

# Investigator Collaboration Agreement

GREGoR Consortium

*Date Approved:* January 19, 2022

*Date of Last Update:* March 8, 2022

*Version:* 1.1

***GREGoR Consortium Investigator Collaboration Agreement***

The Genomics Research to Elucidate the Genetics of Rare diseases ([GREGoR](https://gregorconsortium.org/)) consortium is an NHGRI funded consortium with five research sites ([Baylor College of Medicine](https://mendeliangenomics.org/), [Broad Institute of MIT and Harvard](https://cmg.broadinstitute.org/), [Children’s National/Invitae](https://childrensnational.org/research/center-for-genetic-medicine), [Stanford University](https://gregor.stanford.edu/), and [University of Washington](https://uwcmg.org/#/)) and a [data coordination center at the University of Washington](https://www.biostat.washington.edu/research/centers/gac). The main goals of the GREGoR consortium are: to discover genes underlying Mendelian conditions, particularly those not identified using whole exome sequencing; to develop approaches to inform variant interpretation, functional follow-up of candidate variants; and to disseminate the findings to the research, clinical, diagnostic laboratories, and patient community.

To accomplish this, we offer research exome sequencing (ES), genome sequencing (GS) using either short- or long-reads (srGS, lrGS), RNA-seq, methylation profiling, comprehensive analysis, and/or options for functional validation of candidate variants, at no cost, to investigators and clinicians worldwide. Only samples consented for broad research use (GRU, HMB) and sharing in restricted access databases, e.g.. dbGaP/AnVIL, are eligible for consideration. Specific study design is done in collaboration with the GREGoR consortium.

The GREGoR consortium is expected to comply with NHGRI program guidelines regarding data release and sharing: the public posting of candidate genes, gene discoveries, causal variants, and information about conditions on which we are working, without identifying specific individuals, and the publication of discoveries in a timely manner. We are also required to submit regular progress reports to the NIH and its Scientific Advisory Panel.

**Benefits to collaborating investigators:**

* Provide feedback from our review of your proposed Mendelian project, typically within 10 business days.
* Work with you to determine a study design/analysis plan that maximizes the opportunity for novel discovery or diagnosis, within available resources.
* Provide centralized services for DNA extraction (if required) and storage, sequencing, alignment and variant calling, quality control, and interpretation of appropriately consented samples.
* Facilitate direct access to data generated from your samples through AnVIL and/or through services managed by the Consortium site.
* Assign one of our analysts to conduct collaborative analysis with your team.
* Provide analysis information back on cases through a written or verbal report or discussion in a meeting.
* Submit data to an NIH-designated restricted access database (e.g. dbGaP, AnVIL) promptly.
* Data will be available for analysis, including an intuitive online platform that enables collaborators to analyze their own data.
* Submit pathogenic and likely pathogenic variants in ClinVar in known disease genes, assigning priority to variants included in a publication.
* Accelerate your path to publication by:
  + Releasing de-identified aggregate rare variant and phenotype data through publicly available databases (e.g., Geno2MP, seqr)
  + Submitting candidate genes linked to an HPO profile to a node of the MatchMaker Exchange shortly after identification,
  + Releasing candidate genes via a public list maintained by the GREGoR Consortium, and
  + Facilitating collaboration as appropriate between investigators working on the same condition(s), including providing support for searching gene candidates across the GREGoR consortium.
* Support the generation of manuscripts by providing publication-quality text and figures and by connecting collaborators with sources of additional cases with variants in the same gene.
* Make connections with GREGoR sites and external collaborators who have potentially relevant functional studies.

**Expectations for investigators:**

* Samples and/or data must be:
  + high-quality,
  + appropriately consented (general research use/GRU or health, medical, biomedical/HMB accepted; disease-specific consent not accepted),
  + consented in a way that allows sharing with other researchers through dbGaP/AnVIL, including commercial groups (e.g. Invitae), and
  + acquired in accordance with local, state, federal, and international regulations.
* Provide documentation confirming IRB and data sharing approvals prior to submitting samples:
  + Blank copy of consent form(s) or Genomic Data Sharing certification from your IRB/local ethics committee,
  + Genomic Data Sharing certification or Data Use Limitation (DUL) form from your IRB/local ethics committee, and
  + Material transfer agreement (MTA) if required by your institution.
* Follow all local, state/provincial, and federal regulations/laws related to shipping samples within and to the U.S.
* Complete a sample manifest and provide detailed phenotype information in the requested format (varies by center) that includes sex, affected status, relatedness information, tissue type, ancestry, detailed phenotype data, clinical diagnoses, age of onset, and prior testing. No sequence data will be delivered until this metadata is shared.
* Respond in a timely manner to requests for additional phenotype data, which could involve recontacting participants or reviewing their records, to ask about specific findings/features.
* Participate in a conference call prior to release of data to review study design, analysis plan, etc., with follow up analysis calls as needed.
* Provide regular progress updates in the requested format as requested and at least quarterly.
* Investigators are responsible for validation of results in an appropriately regulated clinical setting (e.g. a CLIA laboratory) before using them in clinical practice.
* Include the grant number in the acknowledgements and funding sections of publications and presentations.
* Follow the GREGoR data sharing and publication policies which outline how data is shared and who should be a coauthor on resulting manuscripts.

**AGREED AND APPROVED**

Submitting Investigator Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

## Change Log

* V1.1 - Added expectation for investigators to respond to requests for additional phenotype data
* V1.0 - Initial Version