

## Creation of a Biobank with Specialization in Kidney and other Genetic Diseases

A Biobank was founded by the University of Cyprus, governed by the Molecular Medicine Research Center of the School of Pure and Applied Sciences, for collecting and archiving biological material and personal data of donors, totally on a voluntary basis, regardless of age, sex, religion, language, ethnic origin or community minority. Volunteers may be patients or healthy people, who may or may not be members of families with a history of an inherited disease or a disease with a small or large genetic component. The material and records to be archived in the Biobank, which is of Pancyprian coverage, is considered as National Wealth and every effort will be exercised to maximize the utility and the benefit towards the Cypriot citizen, the European citizen and the society in general.

The creation of the Biobank was made possible by funding primarily from two sources. The first was a Strategic Research Infrastructure program entitled:

### **Creation of a Kidney Specific Biobank and Infrastructure for Genomics/Proteomics Research [ΝΕΑ ΥΠΟΔΟΜΗ/ΣΤΡΑΤΗ/0308/24]**

The coordinator is Prof. Constantinos Deltas, of University of Cyprus, who had submitted a proposal and obtained a grant co-funded by the European Regional Development Fund and the Republic of Cyprus through the Cyprus Research Promotion Foundation. The second source of funding is the University of Cyprus. The researchers involved and the Coordinator of the Biobank do not intend to use the biobanked material for commercial purposes.

In recent years, in Europe and other countries worldwide, there is significant funding and intense effort made for the creation and maintenance of national and transnational Biobanks with high standards. It has been realized that it is imperative to have access to high quality biological materials and detailed medical records in order to develop ambitious research programs aimed to promote and improve the health of European citizens and provide personalized medical care (personalized medicine). Also genuine efforts have been made and actions have been funded for harmonizing the activities of various European biobanks in order to facilitate the exchange of samples or information about samples and medical records from different biobanks (Biobanking and Biomolecular Resources Research Infrastructure (BBMRI, URL address: [www.bbmri.eu/bbmri/](http://www.bbmri.eu/bbmri/)).

The objectives of the Biobank are:

1. To develop, promote and enhance research or diagnostic or therapeutic programs for the benefit of the Cypriot and European citizens.
2. To create new prospects for research in areas that either already there is some research activity, or in areas where there has not been any remarkable research activity yet, and therefore there is insufficient care for some categories of patients.

It is the thesis of people involved in this Biobanking operation that every patient should be encouraged and given the opportunity to participate and contribute, if they so wish, in relevant research programs that can benefit either themselves or other members of their family or other members of our society.

## Sources of Biobank Material and Potential Uses

Samples for the biobank can derive:

- From individual persons who will be recruited for specific research projects in the framework of wider collaborations
- From people under investigation for diagnostic or therapeutic reasons
- From people who receive some new therapy under a separate research protocol
- From people who are taking an accepted treatment for evaluation purposes in the framework of a research program
- From healthy individuals who voluntarily agree to participate as controls in various research protocols or in prospective studies (eg twins pairs)
- Persons with any hereditary disease or disease with a genetic component for future research

The Biobank is created to prepare material, useful files and scientific tools that will be available to be used for the benefit of the society not only by the present but also by the future generation of researchers. Samples and data in the Biobank can be used for any research connected or related to the disease of the donor who will provide his/her biological sample and personal data. The same will apply for the samples and data that will be from healthy volunteers. The intention for broader and unlimited usage of samples of the Biobank files for approved research projects will be explicitly mentioned in the information notice and consent form that volunteers will freely sign (EEBK03). Such uses are notably envisaged regarding the following kind of activities (indicative list):

- Clinical research
- Pharmaceutical research
- Genetics/genomics research using molecular biology techniques
- Proteomics research using biomarkers
- Epidemiological, phylogenetic research, targeting specific genes or scanning the human genome to define the frequency of related and unrelated genetic and proteomic biomarkers
- Control studies in other research projects

This list being not limitative biobank materials could be accessed for other useful purposes that may not be evident at this stage provided that the projects complies with relevant legal and ethical requirements at European, National or Local levels.

Access to the materials of the Biobank can be requested by many researchers and research groups from Cyprus and abroad, upon approval of the Academic Council, in order to maximize the social benefits resulting from its usage. It is a prerequisite that no project can be developed and materialized without first applying and obtaining the approval of the Cyprus National Bioethics Committee.

## Data Protection and Measures of Security and Confidentiality

The infrastructure is under the supervision of the Technical Services and the Office of Information Systems of the University of Cyprus. The safety of the premises, infrastructure, technological equipment and IT systems are checked and guaranteed by those services. Regarding confidentiality, every effort will be made with available technology to be guaranteed by advanced software systems and mechanisms according to which all samples are coded and data cannot be accessed without using passwords, which will be in the possession of the Director and the

Supervisor of the Biobank. The biological materials such as DNA, RNA, urine, or other to be collected, are kept in a separate dedicated area from the software systems that contain the sensitive personal and medical data. All data is also kept on paper in a special archive with restricted access. The access to biological samples and paper records is secured by electronic locks and passwords. Passwords for access to personal data are available to responsible researchers whenever this is deemed necessary, in the framework of preparing research programs. The Biobank may also include samples that have been collected anonymously in case the researchers do not want or do not require connection of the biological material with the donors and provided that the volunteers were aware of this settlement, in which case no bioethical issues are raised.

The researchers' access to the samples of the Biobank depends on the arrangements made for each research program and is based on the agreement between the researchers and the Biobank and may be subject by the following relationship:

- I. Access to anonymous or fully anonymised material and archive, i.e. electronically unconnected material with no possibility to connect with a specific person.
- II. Access to pseudonymised (coded) material for which a code key and special permission is needed for connection to personal data files, and which are not held by the researcher.
- III. Access to pseudonymised (coded) material with the right of obtaining the code and hold permission for the acquisition of files with personal data. This case necessitating special justifications and guarantees.

There will be possibility for access to the encrypted files via a closed circuit network or via the internet, for a narrow number of partners with a hierarchical and graded accessibility with the use of specific codes. For example a doctor, who is participating in this, can see and study any patient records remotely if the Academic Council allows it. For greater security purposes, passwords will be changed frequently to prevent unwanted access. The access authorization software will be such as to ensure the confidentiality of data and making them available to authorized researchers according with the consent of each volunteer, which is utterly respected. At the same time, for purposes of facilitating any research which aims to advance the general good, and provided that it has obtained approval for implementation, each researcher will have easy access to the samples and the medical archives that he will be given permission (depending on the access mode as indicated above), while the laboratory infrastructure and the expertise of the personnel of the Center will be available to him.

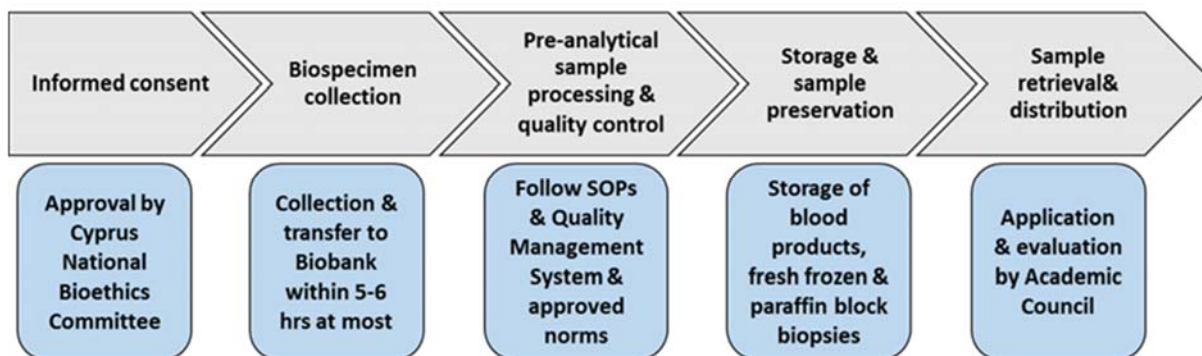
In general, researchers should be aware of, and act by taking into consideration, the guidelines 95/46/EC of the European Parliament and Recommendation 2006 (4) of the Council of Europe relating to access, management, use and protection of personal data.

### **Collaborations, Usage of the Biobanked Material**

Researchers that will request to have access to the archived material can be scientists-researchers of any specialty of the medical/biological sciences who will submit their specific research protocol, after approval by the Cyprus National Bioethics Committee. Every research protocol submitted with the request for implementation using Biobank material will have to undergo evaluation and approval by the Academic Council. All applicants who wish to receive biological material are requested to file at minimum, a summary of their research proposal, in order to ensure to the Academic Council the right to manage and control Biobank samples, to the mutual benefit of all parties involved, including volunteer donors. It may also require payment of a compensation for the usage of archived materials to ensure the maintenance of the Biobank, in accordance with the decisions of the Academic Council.

Researchers requesting access to material gathered by other researchers under a specific research program are encouraged to contact the responsible researchers and enter into collaborations, with the catalytic intervention of the Academic Council, for maximizing the benefit. Special agreements and arrangements may be made between the Academic Council and researchers in Cyprus and abroad who wish to work with the Biobank. The management of the Biobank will seek to enrich the Biobank and encourage partnerships with many researchers. In case of refusal from the Academic Council to grant to the applicants biological sample, the request shall be referred for discussion and consideration by the Research Unit Council.

### Biological Samples and Procedure for Receiving / Giving out Samples



*Work flow depicting the sequential steps for donor enrolment, sample collection and archiving, and sample retrieval*

The biological samples that can be archived are DNA, RNA, plasma, serum, urine, and tissues from biopsies (or other, e.g., hair). After the volunteers are adequately informed by responsible researchers or appropriate collaborators of the Biobank or specific research project, they have to sign a consent form approved by the Cyprus National Bioethics Committee. The samples will be received and transferred to the Biobank for recording and storing in the right conditions, depending on the sample, in a coded manner. At the same time, and according to the specific research protocol, the personal details and medical history or other relevant information of the volunteer, will be recorded and archived electronically and in printed form. For the collection and storage of specimens, directly responsible are the Supervisor of the Biobank and his/her assistant, who are qualified in the field of biological/biomedical sciences, with postgraduate studies.

The privilege and the right to receive samples from the Biobank is realized only after the submission of a written or electronic request to the Director of the Biobank. The samples will be recorded and followed through the Biobank Laboratory Information and Management System (LIMS) so that it is possible at any time to know who the scientists that use the samples are and for what purpose, and thereby assess the pace of sample use.

### Consent Forms of Volunteer Donors

Each volunteer will be informed orally and in writing for the purposes of the Biobank and of the intentions to use the information and samples for the above described studies. If the volunteer agrees, he/she signs freely an approved consent form (EEBK03; [http://www.bioethics.gov.cy/moh/cnbc/cnbc.nsf/DMLapplform\\_en/DMLapplform\\_en?OpenDocument](http://www.bioethics.gov.cy/moh/cnbc/cnbc.nsf/DMLapplform_en/DMLapplform_en?OpenDocument)), thereby expressing his/her will to provide details of his/her medical record and the

biological material to the Biobank. The reason for making the record and biological material available to the Biobank and therefore be used in several different future research, diagnostic and therapeutic protocols and clinical trials, lies on the fact that our Biobank aspires to be the first Biobank of Cyprus to serve the wider research and medical community. As every other Biobank in the world, it will have large operational and maintenance costs, so it should be able to serve as many researchers and research projects as possible, always with the prior approval of volunteers that will participate. If a volunteer expresses a different opinion regarding the usage of his/her biological samples and personal data, his/her wish will be fully respected. The widespread usage in research of archives and biobank material for the benefit of citizens, is of particularly great importance for Cyprus where research in the various sciences and especially in biological/medical sciences is at relatively lower level compared with other countries of the European Union.

Personal data of volunteers who will decide freely to participate in the creation of the Biobank will include their personal medical history and the entire contents of their health records, medical information and data relating to diet and medications, demographics and everything else deemed necessary depending on the specific research programs that will be implemented through the Biobank.

### **Lifespan of the Biobank and Destruction of Samples**

This is the first Biobank created in Cyprus and it is of Pan-Cyprian range and committed to serve the present and future generations of researchers acting for the public good and general interest. Initially it is approved to have a lifetime of 25 years, after the expiry of which it may or may not require a renewal of the approvals by the Cyprus National Bioethics Committee, depending on the situation at that time. A relatively short lifespan is not to the benefit of the Cypriot society and the Cypriot taxpayer.

International experience shows that Biobanks are becoming much more useful and their scientific value increases tremendously as time goes by, thereby giving the opportunity for recruitment and participation of thousands of volunteers. This in turn, relates to the fact that contemporary research projects of epidemiological or other medical character of multifactorial diseases with a genetic component require thousands of patients to increase statistical power. This is why many times researchers and patients contribute samples and data from different registries and Biobanks to increase reliability and maximize the chances of success in reaching firm conclusions.

If a serious maintenance problem arises or there is weakness of retaining the Biobank, the possibility will be explored for transporting the samples to another safe place to protect records and samples and continue the contribution to research.

If a decision is ever taken for the destruction of archived samples, the intervention of the Cyprus National Bioethics Committee and that of the Data Protection Commissioner is going to be asked, to supervise the destruction process in the presence of the Academic Council of the Biobank.

If a volunteer expresses the desire to withdraw his/her samples and the archive from the Biobank, it will be required to sign a written request, without being necessary to justify his/her decision. This document will be recorded by the Biobank. If the volunteer wishes so, he/she can be present during the process of erasing the record from the electronic system, during the destruction of the printed copy, and the destruction of the biological samples by pouring them down in the sink of the laboratory of the Biobank. Before making the destruction of the above, the volunteer will be given the option for full and irreversible anonymization of the file including the destruction of the mechanism that associates the biological sample with the personal medical information in order to maintain at least the biological sample for use in cases that do not require further follow-up and

contact with the individual. This alternative option is mentioned in the consent form EEBK03 and it is a legitimate option in order to minimize the loss of the Biobank, without any psychological, social or other cost for the volunteer.

### **Governance of the Biobank**

The Biobank is an integral part of the Molecular Medicine Research Center which operates as an independent Research Unit and therefore managed by the Academic Council, as stipulated by the Regulations of the University of Cyprus (General Regulations for Research Units, 1999 and 2010). The election of the Director of the Molecular Medicine Research Center, as an independent research unit, is subject to the approval of the Senate, which is responsible for filling that position. The full composition of the Academic Council is as follows:

Chairman: Prof. Constantinos Deltas

Members: In accordance with the law and regulations concerning the governing of the Research Units, members of the Academic Council can be group leaders who supervise ongoing research programs and academic faculty members, with a total of 3-9 members.

An advisory and supervisory role is exercised by a separate council which is also provided by the same regulation according to which a Research Unit Council is established, of 5-9 members that are coming from both the academic community and outside of it, provided they are not members of the Academic Council. The Director of the Research Unit is a member but cannot be President of the Research Unit Council. The composition of this Board, which is approved by the Senate, is proposed to be as follows:

- Head of the Department of Nephrology of a Public General Hospital or his/her representative
- Representative of the Rector's Council, University of Cyprus
- Chairman of the Pancyprian Medical Association or his/her representative
- Director of Medical Services and Services for Public Health, Ministry of Health, or his/her representative
- President or representative of the Organization for Protection of Patients' Rights
- Other Personalities of the Cyprus Research community

The term for members of the Academic Council and the Research Unit Council is four years. Each academic or non-academic member of Councils may be re-elected only for a second consecutive term, except for the Chairman of the Academic Council and group leaders of research, who may be re-elected without limit, upon the approval of the Senate.

Decisions are taken by simple majority and in case of a tie, the President will have a casting vote.

### **Evaluation of Research Programs seeking to Use Biobank Material**

If a researcher or team of researchers apply for the access and the use of Biobank material for the purposes of their research, the Academic Council will evaluate the proposal, provided that it has been approved by the competent Committee on Bioethics, and decide on the usefulness and utility of the research as well as on the benefits to derive from the proposed project. The Academic Council has the right to approve or reject by majority vote research proposals submitted. If the Academic Council considers it necessary, it has the right and the power to appoint an external Ad Hoc committee of three members with a mandate to assess the usefulness of a research project submitted which asked for using material of the Biobank. This process is necessary to ensure that this national wealth that is being created and maintained at great cost

and with the participation of tens of scientists and thousands of volunteers, will generate benefit from its optimal exploitation, with a maximum degree of reliability and confidentiality.

The Biobank will be inspected once per year by the Research Unit Council. Also, once per year or more frequently, if it is necessary, a report on the activities and progress of the Biobank will be prepared and submitted to the Research Unit Council, with the responsibility of the Coordinator.

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The establishment of the Biobank and the approval of this Constitution was confirmed by the decision of the Cyprus National Bioethics Committee, on November 1, 2011, after submission of our application.