2016 BBMRI-LPC Whole Exome Sequencing Call

Sequencing the exome of 500 rare disease samples
in collaboration with EuroBioBank

Summary

A disease is considered rare when it affects less than 1 person in 2000. Although each disease may affect few people, there are over 9000 rare disorders and over 30 million European Union citizens may be affected by one (1). Most rare diseases have a genetic origin. The two main objectives of the International Rare Disease Research Consortium (IRDiRC) are to have means to diagnose most rare diseases and to develop and authorize 200 new medical products by 2020 (2).

BBMRI-LPC (3) will contribute to the achievement of these objectives by offering a unique opportunity to genetically diagnose rare disease patients with samples deposited in Biobanks from the EuroBioBank network (4). EuroBioBank is a network of 23 rare disease (RD) biobanks holding close to 150.000 biological samples. It is the oldest RD network in Europe with established governance and quality assurance for biobanking. A significant percentage of these biological samples come from patients without a molecular diagnosis for their diseases.

The program will provide free-of-charge Whole Exome Sequencing (WES) and bioinformatics analysis to 10-30 coordinated projects each with 2-3 principal investigators (PIs) from different countries (indicative 15-50 samples per project), for a total of 500 samples. Each project will focus on a particular disorder and will include at least 3 genetically undiagnosed index cases and additional samples from case relatives in order to facilitate the identification of the causative variant/s. The sequencing and analysis will be carried out at the Centro Nacional de Análisis Genómico (CNAG-CRG, 5) and at the Wellcome Trust Sanger Institute (WTSI, 6). CNAG-CRG is a genomics research platform based in Barcelona (Spain) that has the mission to carry out large scale projects in DNA sequencing and analysis in collaboration with researchers from Catalonia, Spain and from the international research community. The Wellcome Trust Sanger Institute is a world leader in genome research and aims to deliver new insights into human and pathogen biology that change the course of biology and medicine. Our mission is to use genome sequences to increase understanding of human and pathogen biology in order to improve human health.
Given the high fragmentation of the rare disease field (by geography, disease and research group), this call will promote data sharing to maximize its usage and enable future discoveries, through research activities or platforms such as MatchMaker Exchange (7). Therefore, all samples will need a signed informed consent allowing them to be deposited in controlled access repositories and databases such as the European Genome-Phenome Archive (EGA, 8) and RD-Connect (9).

Objectives

The goals of this high impact initiative are:

- to promote the usage of biobanks for rare diseases
- to promote the utilization of cutting-edge next-generation sequencing technology for the identification of novel causative variants and genes
- to molecularly diagnose rare disease patients
- to promote data sharing for rare disease research to enable future discovery

Eligibility

1. Coordinated projects, with 2-3 PIs from different countries.
2. PIs must hold a PhD or MD degree and a work contract with a European Institution at the time of application.
3. PIs must have their own research lines and experience in leading research groups.
4. DNA samples must be available in some of the biobanks from the EuroBioBank network, please check the sample catalogue from EuroBioBank at:
   http://www.eurobiobank.org/en/services/CatalogueHome.html
   Alternatively, researchers must commit to deposit them in the EuroBioBank network if the project is awarded.
5. Phenotypic description of the donors will have to be provided using the Human Phenotype Ontology (HPO, 10)
6. Samples must have been obtained with "informed consent" of donors, both for collection and for their use, including conservation and / or manipulation / sequencing by entities such as CNAG. Informed consent from the participants must allow sharing of the data in controlled access repositories and databases such as the EGA and RD-Connect.

Application Process

Complete and submit the online form that you will find in the following link:

http://apps.crg.es/content/internet/events/webforms/2016-bbmri-lpc-whole-exome-sequencing-call

One applicant can submit only one project proposal to this call. Applications should be written in English. The **submission deadline** is 25/07/2016 (12pm, noon, GMT+1 hour).

Review Process

A selection committee comprised of 2 BBMRI-LPC researchers, 1 EuroBioBank member as well as 2 external referees, will review the proposals and select the award recipients within 5 weeks of submission deadline. The selection results will be communicated by mail to the principal investigator. The title of the selected projects and name of their principal investigator will be published on BBMRI-LPC's website (3).

Projects will be chosen based on scientific quality and on the chances of success of the exome sequencing approach based on sample availability, pedigree structure, clinical phenotype, availability of additional information, etc.

DNA samples and sequencing

All samples must have been obtained with the corresponding approval of the Bioethics Committee and/or specific signed "informed consent" from each donor, both for collection and for their use, including conservation and manipulation/sequencing by entities such as the CNAG-CRG, and controlled access distribution in the databases mentioned below. Samples should be anonymized and linked to diagnostic categories and Human Phenotype Ontology (HPO) terms.

A minimum of 6 ug of high quality DNA at around 50-200ng/ul is required for Whole Exome Sequencing. DNA samples that fulfill the quality requirements **MUST BE AVAILABLE** at time of project submission. All samples from one study will be processed as a single batch and sequenced following CNAG-CRG's Standard Operating Procedures (ISO-9001, ISO 17025, Illumina Certified Service Provider, Agilent Certified Service Provider) or the WTSI standard operating procedures.

Analysis, databases and tools

Raw data from WES will be deposited at the EGA and analyzed by the CNAG-CRG and WTSI using the standardised state-of-the-art RD-Connect analysis pipeline. Phenotypic information (using controlled vocabulary such as HPO and ORDO, 11) and processed data will be made available through the RD-Connect platform, which provides a user friendly interface to aid in the identification of known and novel causative variants and genes. Data analysis: BBMRI-LPC will support bioinformatics analysis.

Publication and acknowledgement Policy

The results from each project will be published as a collaborative effort between the applicant's group and the supporting investigators. BBMRI-LPC funding, CNAG-CRG and WTSI support and collaboration will be properly acknowledged in any communication or publication.

References and links

(1) http://www.eurordis.org/about-rare-diseases
(2) http://www.irdirc.org/goals/
(3) http://www.bbmri-lpc.org/
(4) http://www.eurobiobank.org/
(5) http://www.cnag.eu/
(6) http://www.sanger.ac.uk/
(7) http://www.matchmakerexchange.org/
(8) https://ega-archive.org/
(9) http://rd-connect.eu/, https://platform.rd-connect.eu/
(10) http://human-phenotype-ontology.github.io/
(11) http://www.orphadata.org/cgi-bin/inc/ordo_orphanet.inc.php