

BIORESOURCE PAPER

# Genomic and Genetic Disorders Biobank

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The Genomic and Genetic Disorders Biobank (GGDB, formerly Genomic Disorders Biobank) was established in 2006 as an internal bioresource to the Medical Genetics Unit at Casa Sollievo della Sofferenza Hospital (Italy) to collect and store biospecimens from affected individuals with genomic-disorders (e.g. microdeletion and duplication syndromes). Since 2009 the Bioresource has joined the Telethon Network of Genetic Biobanks and has expanded the collection to also include Mendelian genetic diseases. The GGDB now gathers wholly annotated clinical and longitudinal data and biological samples from affected and healthy donors, according to standard ethical principles. Biospecimens are available to the international scientific community for research projects in the field of the pathologies collected and stored in the GGDB.

**Keywords:** biobanking; genomic and genetic disorders; biospecimens; data sharing

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## (1) Bioresource Overview

### Project description

Biobanking is an important resource as support to many types of biomedical research, including research in personalized medicine. Since 2006 the Medical Genetics Unit at Casa Sollievo della Sofferenza (CSS) Hospital created a private internal repository of biological samples (mainly DNA, RNA and cell lines) from individuals affected by different genomic disorders [1–3]. The Ethics Committee of CSS approved the repository in 2006 (protocol n. 12736/06). Afterwards, in 2009, following to a peer-reviewed Italian Telethon Foundation granting call, the GGDB (<http://www.operapadrepio.it/ggdbbank/>) joined the Telethon Network of Genetic Biobanks (TNGB, [www.biobanknetwork.org](http://www.biobanknetwork.org), grant #GTB12001) [4] and in 2012, became a partner of the EuroBioBank (<http://www.eurobiobank.org/index>), the first European Network of Biobanks of Rare Diseases [5]. Finally in 2013, the GGDB joined the Italian node of BBMRI-ERIC consortium (<http://www.bbmri.it/home>). The main goals of GGDB include: i) centralizing the collection, management, and storage of biospecimens and associated clinical data of affected and healthy individuals; ii) maintaining an essential service by distributing biological samples and making them available to the scientific community; iii) implementing new and already established agreements with the Patients' Association; iv) elucidate and study the molecular characterization of GGDB samples to improve the scientific knowledge on genomic and genetic disorders.

Regarding phenotyping, importantly, the GGDB can rely on the activities of the host laboratory, which is skilled in pre- and post-natal diagnosis of genetic disorders. As result of the Biobank staff's consolidated expertise on rare genetic diseases, as well as, the increased interest of the Patients' Associations, the collection of the Biobank has been recently expanded. Indeed, an agreement has been signed between GGDB and Italian Federation of Prader-Willi syndrome in 2012.

To date, the GGDB has recorded and stored clinical data and biospecimens from approximately 1700 individuals (1000 affected patients and 700 healthy controls, of which 98% matched with patient) for a total of 2300 biospecimens collected so far. The great majority of healthy members are not carriers.

### Classification (1)

Human rare genomic and genetics diseases

### Species

Human

### Classification (2)

GGDB collection includes biospecimens with associated clinical, molecular, and biochemical data for genomic disorders, such as Di George syndrome, Prader Willi syndrome, Williams Beuren syndrome, WBS Duplication syndrome, and genetic diseases (including Kabuki syndrome, Supravalvar aortic stenosis, Charcot-Marie-Tooth disease

type 1A, Split-Hand/Foot Malformation with Long Bone Deficiency, Aicardi syndrome, Wolfram syndrome type 2).

### Context

#### **Spatial coverage**

Medical Genetics Unit, IRCCS Casa Sollievo della Sofferenza, Poliambulatorio Giovanni Paolo II, viale Padre Pio, 71013 San Giovanni Rotondo (FG), Puglia, Italy:

Latitude: 41 degrees, 42 minutes, 31.4346 seconds

Longitude: 15 degrees, 42 minutes, 7.1418 seconds

#### **Temporal coverage**

From 2006 to present, on-going with no fixed expiry date.

#### **Temporal coverage for accessibility**

N/A

## **(2) Methods**

GGDB strictly follows the Standard Operating Procedures (SOP) approved by all members of TNGB ([http://biobank-network.org/documents/0-TNGB\\_SOPs\\_Aug2012\\_online.pdf](http://biobank-network.org/documents/0-TNGB_SOPs_Aug2012_online.pdf)).

### Steps

The GGDB Biobank's centralized process enables researchers to access to the service by an initial contact with the staff manager(s) of the Biobank.

### Depositing samples

To deposit samples, users must fill in the Submission form available on the GGDB website providing anamnestic and clinical data of the patient/donor along with a signed copy of the Informed consent form. Signing the Submission form, the user agrees to accept the rules and policies of the Biobank, as reported in Guidelines document at <http://www.biobanknetwork.org/documents/GUIDELINES.pdf>.

After sample acceptance and registration, the Director of Biobank assigns an individual and unique code to each sample. Coded samples, recorded in the Bioresource database are protected by a password chosen by the Director and shared with the Biobank staff member only. The personal data related to the each sample are accessible only to personnel of the Biobank and are protected by security systems. Consistently in the sheet file, the code linked to the donor and his/her data is registered and stored separately. GGDB staff properly manages samples only.

### Requesting samples

The GGDB, as member of the TNGB, manages all samples requests through a dedicate website upon users' registration. All the submitted requests are gathered in a unique Request Control Panel, a tool where each Network Partner can manage their own requests. The applicant must log in and complete the request online appropriate forms provided by GGDB Staff by declaring the reason for use, describing the research purpose and the expected results. Furthermore, as stated on the sample request form, the applicant should be in agreement with the following conditions:

- The material cannot be used for commercial purposes
- Materials cannot be distributed to other investigators without GGDB permission
- The samples should be quoted in any publication and must include acknowledgement to the GGDB, the TNGB, and the support of Italian Telethon Foundation
- No materials are released prior to receipt of the signed agreement form
- Project employing the samples in agreement with the Biobank mission
- All applications must have ethical approval for the proposed research and the Material Transfer Agreement (MTA) must be signed before material release.

### Stabilization/preservation

- Cell lines in DMSO and Medium (for cryopreservation)
- Peripheral blood in RNAlater (LifeTechnologies) solution (for RNA preparation)
- Peripheral blood in PAXgene (PreAnalytiX) tubes for RNA preparation)
- Peripheral blood in EDTA (for DNA preparation)

### Type of long-term preservation

- Frozen (for DNA and RNA preservation) and DMSO (for cell lines cryopreservation)

All samples are stored in temperature-monitored freezers that are locked and accessible only by GGDB staff.

### Storage temperature

- - 20°C (DNA)
- - 80°C (Serum, DNA, RNA)
- - 180°C (cell lines)
- Storage length: until the sample is available, undegraded (DNA/RNA), and/or viable (cell line)

### Shipping temperature from patient/source to preservation or research use

- Room temperature (18–25°C) for flask of cell cultures, skin biopsy and peripheral blood samples
- 4–10° for DNA samples
- Dry ice for frozen cell lines, serum and RNA samples

### Shipping temperature from storage to research use

- Room temperature (18–25°C) for cultured cell lines (not frozen) and DNA samples
- Dry ice for vials of frozen cell lines, serum and RNA samples

### Quality assurance measures

Rigorous quality control measures are applied to all procedures performed by the GGDB. The host laboratory's operational quality system has been certified for Quality Management System (UNI EN ISO 9001) in order to

guarantee high quality standards in terms of procedures, sample preservation, security and privacy. The principal measures for ensuring the quality of the samples include a number of procedures to:

- Govern the sterilisation of reagents and laboratory materials
- Guarantee that cell lines are free from mycoplasma, bacteria, and fungi contamination during all the procedures (preparation, expansion, storage, and distribution)
- Guarantee the integrity of nucleic acids using Nanodrop, Bioanalyser, and agarose gel analysis
- Ensure an immediate intervention in case of an electrical blackout to safeguard samples by proper alarm systems for all freezers
- Have a back-up storage for each sample in separate freezers and boxes
- Keep temperature and monitoring variations of CO<sub>2</sub> by an alarm system
- Keep up-to-date both local and online databases

#### Source of associated data

- Medical records
- Laboratory reports
- Previous studies on samples stored
- Patients' Registry after *ad hoc* Agreement

#### Ethics Statement

The GGDB adopts appropriate security measures at different levels:

- Sample cryptification (identifiable samples)
- Confidentiality and data protection by restricting the access only to the personnel of the bank and protect by security systems
- Written informed consent for collection, storage and distribution
- Distribution to scientific community regulated by evaluation and approval of the project for which the samples are requested

For all the ethical, legal and societal issues the GGDB follows the principles adopted by TNGB Network. Reference documents are:

- **Recommendations issued by the Oviedo Agreement, 1997** (Convention on Human Rights and Biomedicine, Oviedo, 4<sup>th</sup> April 1997) <http://www.portaledibioetica.it/documenti/001316/001316.htm>
- **Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes (CETS n. 203), 2008** (Strasbourg, 27<sup>th</sup> November 2008) <http://conventions.coe.int/Treaty/EN/Treaties/Html/203.htm>
- **Telethon - SIGU Guidelines for Genetic Biobanks, 2003** <http://www.biobanknetwork.org/documents/GUIDELINES.pdf>

- **International Declaration on Human Genetic Data, 2003** (16<sup>th</sup> October 2003, 32<sup>nd</sup> session, the General Conference of UNESCO - The International Declaration on Human Genetic Data) [http://portal.unesco.org/en/ev.phpURL\\_ID=17720&URL\\_DO=DO\\_TOPIC&URL\\_SECTION=201.html](http://portal.unesco.org/en/ev.phpURL_ID=17720&URL_DO=DO_TOPIC&URL_SECTION=201.html)

The Network operates abiding by the Italian Privacy and Data Protection Laws in force, including:

- **Italian Data Protection Authority (Garante Privacy), Personal Data Protection Code**, Legislative Decree no. 196, 30<sup>th</sup> June 2003, published in *Official Gazette No. 174 of the Italian Republic*, 29<sup>th</sup> July 2003 and possible subsequent amendments;
- **Italian Data Protection Authority (Garante Privacy), General Authorisation for the processing of genetic data**, 12<sup>th</sup> December 2013, published in *Official Gazette No. 302 of the Italian Republic*, 27<sup>th</sup> December 2013 and possible subsequent amendments;
- **Italian Data Protection Authority (Garante Privacy), General Authorisation to process personal data for scientific research purposes**, 1<sup>st</sup> March 2012, published in *Official Gazette No. 72 of the Italian Republic*, 26<sup>th</sup> March 2012 and possible subsequent amendments.

#### Constraints

Funds to support the GGDB originate mainly from Italian Telethon Foundation, followed by peer review grants. The maintenance and development of GGDB does greatly depend on the possibility to get additional funds supporting the bioresource.

### (3) Bioresource description

#### Object name

Human Genomic and Genetic disease oriented samples and data

#### Bioresource name

- The Genomic and Genetic Disorders Biobank
- Bioresources acronym: GGDB

#### Bioresource location

Medical Genetics Unit, IRCCS Casa Sollievo della Sofferenza, Poliambulatorio Giovanni Paolo II, viale Padre Pio, 71013 San Giovanni Rotondo (FG), Puglia, Italy

#### Bioresource contact

Staff: [ggdb@operapadrepio.it](mailto:ggdb@operapadrepio.it)  
 ph +39 0882 416350/6353  
 fax +39 0882 411616  
 Dott. Giuseppe Merla, Director: [g.merla@operapadrepio.it](mailto:g.merla@operapadrepio.it)

#### Bioresource URL

<http://www.operapadrepio.it/ggdbbank/>  
<http://www.biobanknetwork.org/>

<http://www.eurobiobank.org/en/partners/partners.htm#22>

#### Identifier used

N/A

#### Bioresource type

Genomic and Genetic Biobank

#### Type of sampling

Disease based

#### Anatomical site

N/A

#### Disease status of patients/source

Patients affected by rare genetic and genomic diseases

#### Clinical characteristics of patients/source

For any patient we have general and anamnestic data (age, gender, disease, and other), and the entire general features for a given pathology, including record of clinical, cognitive, and behavioural profiles and available molecular analyses (on request).

#### Size of the bioresource

- To date approximately 1700 individuals (1000 affected patients and 700 healthy controls, of which 98% matched with patient) for a total of 2300 biospecimens have been collected so far. The great majority of healthy members are not carriers.
- Average of the incoming samples per year: approximately 350 samples
- Average of the outgoing samples per year: approximately 50 samples

#### Vital state of patients/source

All patients are alive at the sampling. The patient collection stands as a heterogeneous population including children.

#### Clinical diagnosis of patients/source

Rare genetic and genomic disorders characterized by dysmorphisms, mental retardation and intellectual disability and other anomalies affecting different tissues and organs, such as cardiovascular, gastrointestinal, muscular and skeletal anomalies.

#### Pathology diagnosis

N/A

#### Control samples

Healthy patients relatives and unrelated individuals.

#### Biospecimen type

Cell lines (lymphocytes, EBV-lymphoblastoids, and skin fibroblasts), nucleic acids (DNAs and RNA), and sera.

#### Release date

N/A

#### Access criteria

Access to the database is restricted to limited number of member staff of the Biobank only. The distribution of samples stored in GGDB is reserved to donors (strictly limited to their samples) and researchers working in qualified and certified institutions engaged in health-related research or health care.

The justification for use (description of the research project, grant sponsor, and expected results) should be properly declared and the project employing the samples should be in agreement with the Biobank and TNGB mission. Proper acknowledgments in the resulting scientific publication, as follows “We thank the Genomic and Genetic Disorder Biobank, member of the Telethon Network of Genetic Biobanks funded by Telethon Italy (project no. GTB12001G) for the biobanking of specimens” should be guaranteed for the Biobank. Payment for shipping cost and a cost recovery to partial coverage of the cost of some basic procedures, related to the sample preparation and distribution service, could be applied.

#### (4) Reuse potential

GGDB samples linked data can be used for both diagnosis and research purposes in the field of the disease for which they have been stored, and never for financial gain.

In the case that a sample is requested with a purpose other than those specified above, the Biobank would contact the donor's family for a new specific consent. The GGDB Biobank preserves an adequate aliquot of the samples to the advantage of the donor and/or their relatives.

#### Author roles

Carmela Fusco, Bioresource Staff, drafts the manuscript  
 Lucia Micale, Bioresource Curator, drafts the manuscript  
 MariaTeresa Pellico, Bioresource Staff, Cell line processing, Sample request and Shipping management, Quality control  
 Valentina Ester D'Addetta, Annotation of data and DNA/RNA sample processing  
 Bartolomeo Augello, DNA/RNA sample processing  
 Barbara Mandriani, Cell line processing  
 Pasquela De Nittis, Collector of samples  
 Dario Cocciadiferro, Collector of samples  
 Natascia Malerba, DNA/RNA sample processing  
 Michele Sacco, Clinical record and patients recruitment  
 Leopoldo Zelante, Clinical record and patients recruitment  
 Merla Giuseppe, GGDB Director, drafts the manuscript

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