Request for Proposals
Research Utilizing the My Life, Our Future Research Repository

ATHN, in collaboration with the NHF and BWNW, is pleased to announce the availability of the My Life, Our Future *(*MLOF) Research Repository to United States-based researchers in support of scientific discoveries**.** The MLOF Research Repository includes biologic samples and genetic data linked to phenotypic data from patients with hemophilia A and B receiving care in the U.S., as well as potential and confirmed carriers.

- Interested investigators must apply for access to the research repository and receive an invitation to submit a research proposal.
- Applicants interested in submitting a Pre-Proposal for the 2020 cycle can do so starting **Monday, November 30, 2020** with all Pre-Proposals due no later than **Friday, January 15, 2021 by 8:00 p.m. EST**.
- Investigators will be notified by **Monday, February 15, 2021** if they are invited to submit a Full Proposal.
- Invited proposals will be due **Thursday, April 1, 2021 by 8:00 p.m. EST**.
- Applicants with approved research proposals will be notified by **Friday, July 30, 2021.**
- Confirmation of funding and source must be confirmed prior to the release of biologic samples or data. For approved projects that are yet to secure funding, a letter of commitment for biologic samples and/or data will be provided; however, funding must be secured within one year of project approval.

Additional details related to the application process are provided below.

My Life, Our Future Project Description

In 2012, the MLOF project was created as a collaboration between four founding partners – the American Thrombosis and Hemostasis Network (ATHN), Bloodworks Northwest (BWNW), the National Hemophilia Foundation (NHF), and Biogen (later Bioverativ) – to advance and improve care for individuals affected by hemophilia. The primary goal of the MLOF project was exceeded with more than 11,000 people receiving free hemophilia genotyping. In addition, the MLOF Research Repository was established and is the largest hemophilia scientific resource of its kind in the world. Although the MLOF project concluded in 2018, ATHN is committed to working with BWNW and NHF to ensure the longevity of the research repository and has therefore incorporated the repository into ATHN's research portfolio. This enables ATHN to leverage its existing infrastructure to support use of the repository by researchers in support of scientific discoveries.

Research Repository Cohort Description

The research repository cohort represents more than 9,000 patients with hemophilia A and B, as well as potential and confirmed female genetic carriers receiving care at one of more than 100 ATHN-affiliated hemophilia treatment centers (HTCs) across the United States. Patients or parents of patients gave Institutional Review Board (IRB)-approved written informed consent to participate in the research repository part of the project, including consent for whole genome sequencing and deposition into databases such as the National Center for Biotechnology Information (NCBI) database of Genotypes and

Phenotypes (dbGaP). After consent was obtained, blood samples and limited data were sent to BWNW. Samples are maintained in the MLOF Research Repository which holds DNA and serum samples from most and plasma samples from many participants. For many participants blood was collected for RNA extraction which is being performed through the NHBLI Transomics in Precision Medicine (TOPMed) program (see below). Clinical genotyping included targeted *F8* and *F9* DNA variant analysis performed utilizing a next-generation sequencing (NGS) approach targeting all exons, splice sites, and sequences 5' and 3' to the coding region, and intron 22 and 1 inversions. Variants were confirmed by another method specific to the variant. The associated phenotypic data is derived from the ATHNdataset, a de-identified data set. Patients authorized use of their data for research, including its use in conjunction with the genetic data. Enrollment in the MLOF project ended on December 15, 2017, and the project was closed at the HTCs in December 2018.

MLOF is a cohort of the National Heart Lung and Blood Institute (NHLBI) Transomics in Precision Medicine (TOPMed) program. Samples from 5117 subjects have whole genome sequencing (WGS) data which is now deposited in dbGaP. Samples from 4,000 additional subjects are approved to undergo WGS, and 4,500 subjects are approved for whole blood RNASeq. These data will subsequently be deposited in dbGaP (Please note, it is unknown at this time the approximate date of availability of the data). Linkage between MLOF and dbGaP identifiers will be provided to approved projects that request these data as part of their research.

Research Repository Materials

The following genetic and phenotypic data are available through the research repository. All participant biologic samples and data are de-identified to ensure anonymity to researchers.

- *Phenotypic data*: The list of ATHNdataset Core data elements is on page 6 of this RFP and is also available at www.athn.org.
- *Genetic data*: *F8* and *F9* variants identified, *F8* and *F9* sequence data from MLOF genotyping. Linkage to TOPMed WGS and RNASeq data (as available in dbGaP).
- *Specimens*: DNA and serum (for most of the entire cohort); plasma (for ~75% of cohort).

Application Process

Eligible Applicants

Applications will be considered from U.S.-based investigators associated with academic, government, or commercial entities.

Application Cycle Timeline

Milestone	Date
Announcement of Repository Availability	November 9, 2020
Pre-Proposals Due	January 15, 2021
Invitation for Full Proposals	February 15, 2021
Full Proposals Due	April 1, 2021
Full Proposal Review Decision	July 30, 2021

Application Submission
Research proposals will be submitted to ATHN and will undergo feasibility and scientific review**.** A Pre-Proposal is required to test responsiveness to eligibility requirements, technical feasibility as proposed, and scientific integrity. Full Proposals will be invited for submission.

Pre-Proposals must be submitted to ATHN no later than January 15, 2021 at 8:00 p.m. EST. Proposals will be submitted through ATHN's online application process. Contact support@athn.org with the subject line "2020 Research Repository Application Request" to request a link to the application. Please include your name and the name of your institution/company. All uploaded documents must follow NIH formatting guidelines.

Pre-proposals must include the following components:

- Completed online application
- Abstract/Project Summary (100 words maximum)
- A research concept that includes:
    - Scientific background and rationale (200 words maximum)
    - Main hypothesis (200 words maximum)
    - Proposed research aims (200 words maximum)
    - Characteristics of the study population
    - Data elements of interest (ATHNdataset core data elements, genetic data)
    - Biologic samples of interest (Sample types and an estimation of the number of samples)
- Expected project initiation and completion dates
- List of collaborators, if applicable
- Funding status relevant to the application

Invited Full Proposals must be submitted to ATHN no later than April 1, 2021 at 8:00 p.m. EST. All uploaded documents must follow NIH formatting guidelines. Proposals must include the following components:

- Completed online application
- Technical abstract (200 words)
- Lay abstract (100 words)
- A research plan that includes:
    - Scientific background and rationale (500 words maximum)
    - Main hypothesis (200 words maximum)
    - Proposed research aims (500 words maximum)
    - Characteristics of the study population
    - Biologic samples and data elements of interest
    - Methodology including a rationale for measurements, data elements and/or number/volume of biospecimens requested, use of co-variates and statistical analysis plan. (1,500 words maximum)
- Literature cited
- NIH biosketch (for the Principal Investigator and collaborators)
- Local resources and environment information (description of the applicant's research resources

and environment)
- Project budget and source of funding
- Letters of support from collaborators, if applicable

Proposals that do not adhere to the requirements listed above will not be considered.

Full Proposal Criteria

Applications will be reviewed and scored under the direction of an ATHN Scientific Review Committee, consisting of a multi-disciplinary, expert panel. Any reviewer with a conflict of interest (such as a close professional relationship with any applicant, or previous involvement in applicant's proposed project) will be recused from reviewing the specific application in question.

Applications will be judged based upon the following criteria:

- Overall quality of applicant **(30%)**
  - Evidence of relevant research experience
  - Sufficient research funding secured
  - Evidence of research productivity
  - Research environment
- Scientific merit of proposal **(60%)**
  - Relevant and timely research question
  - Research likely to contribute new knowledge
  - Availability of biologic samples (e.g. DNA, plasma, serum)
  - Biologic samples requested proportional to scientific gain
  - Availability of phenotypic data
- Level of benefit to the bleeding disorders community **(10%)**
  - High priority given to studies directly benefitting the bleeding disorders community vs. indirect benefit vs. unlikely benefit

ATHN reserves the right to determine the number and category of applications approved, the basis of which includes but is not limited to, the quality of submitted proposals, the scientific feasibility, sufficient research funding secured, and the availability of biologic samples and data.

Biologic samples and data will be prepared by ATHN and BWNW and transferred to the investigator following execution of a Data Use and Materials Transfer Agreement. Verification of funding must be provided prior to the release of biologic samples or data.

Quarantine of Research Materials

If funding has not been secured at the time of application approval, a letter of commitment for biologic samples and/or data must be provided. Biologic samples will be reserved for up to a one-year period.

Actions After Approval: Administrative Requirements for Approved Projects

Prior to initiating a project and throughout the project period, the approved applicants will be expected to meet certain administrative requirements.

Human Subjects Protection: The MLOF repository was collected under an IRB-approved protocol with written informed consent. Data and samples will be sent to the researcher with a research ID only. Human subject identifiers will never be given to the researcher, and thus use of the data and samples by the researcher would not be considered human subjects research. MLOF whole genome and other –omic sequence obtained through dbGaP is restricted to use for health, medical and biomedical research and cannot be used for population genetics.

Project Funding should be adequate to ensure the proper conduct of the proposed research. There could be possible fees related to sample shipping and acceptance from your institution. Funding is the responsibility of the approved researcher. Confirmation of funding and source must be confirmed prior to the release of biologic samples or data and must be secured within one year of project approval.

A **Data Use and Materials Transfer Agreement** governing materials transfer and data sharing will be executed by the investigator, a legal representative of the researcher's institution, and an ATHN representative before biologic samples or data will be released. ATHN reserves the right to notice of any patent or other intellectual property filing involving use of the biologic samples or data.

In any **Publication of Findings** including peer-reviewed journals, theses, or presentations utilizing information or data derived through the research repository, acknowledgment of support of the MLOF project and the founding partners is required. ATHN reserves the right to review publications derived from the repository for purposes of patentable subject matter.

Questions?

All questions about the research repository, including questions about the preparation and submission of Pre-Proposals and invited Full Proposals should be directed to support@athn.org.

athn™
american thrombosis & hemostasis network

ATHNdataset Core Data Elements

DATA CATEGORY	CORE DATA ELEMENT
Record Status	Record Status - Active vs. Inactive
	Date Made Inactive
	Inactive Reason
Mortality Status	Mortality Status - Alive vs. Deceased
	Date of Death
	Primary Category of Death
	Primary Cause of Death
Demographics	Date of Birth
	Gender
	Race
	Ethnicity
	Education Level
	Employment Level
	Zip Code
Consents	ATHNdataset Patient Authorization
Insurance Information	Category
	Start Date
	Payer Name
	Type
Diagnoses	Primary Bleeding or Clotting Disorder Diagnosis Name
	Status
	Primary Diagnosis Indication
	Start Date
	Reason for Diagnostic Testing
Complications and Co-Morbidities	History of Other Diagnoses
	Inhibitor
	HIV
	Hepatitis A
	Hepatitis B
	Hepatitis C
Surgeries/Procedures	Date
	Surgery/Procedure Type

DATA CATEGORY	CORE DATA ELEMENT
Medications	Primary Bleeding or Clotting Disorder Medication Names
	Start Date
	Primary Regimen Indication
	Treatment Type
	Dose
	Frequency
	End Date
	Reason for Discontinuation
Immune Tolerance Regimen	Start Date
	End Date
	Response
Immunizations	Immunization Type
	Immunization Status
Bleed/Infusion Data	Product Usage
	Bleed Events
	First Product Exposure
	Historical Product Exposure
	First Bleed Information
	Infusion Administration History
	Target Joint History
Visit Information	Type of Visit
	Date of Visit
	Visit Disposition
	Report sent to PCP
Vital Signs	Weight
	Height (length for children)
Laboratory Tests	Baseline Diagnoses and Co-Morbidities
	Test Name
	Draw Date
	Lab Results