BBMRI-ERIC
Biobanking and
BioMolecular resources
Research Infrastructure

We invite you to contribute to BBMRI-ERIC Common Service ELSI's

CALL FOR EXAMPLES

'HOW BIOBANKING MAKES A DIFFERENCE IN SOCIETY'

The objective of the call is to collect good examples that illustrate the benefit of biobanks and biobank-related research for patients and their families, the broader scientific community, as well as society at large. In doing so, we intend to highlight the importance of biobanking, as well as collect arguments which we can all use to promote activities in the field, as well as when advocating for appropriate regulation.

As you can see below and from the enclosed attachment, we have provided you with a set of questions and various examples of success stories. With the aim to show where and how biobanking makes a difference to society within the entirety of the BBMRI-ERIC network, we ask you to provide us with abstracts of examples from your countries and/or your biobank (networks) and send them to us by completing the template by **February 20th**.

Why contribute?

The examples you provide will be compiled in a report and made publicly available in order to promote your success stories across Europe andwill serve to highlight biobank achievements to both policy makers and the public. Bearing this in mind, we want to help you to promote the significance of your work on a European level.

How can you contribute?

Please complete the enclosed template, or provide a narrative text of **500 words** (excluding references, images[1] and contact information) of the example you wish to share in a word file, considering a catchy title. As a guide, please consider the following points when responding:

- What successful biobank-based research has been developed by/thanks to your biobank (network)?
- What changes have been directly produced or enabled thanks to your biobank(research)?
- In what way does your example contribute to better health care?
- What is the best way to contact you for follow up questions?

Please limit the number of references to five and the number of images to three.

Be inspired by the exemplary examples provided in the annex!

Contact us

Please submit the examples to, or contact us in case of any questions,:
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[1] When providing images, consider that they: (a) have to appeal to the lay public: (b) specify copyright, as well as what/who we see in the picture); and (c) share them in appropriate quality for print and web (at least 300 ppi).

ANNEX: EXAMPLES OF SUCCESS STORIES

Estonian Biobank – partner in personalized medicine

The Estonian Biobank cohort is a volunteer-based sample of close to 52 000 participants, representing five percent of the Estonian adult population. The Estonian Genome Center is a research institute of the University of Tartu that manages and maintains the Estonian Biobank.

The initial recruitment phase of 2002-2010 was followed by a period of growing and updating the health information through re-contacting of participants and retrieving data from national health registries and databases. By combining information from electronic prescription, electronic health records and genotype data from the biobank we have identified variants associated with adverse drug reactions. Future plans include linking such information with electronic prescription database to inform prescription decisions.

The genome center is one of the partners of the national personalized medicine initiative (2016-2020). In the first phase of the initiative the existing genetic profiles of the biobank participants will be applied, if approved by them. Meanwhile, the Estonian Government has allocated funding for the recruitment of another 100 000 participants.

Since 2012, the genome center has had several ongoing projects involving return of actionable findings to biobank participants. Examples include familial hypercholesterolemia and familial breast and ovarian cancer and projects are conducted in collaboration with clinicians such as cardiologists and oncologists. By the end of 2017, over 130 individuals received results and genetic counseling. Majority of participants informed of familial risk were previously unnoticed by the medical system, hence the biobank and the genetics first approach has an added value. In many cases, return of results resulted in changes in participants medical management. Additionally, feedback from the participants having received unexpected genetic risk information and long term follow up on their medical management allows us to collect much needed empirical data on how such information will be received and what is the psychosocial impact and clinical utility.

Publications:

Leitsalu, L., Alavere, H., Jacquemont, S., Kolk, A., Maillard, A. M., Reigo, A., … Metspalu, A. (2016). Reporting incidental findings of genomic disorder-associated copy number variants to unselected biobank participants. *Personalized Medicine*.

Milani, L., Leitsalu, L., & Metspalu, A. (2015). An epidemiological perspective of personalized medicine: the Estonian experience. *Journal of Internal Medicine*.

Leitsalu, L., Haller, T., Esko, T., Tammesoo, M.-L., Alavere, H., Snieder, H., … Metspalu, A. (2015). Cohort Profile: Estonian Biobank of the Estonian Genome Center, University of Tartu. *International Journal of Epidemiology*.

Contact:

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Risk biomarkers for familial-hereditary cancer: from identification, to prevention and early diagnosis

Biobanking and the Family Hereditary Cancer:

The BBI-IstitutoTumori Bari was born as an ISO certified biobank in 2008: it collects and cryopreserves consecutive samples of liquid and solid left-over human biological samples and collections of ad hoc biospecimens related to specific clinical trials. It comprises of approximately 250 square meters of surface divided into two floors: a reception and micro-macromanipulation floor and a cryopreservation floor. Since 2004, it also interacts with the Family-Hereditary Cancer Study Center and the Molecular Genetics Laboratory of the Istituto Tumori Bari, which cryopreserves tested samples of DNA tumors and blood samples.

A Research Story:

The story started in 2004: an experimental research of genetic factors for hereditary oncological risk lead to the definition of standard procedures for cryopreservation, laboratory and clinical management of biospecimens. In parallel to procedure-standardization-phase, a systematic DNA biobanking for all the women treated for mammary cancer with primary surgery at our Institute begins. After standardizing laboratory techniques for genetic study of family hereditary risk factors, from the Directory of the Institutional Biobank, we identified the subjects with family-hereditary stigmata eligible for the genetic test.

The availability of the Biobank Directory and of blood cryopreserved related to all our women with breast cancer allowed to work on the prevalent, retrospective cases, candidates for oncological genetic counseling to study heredo-familiarity; in addition, a prospective case studies has been routinely assessed since 2008.

Innovation in the healthcare horizon:

Since 2008, all our patients with first diagnosis of breast/ovarian cancer are screened for family hereditary risk. Individuals with specific genetic alterations predictive of hereditary syndrome, specific prevention programs are proposed as well as the involvement of relatives in the preventive-diagnostic process.

Contacts:

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References:

The activity of the Biobank of the Istituto Tumori di Bari can be summarized in about 100 publications produced by their scientists and utilizing cryopreserved biological material. A brief summary can be obtained from the Special Issue of Biopreserv Biobank Journal; Guest Editors: Paradiso A, Daidone MG, Riegman P. Biopreserv Biobank. 2011 Jun; 9 (2): 139-210.

Danza K, De Summa S, Pilato B, Carella M, Palumbo O, Popescu O, Paradiso A, Pinto R, Tommasi S. Combined microRNA and ER expression: a new classifier forfamilial and sporadic breast cancer patients. J Transl Med. 2014 Nov 19; 12: 319.doi: 10.1186/s12967-014-0319-6. PubMed PMID: 25406994; PubMed Central PMCID: PMC4239401.

Digennaro M, Sambiasi D, Tommasi S, Pilato B, Diotaiuti S, Kardhashi A, Trojano G, Tufaro A, Paradiso AV. Hereditary and non-hereditary branches offamily eligible for BRCA test: cancers in other sites. Hered Cancer ClinPract.2017 May 25;15:7. doi: 10.1186/s13053-017-0067-8. eCollection 2017. PubMed PMID: 28559958; PubMed Central PMCID: PMC5445420.

Disease Registry & Disease Driven Biobank: A Success Story for Multiple Osteochondromas

To improve diagnosis, research and development of personalized treatments in rare disease scenario, Medical Genetic Department (MGD) of Istituto Ortopedico Rizzoli created BIOGEN and 4 related diseases registries to collect high quality biological materials and data of patients. Since 2003, the MGD started a collection of data and samples from patients and families affected by Rare Bone Diseases. In the subsequent years MGD has initiated a standardization process of collected data in collaboration with CLIBI Laboratory establishing the Registry for Multiple Osteochondromas Disease (REM). A comparable process has been performed for biospecimens storage and maintenance, leading to the Biobank for Genetic Samples (BIOGEN). Since many years these two entities are working in concert to provide high quality samples connected to high quality data.

The procedures for collection and governance of all data (clinical, genetic, genealogical, etc.) and specimens according to the ELSI standards have been implemented and supported by the cooperation among clinicians, researchers. In addition, the strong collaboration with the MO national patients' association (ACAR Onlus) has supported REM implementation and is involved in REM/BIOGEN governance leading to an empowerment of the patient-centric perspective.

The Multiple Osteochondromas (MO) is an autosomal dominant disease characterized by the formation of multiple cartilage-capped bone tumours (defined osteochondromas, OCs) typically located in the long bones. OCs are rarely present at birth and grow in number and size during childhood, until completed skeletal maturity. The great variability in size and number of lesions reflects the MO clinical heterogeneity. MO is mostly caused by heterozygous mutations on EXT1 or EXT2, implicated in the control of cartilage growth during endochondral ossification. Surgery is the primary treatment for more severe disease, but imposes significant risk for paediatric patients as excision of OCs can cause irreversible damage to the adjacent growth plate, resulting in further growth abnormalities. In addition, multiple X-rays and imaging scans are the only method of monitoring disease progression. Aiming to increase the knowledge on MO, with the support of Clementia Pharmaceuticals Inc., a biopharmaceutical company dedicated to developing treatments for rare diseases, a wide set of elaborations and analyses have been performed on collected data of underage patients. Those multistep evaluations have proven to be fundamental to design a clinical trial for treatment of MO patients with palovarotene, a retinoic acid receptor gamma (RARγ) agonist that inhibits spontaneous heterotopic ossification. In this perspective Palovarotene treatment could potentially reduce morbidity and deformity, preserving functionality in patients affected by MO.

To date a draft protocol for treatment of paediatric patients affected by MO is under FDA evaluation and REM & BIOGEN data are still contributing the advance of this process, aiming to start a clinical trial within few months.
http://clementiapharma.com/our-focus/multiple-osteochondromas/
http://www.acar2006.org/index.php/attivita/registropatologiarem/87-remesostosi
http://www.acar2006.org/index.php/attivita/biobanca/74-biobanca

The combination of data and samples can bring to increased valuable results for patients' diagnosis and treatment. This approach is showing us a way to improve the patients' quality of life, hoping to substitute the invasive surgical treatment with pharmacological therapy. Stories like this besides highlight the fundamental role of collaboration among all potential actors, are also acting as leverage for health improvement.

Keywords: Biobank, Disease Registry, Multiple Osteochondromas, Systemic Empowerment, Patient-centric approach

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ANNEX: EXAMPLES OF SUCCESS STORIES

Swiss Biobanking Platform identified the CoLaus/PsyCoLaus cohort as one of the good Swiss examples of biobanking-based-research. Below is the story of this study cohort including its impact on healthcare.

The CoLaus/PsyCoLaus cohort is a large population based monocentric study in Lausanne (Switzerland) which includes over 6000 subjects. Initiated in 2003, its main goals are to:

1. Prospectively assess the complex association between cardiovascular diseases (CVD), cardiovascular risk factors (CVRF) and mental disorders
2. Identify new molecular and genetic determinants of these conditions or their association

Assessments:

- Data: All subjects completed a face to face interview with questions on personal and familial history of CVRF, current medical conditions and medication as well as a screen for cognitive problems (in subjects older than 65 years of age). In addition, a screen for psychopathology was performed using the General Health Questionnaire (GHQ-12, Goldberg 1972). Basic anthropometric characteristics were also measured. Over 4000 subjects underwent an interview-based psychiatric assessment (DIGS) allowing to elicit DSM-V psychiatric diagnosis. Finally, additional cardiovascular and blood pressure assessments were performed in a subset of participants.
- Samples: A large array of serum biological variables was measured in the fasting state and in the urine. In addition, all participants from Caucasian origin were genotyped with a 500K SNP (Affimetrix®) DNA chip.

To date, CoLaus/PsyCoLaus has published over 300 articles in peer-reviewed journals. The successful biobanking-based-research that has been developed allows gain of knowledge in the genetic and epidemiological field of cardiovascular diseases and mental health.
This list of publications is available by clicking here:
http://www.researcherid.com/ProfileView.action?returnCode=ROUTER.Success&Init=Yes&SrcApp=CR&queryString=KG0UuZjN5WnJscYjPYkIdEuHtajPak9XYyGj9MQ7nQE%253D&SID=C1fUIHibJSXyV1N99tT

CoLaus/PsyCoLaus study provides a unique opportunity to gather prospective data on the interplay between CVRF/CVD and mental disorders. A better understanding of the psychological, physiological and behavioural links underlying these conditions will result in the development of more specific and efficient strategies of prevention and treatment.

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