

The Regional Research Biobank of Central Norway – “One biobank, many collections”

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INTRODUCTION

The term biobank is used to designate a systematized collection of biological specimens, often restricted to specimens of human origin (1). Population biobanks, which mainly receive blood samples from large cohorts, have their value primarily in an epidemiological setting, as they are especially useful in identifying causative agents and risk factors, the practical scope of which is prevention. Clinical research biobanks, which contain samples from patients, are often established *ad hoc*, as part of a particular research project, aimed at shedding light on disease mechanisms and factors determining the course of disease, their practical scope being mainly to improve diagnosis and treatment.

In the central part of Norway, we have established one clinical research biobank which is meant to serve the whole region. In this paper we will describe the background for this rather unusual construction, the principles which have governed its organisation and policy, and the results which we have achieved so far. Finally we discuss a couple of issues which open perspectives into the future.

BACKGROUND

Although Norway has a well developed health care system and although its hospitals are holding high standards, the country has weak traditions in medical and health related research, its scientific production being inferior to the ones of neighboring countries. In recent years, the national government has requested that increased efforts be put into medical research. Official documents point to health registries, biobanks, and health surveys as the fields where Norwegian medical research has its greatest potential (2). Thus, translational research, which seems to be the common denominator of these fields (3), is deemed the most promising area for the demanded surge in research activity. In keeping with this, research has been declared as one of the main tasks of the public hospitals, which constitute the overwhelming majority of such institutions. In order to realize the expectations, collaboration between institutions is strongly encouraged, and there is a special emphasis on the establishment of positive interactions between the health care and university sectors, as well as between large city hospitals and the smaller, peripherally located ones. However, there are several challenges which must be overcome before this can be realized.

During the last decade it has become more complicated to initiate research projects involving human beings and human biological material. Like many Western countries, Norway has had its share of new legislation, with more explicit regulations and formal approval schemes. The application and reporting processes are more cumbersome and time-consuming than they used to be, and the risk of making a misstep is felt as a real threat, not only for novices in the field, but also for more experienced scientists (4). Meanwhile, the hospital wards meet increasing demands in terms of productivity, economic efficiency, and budget discipline. More time is spent with planning and reporting. In general, hospital personnel feel themselves tightly squeezed between the official requirements and patients' expectations on one hand, and the available resources, especially time, on the other. Thus, there is an obvious need for a robust support service, which can help researchers navigate through the bureaucratic maze, so they can concentrate their efforts on the production of scientific hypotheses and devising ways to test them.

Many hospital based research projects have been of limited size. In small and medium sized hospital departments there may not be available expertise on all the practical issues which must be resolved before a project involving the collection and analysis of biological samples can start. A number of decisions must be taken and many arrangements must be made, concerning the recruitment of study participants, the collection and transport of samples, their preservation and storage, annotation and labeling, data storage and security. The methodological solutions are often decided *ad hoc*, and the risk of making suboptimal choices which may jeopardize the project is looming. Many such projects have been abandoned, leaving a collection of useless samples, which end up being destroyed without ever having been put to the intended use, let alone being reused for new purposes after completion of the initial investigation. Thus, there is an obvious need for a consulting service, which will keep an updated inventory of quality checked practices and solutions in relevant areas and which will put this accumulated experience to the researchers' disposal, along with guidance and recommendations.

The numerous steps involved in specimen logistics, as well as in the storage and protection of data about the samples, their donors and the analytical results necessitate to varying degrees personnel with diverse

competences, storage containers and buildings, computer hardware and software systems. In a large project this will typically be covered within the financial plan. In projects of more modest size – or in projects in which the biospecimen analysis plays a small part – it may not be worthwhile to establish a comprehensive infrastructure for this sole purpose. Thus, there is an obvious need for a practical service, which can provide the researchers with access to necessary, basic equipment and assistance by competent operators, according to the needs of each particular project.

Summing up, a service is needed within the hospital organization, which can assist with formalities, methodologies and infrastructure, thereby promoting biobank research activity. Since 2002 ownership and the administrative responsibility of Norwegian public hospitals has resided with the central government (5). The whole country is divided into four regions, each region endowed with a regional health enterprise administered by a Chief Executive Officer (CEO), who operates under the instruction and control of a professional board. In each region there are one or more large, highly specialized and broadly staffed teaching hospitals, plus several institutions of lesser size. The hospitals are organized as local health enterprises under the patronage of the regional enterprise. The latter is an administrative entity, which has been given the explicitly stated responsibility for research in the hospitals under its jurisdiction. This organizational background provides an opportunity to address the three challenges outlined above. In Central Norway, the University and the Regional Health Enterprise have established a Regional Research Biobank of Central Norway (hereafter: the Biobank). The Biobank is intended to provide an organizational framework for all research which involves biological material from patients in any of the public hospitals of the region.

PRINCIPLES

A general biobank

In clinical research, a formal biobank is often established for every new research project, only to be closed down at the end of the project period. The expressed aim of the Biobank is to become the only formal clinical research biobank in the region of Central Norway, by offering procedural and practical support to research involving the use of patient samples. The strategy is formulated in the slogan: “One biobank, many collections”. The Biobank is conceived as a durable umbrella structure, of undetermined duration, whereas individual research projects are thought of as collections, somewhat similar to bank accounts – to extend the bank metaphor. This is one of the most important aspects of the Biobank. The project groups are primary responsible for storing their own samples, but all handling of samples and data must comply with Biobank policies. Thus, the Biobank is more an organizational structure than a physical bank.

Current law requests that a research biobank be formally approved before a project can start, and the application process is somewhat cumbersome, involving approval of the Regional Ethical Committee (REC). In contrast, we consider that a permanent biobank with a continuous activity, allowing temporary support for any project, is a model which will contribute substantially to the objectives expressed by the national government (2). By establishing a general biobank with a sufficiently wide scope, which will encompass all conceivable research activity, the application process is simplified for any future project. Furthermore, the individual project leader will not be formally responsible for the biobank material, as the CEO of the Biobank assumes that role. Our idea was met with scepticism and resistance in various regulatory bodies, but finally the concept has been approved by all relevant instances, i.e. the REC, the Ministry of Health and the Data Inspectorate. If the purpose of the law is to ensure sound handling and use of biological material, the regulations should not be more complicated than what is necessary to achieve this objective (6).

Several projects

The most important resource in any kind of research is the human factor: the curiosity, the creativity, the ingenuity and the enthusiasm of individual researchers and research groups. In the case of medical and health related research this is all the more true. Any research activity hosted in a clinical setting will depend on the eager contribution from various hospital professionals. The chances of success are maximized if the project idea is firmly rooted among those who must do the job. Since the Biobank is not sufficiently staffed to take care of all aspects of material collection, we are dependent on the initiatives taken by others. The role of the Biobank is rather to encourage and provide support to local initiatives. Although the Biobank has a general approval without time limit, it is a matter of policy that every new collection and every new use of stored material shall be described as a separate project, which must be individually approved by the REC. The Biobank assists in preparing the necessary documents for the ethical review application, but in the material collection phase the Biobank itself will often hold the formal project leadership. In that case the CEO of the Biobank will be the prime manager of the stored specimens. This way of operating requires a formal distinction between collection and use of biobanked material as two different kinds of project, although projects of both types are usually planned concomitantly, and in the eyes of researchers appear as two sides of the same coin.

A main function of the Biobank is to make it easier to start a research project, but this is part of the more general objective, which is to contribute to an increased research activity within the hospitals. Whenever possible, a collection project should seek to collect more material than what is envisaged for immediate

use. Experience has repeatedly shown that new questions and new hypotheses turn up as a project is evolving, so more material will regularly be wanted. Similarly, clinical information is also stored and organized with further use in mind. Whenever biological samples are analysed, we require that the primary results are stored in the Biobank database in a format which permits retrieval and further processing. As a general rule one should in each case collect and keep as much material as possible, within the practical limits of storage capacity and within the limits imposed by the needs for diagnostic or other clinical purposes. The latter condition is an issue of utmost importance, and the Biobank will not accept any collection project unless the procedure has been approved by those who are in charge of the diagnostics. If material still remains after a project is completed, this will constitute a valuable resource for further examination by others. When a patient has consented to the scientific use of a sample, this must be understood as the expression of a genuine wish to support the advancement of medical knowledge. The best way to respect the patient is to use the material and associated information to gain as much scientific insight as possible, within eventual limits imposed by the consent.

Moreover, one should collect and handle the material in such a way as to maximize its future usability. Even if the use which is planned at the moment of collection can be well served by a certain quality standard, one should always seek a higher standard if that is practical, since an investigation which becomes desirable in the future may well require more stringent preservation and storage conditions. The procedure should therefore be chosen so as to ensure the best possible preservation of all aspects of the material's chemical and structural integrity. To the extent of what is possible, one should strive for short handling times, low storage temperature, avoidance of chemical and other contamination etc. This includes the adoption of well documented standard operating procedures, and careful recording of any deviation from the protocol.

Broad consent

Until 2009 Norwegian law held the informed consent as an absolute prerequisite for the use of biological material in research, and that the information must include a description of the purpose of the project. Blanket consent was not permitted, by the argument that consent without limits cannot be qualified as informed, since no information is given. However, whenever suitable the Biobank will use a generic and standardized information pamphlet and consent form, with the broadest possible scope. Since it is under no circumstance possible to describe absolutely all thinkable aspects of a project, one must necessarily make some delimitation. We argue that relevance is a practical and safe criterion to apply. This is to say that the patient must receive all relevant information about the project, but need not be exposed to irrelevant informa-

tion (7), although relevance can not be defined in absolute terms. In the case of a mature and mentally adequate human being, the only standard that seems meaningful is a psychological one. This means that a piece of information is relevant to the extent that the individual patient considers it necessary for him or her to make the decision whether or not to consent. Thus, if a given patient gives his or her consent, that patient must have considered the given information sufficient, and therefore fulfilling the relevance-criterion. Disallowing a patient's consent in this circumstance is overruling that patient's ability to make decisions about his or her own personal matters, which is a depreciation of the person and therefore an unacceptably contemptuous attitude. We propose that the vast majority of patients will find it acceptable that the biological material can be used to: "... produce new knowledge about causes of disease, thereby contributing to improved prevention, diagnostics and treatment of disease". This description would obviously not be compatible with all kinds of scientific investigation, and as such it is not blanket consent. However, it would certainly fit into what many classify as a "broad consent" (8), a concept which in 2009 received explicit legal status with the new Health Research Act.

Generic database

A tremendous challenge to the Biobank concept has been the great diversity of the material collected in various projects, which demands specially designed schemes for the organization of the associated information. We have developed a customized database system with a multilayered architecture, comprising a central Microsoft SQL database. The database communicates with a web application written in Java, implementing a rich user interface. The application is thus accessible from any PC connected to the internet, but protected by several layers of log-in security and control measures. Both the underlying persistence and service layers and the user interface have been refurbished and fine-tuned on several occasions, mostly as a reaction to criticisms and suggestions from the users.

The data model needs to cater for a virtually unlimited variety of sample types and analytical results, as well as a multitude of different kinds of clinical data, each project defining its own set of variables. Nevertheless, the Biobank wants to assure that recorded information is globally accessible, so that in the future one may conduct research based on data-mining across projects. This requires strict and well-defined rules for variable definitions and precise naming conventions. Thus, if the same concept appears in two different projects, it must be designated with the same variable name and be quantified using the same unit of measure. Before a project can start recording data the Biobank administrator must define the project's workspace in the database, with a specification of the variables which are going to be used, thereby defining the project schema. All standard variable types are allowed, and in

the database layer all numeric values are stored as base units of the SI-system, if applicable. In the user interface seen by the project members, i.e. the graphical representation of the project schema, the project group itself decides in which multiple of the base unit the value will appear. Similarly, if the project group prefers to designate the variables with unconventional names according to internal tradition or jargon, that wish may be accommodated by defining a project specific alias for the variable name. This alias will then appear in the user interface.

All actions performed in the database are recorded with a timestamp and the login identity, so it will always be possible to track every move, every change to a sample, every alteration of a variable. Any attempt to perform an unauthorized or forbidden action will be recorded. In addition to the physical measures to protect the hardware installations and the quality-checked, high-security login procedures, this provides additional layers of security to ensure protection of the data against accidental or intended corruption or destruction as well as against inadvertent leakage and intentional theft. We feel confident that any conceivable risk is kept at a minimum, which was the conclusion of a formal risk-and-vulnerability analysis undertaken by the IT-department of the Regional Health Enterprise.

Confidentiality

It is mandatory that all personal information about patients is immediately de-identified at the moment a sample is left under Biobank custody or another piece of information is entered into the Biobank information system. The database is constructed in such a way that the personal identification number is automatically encrypted using a strong encryption algorithm. Thus, to the investigator the samples and the associated additional information appear as completely anonymous. The key files, which contain the links between the patient identity and the encrypted number, are kept separated from the project data, under strict access control. Nevertheless, since the encryption process yields the same result each time for the same person within one project, new information about already registered participants can be added at any time.

The database generates a unique identification number for every new sample unit, which is by definition any physically separate unit of biological material destined for storage. The number is a combination of the biobank identification number, a project number, i.e. the identification number of the collection project in which the original specimen was acquired from a patient, and a sample identifier, i.e. a serial number. The unique sample identification number can be converted to a machine readable barcode and printed on a label sticker to be attached to the container. Most projects take advantage of this functionality, although some prefer to use prelabelled tubes, in which case the value of this code must be entered into a variable in the database.

Before they are granted an account in the Biobank database system, potential users must sign a declaration stating that they will not keep any private lists which might permit them to link samples to the personal identity of the donor. Although this does not preclude the theoretical possibility that someone may reidentify a database record and even distribute personal information to others, we find it very unlikely to happen. If someone is found guilty of breaching the Biobank information security rules, their user account may be shut down and they will not be given further access to the database. If the infringement should have a criminal character, the evidence will be reported to the police, and the offender risks a public lawsuit.

ACHIEVEMENTS

General acceptance of the concept

By sticking to the fundamental principles of the original concept, despite resistance from various authorities, the Biobank is today an operative organization as described above, with all the necessary formal approvals as decreed by law and official regulations.

Some clinical researchers may find it difficult to understand why all data are strictly de-identified. Medical personnel are used to think of their interaction with patients in personal terms. In the therapeutic setting this is highly valued, and information is indeed gathered for its relevance for the individual patient. When doctors engage in research, they have a tendency to bring with them the clinical paradigm. In the not too far past, the identity of research samples and data usually was not concealed in any way. The situation has changed dramatically, so that today the focus is on privacy issues, which may be perceived as an inconvenience. However, the purpose of scientific activity is to discover relationships of general validity, and in this context the person as such is irrelevant. At second thought the researchers have always ended up endorsing the principle.

Human biological material is a limited resource, all the more so when it comes to material derived from particular lesions or from patients with a specified disease. In order to gain new insight in pathological processes or disease outcomes, one must have a certain amount of information from a certain number of comparable cases. The less frequent a disease or condition is, the longer it takes and the more laborious it is to obtain a sufficient amount of study material. Consequently, we must encourage and support everyone who wants to engage in the recruitment of patients and the organization of a collection project. In order to enhance and maintain their enthusiasm, which is essential, they must be given some rights and priorities in the use of the material. However, they are not granted an unlimited or exclusive right, in which case one would risk that collected material might not be optimally utilized. Fundamentally, rights must be accompanied by duties. In the case of biobank research this means the obliga-

tion to ensure that collected material is exploited in accordance with the expectations of all contributing parties, including the patients, the health service, the scientific community, and the society at large. As a general rule, the research group which organizes the collection is assigned a three years' period of exclusive right to utilize the material, the period starting when the number of samples is considered sufficient for research use. After this period, the material must be made available also for others who may need it. Also this condition is generally accepted by the researchers. Since 2009 the Health Research Act provides a similar rule.

Contribution to standardization

Two key elements define a necessary condition for effective resource sharing and reuse: Standardization and documentation. Only if material from diverse sources is handled in similar ways can it be analysed together in a single research project. It is therefore of utmost importance that procedures be as standardized as possible. Although one should always strive for optimal quality, similar quality is even more important. A number of voluminous manuals have been published describing "best practices" for a diversity of biobank relevant procedures, and we have adopted these as our standard to the extent we find them appropriate (9,10). By constraining all project groups to make a detailed description of their operating procedures and store these electronically in the Biobank information system, we gradually build an internal collection of documents. New projects are strongly urged to use the same procedures as those employed previously.

There is a high degree of consensus about procedures for the collection and storage of blood and other samples of fluid material. There is much less agreement on the best way to collect and preserve tissue material, which is the kind of samples which make the clinical biobanks unique. Tissue is distinguished from fluid samples by its local heterogeneity, which brings about several challenges. In order for tissue material to be useful, it is nearly always mandatory to know the histological composition and sometimes other structural details of the sample, in addition to the faithful conservation of the genetic, chemical, and morphological properties.

The Biobank has for several years been engaged in the development and optimization of methods for harvesting of tissue samples, using material from total prostatectomies as an especially demanding type of specimen. Although the material was originally meant only for transcription analysis, we wanted to avoid the use of chemical stabilizers, which otherwise might have solved the issue. We managed to develop a method which produces research specimens of the utmost quality for RNA analysis and which furthermore permit the results to be correlated to histopathology. Moreover, the method is perfectly suited to MR spectroscopy, a methodology which would have been precluded had

we chosen to preserve RNA by the use of chemicals (11). The method has recently been adapted to other organs removed by surgical interventions.

Although the Biobank disposes of some storage capacity, which may be used to store the samples if such help is needed, many project groups have their own freezers and keep their samples close to the laboratories where the analysis work is taking place. However, relevant details about local freezers must be recorded in the Biobank database, and they must be connected to an approved surveillance and quality control system. Moreover, the researchers are compelled to keep track of their samples and to update the central database via the project interface whenever a sample is moved or manipulated in a way that affects its status. They also have the responsibility to record and document any deviation from the settled standards. By these measures our solution ensures a sufficient degree of sample quality. Further, we think that our insistence on standardization and quality will make our collections more attractive to external collaborators in the future.

Increasing level of activity

The Biobank is answerable to the Regional Health Enterprise, its task being to assume managerial responsibility for all research use of biological patient material in the health region. A steadily increasing number of ongoing research projects seek assistance and support from the Biobank. Obviously, the Biobank responds to a real need in the scientific community. New projects involving the collection of biological samples are now seldom started without involvement of the Biobank, especially when it comes to questions of organizing the collection logistics and the storage of data. However, the Biobank has also been engaged in salvation operations in order to bring old collections of samples and data in accordance with present laws and regulations. Some of these have been of substantial size, encompassing tens of thousands of samples and thousands of variables.

In addition to serving various research groups supporting their initiatives and helping them with formal and practical issues, the Biobank has also taken the initiative to some collection projects, with the CEO of the Biobank as the formal project leader. One project of this kind involves one of the peripheral hospitals in the region and so serves as a pilot project for developing and optimizing logistics procedures for large scale collection in a small hospital setting. The resulting material collection will be put at the disposal of anyone who can present realistic plans for its use in scientifically sound investigation.

Building relations of trust

The Biobank was established as an instrument to increase and improve medical research. The final aim of the Biobank is to contribute to the large body of knowledge on which health care is built. This activity should expect to be endorsed and actively supported

by anyone, included those who are afflicted by some illness and who are therefore candidates to be enrolled in a study. Provided biobank based research, and the Biobank with it, is understood as this kind of beneficial activity, patients most certainly will be happy to consent to their removed samples being used. The only concern which may reasonably occur to potential donors is that of possible breach of privacy. It is up to the Biobank to build and maintain a widespread confidence among the general public, that our work is for the common good and that we take every possible measure to protect personal information from being unduly disseminated.

In order to make people believe that the Biobank serves their interests, openness and transparency are of the utmost importance (12). We therefore publish information about the Biobank activity on our website, about policy and security measures, about the kinds and amounts of stored material, about ongoing projects and project achievements. We keep open connection lines to the regular press, and at yearly intervals we publish and distribute a brochure reporting on the activity. Furthermore, we are currently planning to establish a routine whereby all patients receive direct information at their arrival in the hospital.

By existing Norwegian law, patients who have donated material to a general biobank may withdraw their consent at any time. The ethical foundation of the right to withdraw has recently been discussed, and there are valid arguments against such a privilege (13). Nevertheless, we think this arrangement constitutes a reasonable basis for the relationship between the Biobank and the donors, not because it is an ethically unquestionable right, but rather because it may serve as a practical instrument to gauge the level of trust among the public. Studies have shown that in the Norwegian population, as well as in other countries where there is a developed sense of national cohesion and solidarity, the proportion of consenters is in the order of 95% (14-16). Thus, by tracking the number of non-consenters and withdrawals we may track the Biobank's reputation, and we may take steps to remedy any decline in public trust (17).

PERSPECTIVES

Clinical research biobanking and personalized medicine

The number of scientific and popular papers abound, in which biobanks are eulogized for their contribution to the progress of medicine. It is not by chance that this expansion of biobanking coincides with the last decade's spectacular advances in genome analysis methodology and stunning achievements in genomic research. One of the tendencies that characterize the development of medicine over the last century is the splitting of old concepts into new diagnostic entities and the subdivision of diagnostic categories into smaller groups, each with their own peculiarities, especially

in terms of prognosis and the response to treatment.

However, despite the tremendous amount of knowledge which forms the basis of modern medicine, there is obviously even more to be discovered. Even within one diagnostic entity, it turns out that the disease process may follow extremely diverse paths, ranging from virtually negligible impairment of the quality of life to severe illness and, sometimes, premature death. Some patients respond well to standard treatment, whereas others do not. The examples are countless (18,19). In some cases we know part of the answer, which may lie in various properties of the disease, at other times it may be linked to properties of the person. But in most cases we do not yet know (20,21). So among the most prioritized areas of contemporary medicine is the search for factors which more precisely determine the future risk of developing any given disease, as well as those which determine the course of the disease, with or without various possible therapeutic interventions (22). A substantial progress in any of these areas will depend critically on the availability of biological samples. Population biobanks will supply scientists with information about genomic and other constitutional background as well as hard data on premorbid exposure to environmental factors, which can be linked to subsequent disease occurrence. The detailed scientific examination of biological material from patients, in combination with clinical data, will be an essential prerequisite for the more targeted therapies we hope to see in the future, those which have become known as personalized medicine (23,24). Thus, available evidence indicates that biobanks will constitute the foundation of biomedical science in coming years, and there is reason to fear that the access to suitable biological material will be the limiting factor.

The ethics of clinical research biobanks

Until 2009 Norwegian law did not distinguish between population based research biobanks and clinical research biobanks. A new law opens the possibility of using an opt-out procedure for the scientific use of biological material, but only for material which has been collected as part of diagnostic or therapeutic procedures within the health care system. A prerequisite for this procedure is that the patients must have had the possibility to refuse. There are ethically sound reasons for this distinction. Whenever someone seeks medical advice for a real or suspected health problem, they demand and expect that their complaint or concern is handled according to the best of current practice. However, medicine is an entirely empirical science. Contemporary medical knowledge and practice is nothing but the result of an unbroken chain of collaborative efforts, kept alive through centuries by thousands of professionals and millions of patients. Our current conception of human biology and the factors which influence on health and disease has been instrumental in establishing the institutions and practices which make inhabitants of modern societies expect to live long and healthy

lives. So when someone demands to receive the best treatment available, that means a treatment based on the accumulated experience with all similar patients up till now. We contend that a person who desirously takes advantage of information about others, and at the same time refuses to let information about himself/herself be used to the benefit of others who are in the same situation, acts in an immoral way. No consistent moral theory will find such a person virtuous. Despite years of intense dispute in the medical literature, this simple argument has – to the best of our knowledge – never been convincingly refuted. Consequently, denial of consent without good reason is immoral. We claim that a rule which takes as the default position that people are immoral is an unethical rule (25). Some have questioned the dogmatic primacy of informed consent altogether (26,27).

Notwithstanding the reasoning presented above, we prefer to keep consent as the general procedure, – not because it is ethically wrong to omit it, but because it is politically right to keep it. We believe asking for consent has the advantage of engaging patients and public in medical research activity. We think it is of societal value to underscore that the continuous process of expanding medical knowledge and improving health care depends on the collaboration between patients, clinicians and researchers. And from this process we all benefit.

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CONCLUSION

The Regional Research Biobank of Central Norway is primarily an organizational framework, established to provide counseling and support for researchers who wish to utilize biological material from patients in their projects. The Biobank has prioritized those areas where the need was seen to be most pressing in the initial analysis, so we can offer advice to the researchers on:

- how to deal with legal and other formal requirements and processes
- how to organize an efficient sample collection workflow to ensure high quality samples
- how to store and secure samples and associated data

We have at all times pursued generic and general solutions, with a high level of reusability.

Although there are still many tasks to be solved and much is still to be improved, we have at present a well functioning unit with the capacity to enhance biobank based research in a hospital setting. We will be happy to share our experience with anyone interested.

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