or cell lines: Applicants must demonstrate all appropriate institutional approvals to receive and work with deidentified human biospecimens. Rationale for number of cell lines to be analyzed must be included in methods section and cost of purchasing cells from biorepositories must be specified in budget.
- If applicant intends to request XDP postmortem brain tissue: Applicants must attach supplementary application outlining amount and type of brain tissue requested, demonstrated mastery of techniques proposed, and access to control tissue. Under project funding please select "CCXDP" and write in "pending" in the adjacent field.
- Completed applications should be submitted as **a single PDF** via email to aalessi@partners.org no later than **5pm EST on October 27th, 2021.**

Please Note:

- Grantees may be required to participate in webinars, teleconferences and/or workshops to provide updates on projects. Written progress reports may also be required.

INVESTIGATOR AWARD - 2 years, up to $250,000/year in direct costs.

- Completed application form.
- Title and abstract of 300 words or less.
- Research plan of up to 5 pages (No less than 0.5 inch margins, 11 point font, times new roman) including specific aims, background, preliminary data (if applicable), methods and expected outcomes. References do not count toward page count.
- Budget not exceeding $250,000 direct costs per year (see attached form). Please include any data analysis costs in budget, if applicable. Please note: subcontracting of CCXDP awards to third parties is not permitted. If two or more institutions are included in the application, separate subcontracts will be executed Please prepare separate budgets for each location in USD. Indirect costs must not exceed 10%.
- Budget must include $2,500-3,000 for one in-person CCXDP meeting in 2023.
- If grant is a resubmission, a one page introduction to revision is allowable.
- Biosketch of Principal Investigator(s) (NIH format, 5 page maximum for each investigator)
- Milestones, deliverables and projected timeline and if applicable, resource sharing plan. Please refer to CCXDP Intellectual Property Policy regarding sharing expectations (sections 2.10-2.13).
- If proposed study involves human subjects: Applicant must demonstrate all appropriate institutional approvals and completion of Human Subjects Research (HSR) training for all study staff. Access to HSR training will be provided, if needed.
- If proposed study will utilize human derived tissue or cell lines: Applicants must demonstrate all appropriate institutional approvals to receive and work with deidentified human biospecimens. Rationale for number of cell lines to be analyzed must be included in methods section and cost of purchasing cells from biorepositories must be specified in budget.
- If applicant intends to request XDP postmortem brain tissue: Applicants must attach supplementary application outlining amount and type of brain tissue requested, demonstrated mastery of techniques proposed, and access to control tissue. Under project funding please select "CCXDP" and write in "pending" in the adjacent field.
- Completed applications should be submitted as **a single PDF** via email to aalessi@partners.org no later than **5pm EST on October 27th, 2021.**

Please Note:

- Grants will be awarded for a one year period with the option for a second year after review of progress toward proposed specific aims.
- Grantees may be required to participate in webinars, teleconferences and/or workshops to provide updates on projects. Written progress reports may also be required.

POSTDOCTORAL FELLOWSHIP - 2 years, $75,000/year in direct costs

- Completed application form.
- Title and abstract of 300 words or less.
- Research plan of up to 3 pages (No less than 0.5 inch margins, 11 point font, times new roman) including specific aims, background, preliminary data (if applicable), methods, and expected outcomes. References do not count toward page count.
- Budget not exceeding $75,000 direct costs per year (see attached form) and budget justification. Please include any data analysis costs in budget, if applicable. Indirect costs must not exceed 10%.

- Budget must include $2,500-3,000 for one in-person CCXDP meeting in 2023.
- Two letters of recommendation emailed directly to Dr. Amy Alessi, aalessi@partners.org Current mentor may not be used as a reference.
- Biosketch of applicant and mentor(s) (NIH format, 5 page maximum for each investigator)
- If grant is a resubmission, a one page introduction to revision is allowable.
- Milestones, deliverables and projected timeline and if applicable, resource sharing plan. Please refer to CCXDP Intellectual Property Policy regarding sharing expectations (sections 2.10-2.13).
- If proposed study involves human subjects: Applicant must demonstrate all appropriate institutional approvals and completion of Human Subjects Research (HSR) training for all study staff. Access to HSR training will be provided, if needed.
- If proposed study will utilize human derived tissue or cell lines: Applicants must demonstrate all appropriate institutional approvals to receive and work with deidentified human biospecimens. Rationale for number of cell lines to be analyzed must be included in methods section and cost of purchasing cells from biorepositories must be specified in budget.
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- Completed applications should be submitted as **a single PDF** via email to aalessi@partners.org no later than **5pm EST on October 27th, 2021.**

Please Note:

- Grants will be awarded for a 1 year period with the option for a second year after review of progress toward proposed specific aims.
- Grantees may be required to participate in webinars, teleconferences and/or workshops to provide updates on projects. Written progress reports may also be required.

COLLABORATIVE CENTER FOR X-LINKED DYSTONIA-PARKINSONISM
MASSACHUSETTS GENERAL HOSPITAL

2021 Grant Application

Principal Investigator		**Position Title**	
Department/ Group		**Degree(s)**	
Institution		**Email**	
Address: **Telephone** **Fax**		**Co-PI(s)**	

EXPLORATORY PILOT GRANT: 1 year, max $100,000 direct costs

POSTDOCTORAL FELLOWSHIP: 2 years, max $75,000/year in direct costs per year

INVESTIGATOR AWARD: 1 or 2 years, max $250,000 in direct costs per year

NOTE: Indirect costs are capped at 10%.

Amount requested:

Year 1 (direct)	Year 1 (indirect)	Year 2 (direct)	Year 2 (indirect)	Total (direct)	Total (indirect)

Grant Title:

Completed applications should be submitted as a single PDF via email to aalessi@partners.org no later than **5pm EST on October 27th, 2021.** Application materials in PDF and Word formats are also available here https://www.massgeneral.org/neurology/xdp-center/research/rfp

Applications Accepted By	Grants Administered by
Amy Alessi, PhD Program Manager (T) 617.643.5007 (F) 617.726.0740 Email aalessi@partners.org Subject Line: XDP Center grant application	Michele Courtright Senior Grants Manager (T) 617.726-5722 (F) 617.643.5769 Email mcourtright@mgh.harvard.edu

INSTITUTIONAL APPROVAL: Appropriate institutional approval must be obtained for any proposed work (e.g. IACUC, IRB) before funding can begin.

I have received the required approval (yes or no):

I have included the appropriate approval documents, if received (yes or no):

Applicant: I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements of claims may be grounds for denying the request. I agree to accept responsibility for the scientific conduct of the project, provide the required progress reports, and meet other requirements specified if a grant is awarded as a result of this application.

Principal Investigator_____**Date:**

Administrative official to be notified if award is made

Name		Title	
Address		Phone Fax	
Email			

Applicant Organization Certification and Acceptance

Official signing for the applicant organization	
Position/Title	
TELEPHONE AND FAX number	
EMAIL address	

I certify that the statements herein are true, complete, and accurate to the best of my knowledge, and accept the obligation to comply with The Collaborative Center for XDP terms and conditions if a grant is awarded as a result of this application.

SIGNATURE INSTITUTIONAL OFFICIAL:_____Date:

NAME: TITLE:

Current and pending funding (attach additional page if necessary)

Suggested reviewers		Excluded reviewers	
LEAVE BLANK – FOR MGH USE ONLY			
Received By		Date	
Board member(s)			
Reviewers		Email	

Year 1 Budget

Program Director/Principal Investigator (Last, First, Middle):

DETAILED BUDGET FOR YEAR 1 PERIOD DIRECT COSTS ONLY	FROM	THROUGH

List PERSONNEL *(Applicant organization only)*
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested *(omit cents)* for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	INST.BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
	PD/PI							
	co-PI							
SUBTOTALS →								

EQUIPMENT *(Itemize)*	
CELL LINES *(Indicate Source, number and type of line, cost per line)*	
SUPPLIES (*Itemize by category*)	
TRAVEL	
INPATIENT CARE COSTS	
OUTPATIENT CARE COSTS	
OTHER EXPENSES *(Itemize by category)*	
TOTAL DIRECT COSTS	**$**
INDIRECT COSTS (*capped at 10%*)	**$**
TOTAL COSTS FOR BUDGET PERIOD	**$**

Year 2 Budget

Program Director/Principal Investigator (Last, First, Middle):

DETAILED BUDGET FOR YEAR 2 PERIOD DIRECT COSTS ONLY	FROM	THROUGH

List PERSONNEL *(Applicant organization only)*
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested *(omit cents)* for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	INST.BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
	PD/PI							
	co-PI							
SUBTOTALS →								

EQUIPMENT *(Itemize)*	
CELL LINES *(Indicate Source, number and type of line, cost per line)*	
SUPPLIES (*Itemize by category*)	
TRAVEL	
INPATIENT CARE COSTS	
OUTPATIENT CARE COSTS	
OTHER EXPENSES *(Itemize by category)*	
TOTAL DIRECT COSTS	**$**
INDIRECT COSTS (*capped at 10%*)	**$**
TOTAL COSTS FOR BUDGET PERIOD	**$**

Consortium Agreement
Appendix D: Intellectual Property Policy of XDP Center

1. Definitions

1.1. For the purposes of this Appendix D:

1.1.1. "**Intellectual Property**" shall mean any of the following (i) patents, patent applications, utility models, design registrations and certificates of invention and other governmental grants for the protection of inventions or industrial designs (including all related continuations, continuations-in-part, divisionals, reissues and reexaminations); (ii) copyrights, designs, data and database rights and registrations and applications for registration thereof; (iii) rights in know-how and unpatented materials (including but not limited to biological materials); and (iv) inventions, invention disclosures and, statutory invention registrations, whether patentable or nonpatentable, whether copyrightable or noncopyrightable

1.1.2. "**Results**" shall mean technical information (including, without limitation, information relating to inventions, discoveries, concepts, methodologies, models, research, development and testing procedures, the results and data of experiments, tests and trials, techniques and specifications, analyses) that is not in the public domain and made in the performance of the Collaborative Center for X-linked Dystonia Parkinsonism

1.1.3. "**Hospital**" is The General Hospital Corporation d/b/a Massachusetts General Hospital

1.1.4. The "**Recipient Institution**" is _____

1.1.5. The "**Center**" is The Collaborative Center for X-linked Dystonia Parkinsonism of Hospital

1.1.6. "**XDP**" is X-linked Dystonia Parkinsonism

1.1.7. The "**Researcher**" is the Recipient Investigator, or any staff members of Recipient Investigator's lab as applicable, of Recipient Institution

1.1.8. The "**XDP Center Consortium**" The Researcher and the Recipient Institution hereby acknowledge and agree that they are participating in a community of investigators and organizations funded by the Center and its affiliates whose objective is to find diagnoses, treatments, cures and preventions of XDP.

2. Intellectual Property

2.1. For the purpose of clarity, the provisions of this article 2 shall apply only to Intellectual Property created or invented after the Effective Date using the funds detailed in Appendix B.

2.2. Ownership of any Intellectual Property shall follow inventorship, which follows US patent law. The place of invention shall not, in itself, create any ownership or other rights in any Intellectual Property.

2.3. Subject to the rights of any third parties, Intellectual Property independently invented or created by employees of Hospital shall be owned by Hospital. Hospital shall, at its own expense, Control the management of the Intellectual Property. “Control” shall mean the control and management of the preparation, filing, prosecution, maintenance and enforcement of patent and other rights for the Intellectual Property and the control and management of the licensing of, or other grants of rights in or to, the Intellectual Property.

2.4. Subject to the rights of any third parties, Intellectual Property independently invented or created by employees of Recipient Institution shall be owned by Recipient Institution (“Recipient IP”). Recipient Institution shall notify Hospital in confidence promptly of any Recipient IP. Recipient Institution shall make best efforts to protect Recipient IP in order to best protect the public interest in such Recipient IP by securing commercialization rights. In cases where the Recipient Institution does not have an intellectual property policy and/or capability to effectively commercialize Recipient IP, Recipient Institution shall assign all rights and interest in its Recipient IP to Hospital.

2.5. Where any Intellectual Property is created or generated jointly by Hospital and Recipient Institution the Intellectual Property will be jointly owned by the Parties. For such jointly-owned Intellectual Property, Hospital shall Control the Intellectual Property management, unless due to special circumstances the co-owners mutually agree for a co-owner other than Hospital to be in Control. The joint owners shall contribute equally to the payment of reasonable expenses related to the filing, prosecution and maintenance of the joint Intellectual Property. Recipient Institution may forgo paying a share of patent expenses for jointly owned Intellectual Property, but if it does it shall provide a perpetual, fully paid up, royalty free, exclusive worldwide, sublicensable, license to the same for all purposes to Hospital.

2.6. Where any third party such as a student or contractor is involved in the Project, the party engaging such third party will ensure that such third party assigns any and all Intellectual Property to the party.

2.7. Within thirty (30) days following the filing of a patent application (including provisional patent applications and each patent application filed corresponding to a previously filed provisional patent application) claiming any Recipient IP, the Recipient Institution shall give notice (a "Patent Notice") to the Center setting forth the date of filing of such patent application and shall include with such notice a complete and accurate copy of the patent application filed.

2.8. With respect to each patent (including any patent application, divisional, continuation, continuation-in-part, substitute, renewal, reexamination, extension or reissue in respect of such patent) claiming Intellectual Property relating only to XDP, the Recipient Institution shall, upon the written request of the Center and to the extent not prohibited by applicable law, grant to the Center a non-exclusive, paid-up, perpetual license throughout the world. The foregoing license (1) shall be for XDP research and development only, (2) shall not include any right to manufacture for sale or sell, (3) shall not be subject to royalties or other fees, and (4) shall include the right to grant sublicenses within the XDP Center Consortium on the same terms; provided, that, such sublicense (a) is granted without payment of royalties, other fees or profit, and (b) prohibits the sublicensee from granting sublicenses.

2.9. Notwithstanding article 2.4, or unless mutually decided otherwise, the Home Institution shall Control the commercialization and the management of the Intellectual Property at the Home Institution’s expense.

Home Institution shall diligently pursue commercialization of Intellectual Property rights. As used herein, "Home Institution" shall be the institution where an inventor is an employee.

2.10. Any licensing income after deduction of out-of-pocket patent and licensing expenses made from the commercialization of Intellectual Property rights ("Net Income") shall be distributed according to the Home Institution's Intellectual Property Policy. However, Recipient Institution shall distribute four percent (4%) of its Net Income to the Center, one percent (1%) as an administrative fee to Hospital and the remaining ninety-five percent (95) percent shall be distributed in accordance with the Recipient Institution's intellectual property policies. All licensing income distributed to the Center shall be used to fund future research benefitting treatments for XDP with investigators of the XDP Center Consortium.

Notwithstanding anything to the contrary in this Agreement, the parties agree and acknowledge that faculty, staff members, or other employees of Center or Recipient Institution will publish or disseminate scholarly articles, books and other publications from time to time and that, subject to the policies of their Home Institution, the authors of all such publications may own the copyrights therein. Nothing in this Article 2 shall be deemed to limit the effect of this Article 2.11. The Researcher shall use reasonable efforts to publish, cause to be published or otherwise publicly disseminate Results as soon as reasonably possible. In addition, the publishing Researcher shall provide copies of published scientific articles describing Results to the Center within sixty (60) days after its publication. The publishing Researcher shall have (a) the sole and exclusive right to publish Results and (b) the sole and final authority over any and all decisions related to publication of Results. The Researcher hereby agrees to provide appropriate acknowledgement of the Center's support of, and contribution to, the Project in any publication and shall provide the Center promptly with the reference of any publication of Results. Researcher agrees to make reagents and research tools developed in the performance of the Study available to the XDP Center Consortium not later than 1 year after initial submission for publication or 6 months after termination or expiration of the Agreement, whichever is earlier.

2.11. Researcher agrees to make reagents described in manuscript available to the XDP Center Consortium no more than 1 year after initial submission for publication.

2.12. Researcher and/or the Recipient Institution shall inform the Center of all Results within a reasonable period of time following the production or discovery of each such Result.

2.13. The Center may disclose Results to any member of the XDP Center Consortium, who has agreed to each of the covenants set forth in this Section 2.13 with respect to any Results disclosed to such member:

2.13.1. to hold all third party results within the XDP Center Consortium in confidence until such third party results are published or otherwise made publicly available so that the disclosure of the third party results among members of the XDP Center Consortium does not constitute a public disclosure; and

2.13.2. to acknowledge other researchers appropriately if the third party results have contributed to a publication or presentation of Results.

2.14. One (1) year after the conclusion of the Project or termination or expiration of the Project, the Center shall have the right to disclose without restrictions all Results to any researcher with the XDP Center Consortium.

NOT FOR SIGNATURE AT THIS TIME. PROVIDED FOR REFERENCE ONLY.

Name:	Name:
Title:	Title:
Date	Date