Case Study on the Economic Impact of Biobanks Illustrated by EuroCryo Saar

November 2009

The following case study presents one part of a joint project of the three partners Technopolis Ltd., Bureau d'Economie Théorique et Appliquée (Beta) at the Strasbourg University and Fraunhofer Institut for Biomedical Engineering (IBMT) to measure the impact of biobanks and their network on the economy. It is the result of the call for proposals for an impact study on biobanks and the biobanking infrastructure BBMRI[1] published in the summer of 2008 and the decision made about the participating partners for this study at the BBMRI WP 7 meeting in Berlin on 27th November 2008. The contract for this case study was signed in March 2009 between Inserm and Fraunhofer-IBMT.

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Contact:
Dipl.-Kfm. Vincent von Walcke-Wulffen
BBMRI Project Manager / Fraunhofer Deputy Representative
CEO of the Alliance of German Cryobanks (GDK)
Fraunhofer Institut for Biomedical Engineering (IBMT)
Industriestraße 5
D-66280 Sulzbach/Saar
Tel: +49/6897/907152
Fax: +49/6897/907151
Email: vincent.walcke@ibmt.fraunhofer.de

[1] Biobanking and Biomolecular Resources Research Infrastructure.

1. Introduction

The goal of this study is to evaluate the economic impact of one individual biobank, namely the EuroCryo Saar / Fraunhofer-Bioarchive at Fraunhofer Institut for Biomedical Engineering (IBMT) in St. Ingbert / Saar. The evaluation of an individual biobank is essential to assess the impact of a biobank on its surrounding economy, which in turn is a necessary prerequisite for the evaluation of the impact of biobank networks. Therefore, in this study we describe EuroCryo Saar / Fraunhofer-Bioarchive and the underlying business models. A successful business model is the basis to reach scientific goals in the field of applied R&D as covered by the Fraunhofer Society.

Basis of this description is the fact, that public investment in R&D infrastructure has in general a positive effect on economic and social issues[2]. The processes and outcomes of innovation triggered by R&D are essential for productivity growth and for sustaining and improving wage rates[3]. The correlation between innovation, productivity growth and prosperity is increasingly well recognized and for example documented in the OECD R&D Overview of 2008[4].

The problem in this field is the lack of possibilities to measure the direct economic effect of R&D in the individual case. Universities and R&D-institutions are often significant units in economic terms, both of income/expenditure flows and employment[5]. Direct effects are, e.g., the number of new jobs directly correlated to the R&D and the return generated by products or services developed. The problem is to measure these direct effects and to correlate them to the R&D done. That's why indirect effects are used like the investment in this R&D area or the number of patents or publications. By using the knowledge documented in patents and publications new businesses can be created, that's why they are used as a measure for the technology transfer[6]. Another way of technology transfer is the education of students. In addition R&D institutions like IBMT or universities have a positive effect on the local economy[7]. Also, these effects can be divided in direct and indirect effects. The direct effect is the employment of the staff, which causes income which is mainly spent on the local economy. An indirect effect is the important role as a public space with all events and educational efforts organized by the university.

2. Economic situation of the Saar region during the founding period of Fraunhofer-IBMT

The Saarland is one of the 16 Federal States in Germany. It is the smallest one, besides the city states of Berlin, Bremen and Hamburg. Its location close to the French border has given the Saarland a unique history. After the Second World War the Saar region was under French occupation and administration. Saarland joined the Federal Republic of Germany in 1959.
The Saar Region was interesting at the time when the coal and steel-industry was very well developed and of major economic and strategic importance. With the declining importance of these industries, the Saar Region fell into a deep economic depression.

[2] Tassey (2008), p 8.
[3] Lester (2005), p 6.
[4] OECD (2008), p.20 ff.
[5] Bleaney et. al. (1992), p 305 ff.
[6] v. Ledebur (2008), p 604.
[7] Bleaney et. al. (1992), p 305 ff.

The Biotech strategy of the Saarland's government was the groundwork to build up a new industry cluster in the academic environment of the universities of the Saar region. This cluster was one of three clusters, which the Saar administration founded to overcome the economic depression. The two others were the automotive and the informatics cluster. In the 1980s, all three clusters appeared to be the rising stars enabling change within the local industry and gave new perspectives for employment[8].

This strategy of the Saar administration started with main investments in the two universities of the Saar region and is trying to win German R&D institutions like the Max-Planck-Society, the Leibniz-Society and last but not least the Fraunhofer-Society to found an R&D institute for a special R&D question related to the three clusters. The universities specialized in the already mentioned subjects to create a cluster of knowledge together with the R&D institutions[9]. In cooperation with the local and foreign industry new business areas were developed, so that the Saar region became the most dynamic federal state of Germany in terms of growth and innovations in the years 2000 to 2002 and again[10] in 2006.

In this context of creating new fields of interest, the Fraunhofer-IBMT was founded in 1987 as a spin-off of another Fraunhofer-Institute for Non-Destructive Testing (IZFP) located in Saarbrücken. By founding the IBMT, the Fraunhofer Society's aim was to develop new medical devices in cooperation with the university.

3. Founding of the Fraunhofer-Institute for Biomedical Engineering

The Fraunhofer-Society (German: Fraunhofer-Gesellschaft) is a German research organization for applied research, which was founded in 1948. By developing technological innovations and novel systems solutions for their customers, the Fraunhofer Institutes help to reinforce the competitive strength of the economy in their region, throughout Germany and in Europe. Their research activities are aimed at promoting the economic development of our industrial society, with particular regard to social welfare and environmental compatibility. The Fraunhofer Society holds 60 institutes spread throughout Germany, each focusing on different fields of applied science. It employs over 17.000 people, mainly scientists and engineers, with an annual research budget of about €1.5 billion.[11]

The non-profit Fraunhofer-Society has a very special business model.[12] The society with all its institutes is awarded 30% of its budget from the German state. This part of the budget is used to finance main investments in building and equipment. All operational costs – the remaining 70% of the budget – have to be covered by R&D-projects, which have to be acquired by the researchers themselves. That means that the researchers are doing contract research for third parties. Main clients of the society are the industry with their applied R&D questions as well as the European and national administration with their R&D programs.

The Fraunhofer Institute for Biomedical Engineering (IBMT) is one of the 60 institutes of the Fraunhofer Society and founding member of the Life Science Alliance of the Fraunhofer-Society. The

[8] Arbeitskammer des Saarlandes (1998), p 46 f.
[9] Hönn (1996), p 26.
[10] Methfessel, (2006).
[11] www.fraunhofer.de.
[12] Rüdiger (2002), p 403 f.

IBMT mainly concentrates on the development of technology in the biomedical sector. The IBMT offers solutions in the areas of biomedical and medical engineering, laser medicine, biotechnology, health telematics, environmental control systems, laboratory development, cryo technology, material testing, home systems, air quality control in homes and cars, security systems as well as industrial process automation and in-line/on-line process control, in particular for the food, chemical and pharmaceutical industry.

From its beginning, this institute grew continuously in its budget volume and staff. This growth was only possible by discovering and investing in new areas of interest, like the area of cryotechnology in the year 2002 (see Fig. 1). About 31 % of this budget is generated with industrial project partners. This last figure shows the importance of cooperation with the industry to enhance the technology transfer from academia to commercial applications.

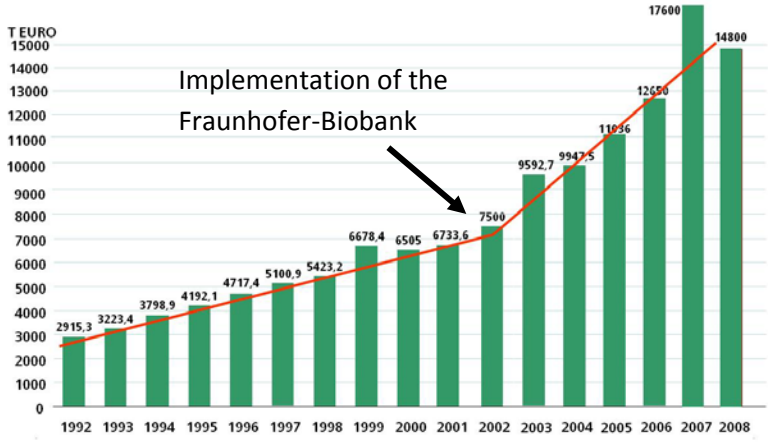

Fig.1: Development of the IBMT-Budget from 1992 to 2008. The effect of the implementation of the biobank can be seen in the change of the line indicating the budget growth of the IBMT[13].

In 1987, the IBMT started operating with three employees in the ultrasound field of R&D. Today, the IBMT has 230 employees at three locations with 40 R&D-groups. Each of these groups specializes in a certain research area. Six of these groups including the Fraunhofer-Bioarchive are correlated to the department Biophysics & Cryotechnology of Prof. Zimmermann.

4. Fraunhofer-Bioarchive and related R&D-Groups

The Fraunhofer-Bioarchive was founded under the old name EuroCryo Saar Biobank in 2002 as a demonstration biobank for new technologies in the biobanking area. Cryopreservation and biobanking themselves were nothing new when the EuroCryo Saar was founded, as these techniques were used for over 50 years in the reproduction medicine to store, e.g., sperm. The way of storing samples didn't change since then and wasn't adequate any more for all developments done in the biotechnology sectors in the past 10 to 15 years with the rapidly increasing amount and variety of samples produced. In 2008, the IBMT-biobank became the storage unit for the whole Fraunhofer-Society and changed its name to Fraunhofer-Bioarchive. The Fraunhofer-Bioarchive is today a

[13] Fraunhofer IBMT 2009.

biobank-holding for many different biobanks at the Fraunhofer-IBMT. So, the EuroCryo Saar Biobank is now one unit of the Fraunhofer-Bioarchive.
The question is, why Fraunhofer-IBMT started running a biobank? In 2001, after having been nominated as new director of the IBMT, Prof. Günter R. Fuhr started with a new R&D group working in the field of cryobiology and cryotechnology. The problem to be tackled in this new group was how to manage this increasing amount of samples, how to connect the data of a sample with the sample by using deep temperature electronics and how to guarantee a 100% safe identification of a sample. This technology part was combined with a biology part, which e.g., developed new cryopreservation protocols. The experience of the biology group was the basis for another new group in IBMT, which started in 2005 doing stem cell research. All these technological and biological R&D approaches could only be done in an environment in which experience in storing samples had been gained and the technology could directly be tested.

To measure the impact of the Fraunhofer-Bioarchive biobank, the environment of this biobank in form of the connected R&D groups has to be included. The connection of the biobank and the related R&D groups is shown in Fig. 2. As the Fraunhofer-Bioarchive biobank acts as an individual research group in the environment of IBMT, this case study allows a separated view of the biobank activities and the R&D activities using the biobank. This study starts with the biobank itself and will continue with the R&D activities using the biobank.

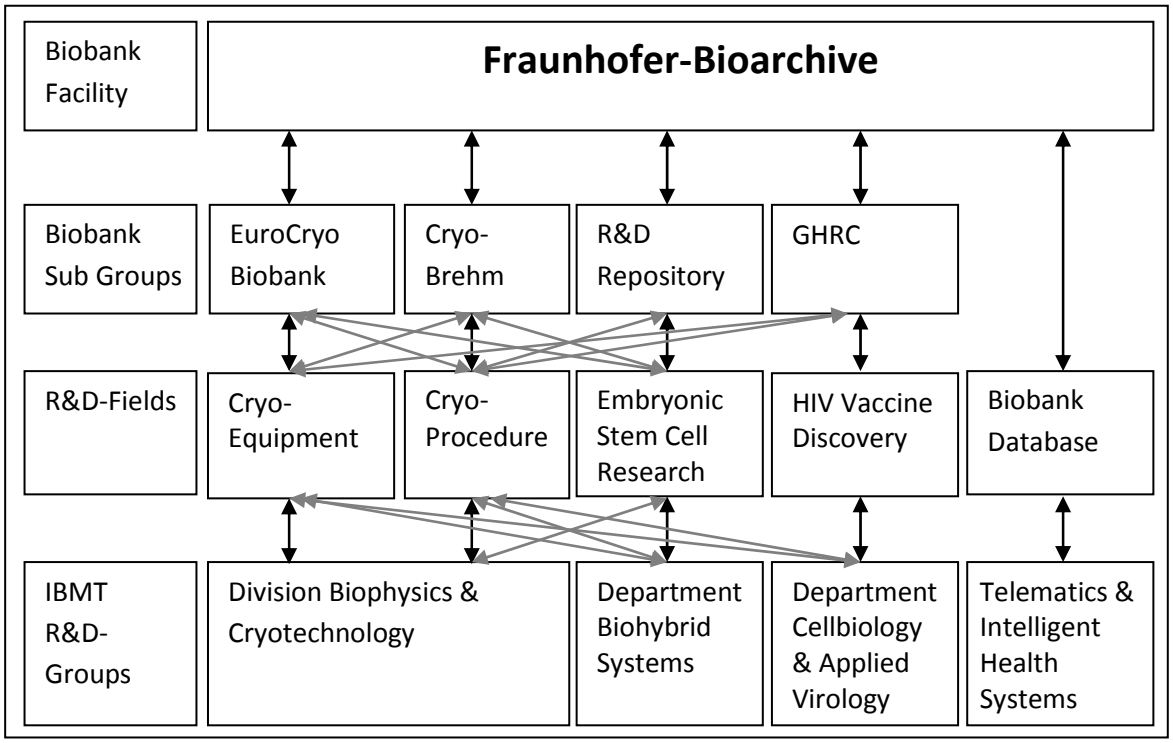

Fig. 2: Chart of the Fraunhofer-Bioarchive and its subgroup-biobanks as well as the involvement of a selected number of R&D fields and R&D groups using the Fraunhofer-Bioarchive.

4.1. Fraunhofer-Bioarchive

In the introduction of this chapter the goal of this biobank was illustrated. Until today, progress in cryotechnology and testing of new cryodevices is one of the major tasks of the biobank. Over the years storing samples gained a greater importance. EuroCryo developed itself to a service provider

for storing samples for clients. These clients are R&D institutions, hospitals and the industry. The kind of samples are:

- Stem Cells
- DNA/RNA
- Animal samples stored e.g., in the project CryoBrehm
- Back up-Samples

Today, over 250.000 samples from clients are stored in this biobank. Most of the samples are for research purposes, but more and more samples for therapeutic purposes are stored. As a service provider for storage, EuroCryo has no scope for decision-making if samples are shared with the international research community. That's why no direct information about the stored samples can be given and no impact on research results can be measured by using these samples in biotechnology, medicine or pharmaceutical industry. Stored tissue samples had been reimplanted twice into a patient within the scope of a therapy by a local hospital.

From 2002 up to now 2.3 Mio € had been invested to build up the building and the first storage capacity. The operational budget started with 270 T€ in 2002 and grew up to 870 T€ in 2008 (see Fig. 3). The number of all involved employees grew to 12 today. This is the staff needed to run the biobank as a service provider and to do basic research in cryobanking.

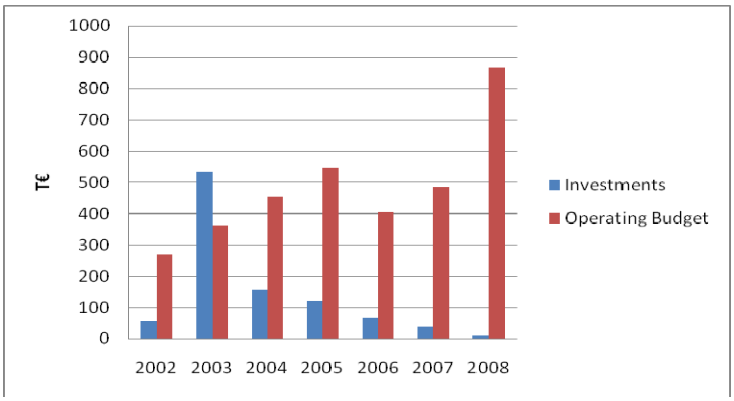

Fig. 3: Development of the Fraunhofer-Bioarchive operating budget and investments.

The Fraunhofer-Bioarchive biobank closely cooperates with the following institutions:

- Alliance of German Cryobanks (GDK)

In 2005, some research, clinical and industrial cryo-banks formed a voluntary network, the Alliance of German Cryobanks (Gemeinschaft Deutscher Kryobanken (GDK)). The common aim is it to enhance transparency to the customer through registering cryo-banks and presenting their individual key aspects of activity. The development of common safety measures, standardized procedures and the dissemination of knowledge should ensure the highest standards of science, technology and therapeutic use. Existing collections are scientific goldmines and, today, each exists in isolation. The Alliance of German Cryobanks (GDK) is necessary to safeguard these national resources, as existing cryobanks can only guard against a disaster by using a network like the GDK. In case of a disaster, time-limited outsourcing of samples at a safe cryobank partner is possible. The GDK is an association, which can stimulate scientific, technical and organizational cooperation and build up a virtual cryo-bank in Germany.

- Saarland University as well as the Saarland University Hospital

The management personnel of IBMT is strongly connected to the Saarland University, as e.g. Prof. Fuhr and Prof. Zimmermann both hold a professorship at the Saarland University. Prof. Fuhr is a member of the medical faculty and Chair of Biotechnology and Medical Engineering. Prof. Zimmermann is member of the faculty of Physics & Mechtronics and professorship of Cryobiophysics and Cellular Bioinformatics. Through this connection, joint R&D projects have been realized and both sides benefit in their R&D-quality and student education.

- Zentrale für Produktivität und Technologie Saar e. V. (ZPT)[14]

The ZPT offers a wide range of services to support enterprises from the Saarland in promoting their competitiveness and innovation as well as tapping new sales market. Under the ZPT's roof, you will find an enterprise europe network, the Innovation Relay Centre for Research and Technology as well as a Patent Information Centre. The comprehensive services the ZPT provides for the Saarland Industry in terms of advice, training, transfer of technology and promotion of innovation, are mainly aimed at small and medium-sized enterprises to help them improve their competitiveness and develop new products and processes.

4.2. Division Biophysics & Cryotechnology

This division started in 2001 with four employees under the direction of Prof. Dr. Heiko Zimmermann[15] to develop new devices in cryotechnology. Shortly after this group had been founded it was supported by the German Federal Ministry of Education and Research (BMBF) by financing a research talent group for more than five years. This initial support was necessary to gain essential experience in this field by doing basic research. Over the years additional projects were acquired, so that the group grew from 4 to 35 employees today (see Fig 4.), which are divided into six R&D groups today. The budget of this division is about 3.5 Mio € today.

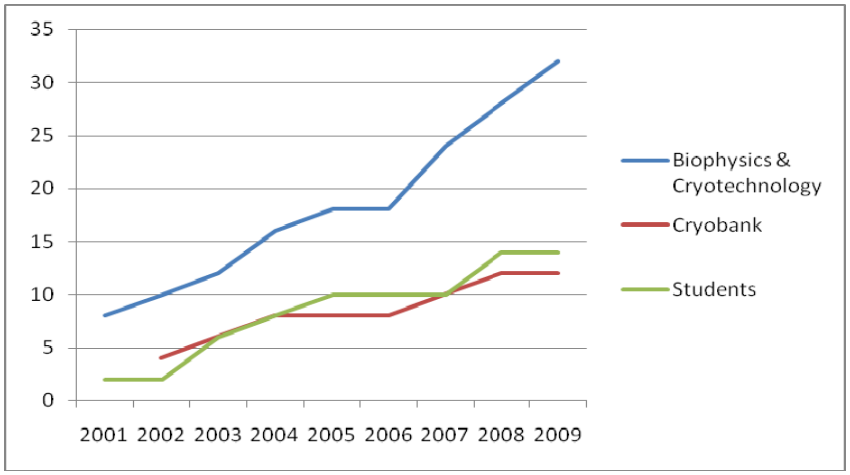

Fig. 4: Development of the number of employees in the division Biophysics & Cryotechnology as well as the Cryobank.

The development of the budget and investment of this division can be seen in Fig 5.

[14] www.zpt.de.

[15] BBMRI Representative for the Fraunhofer-Society.

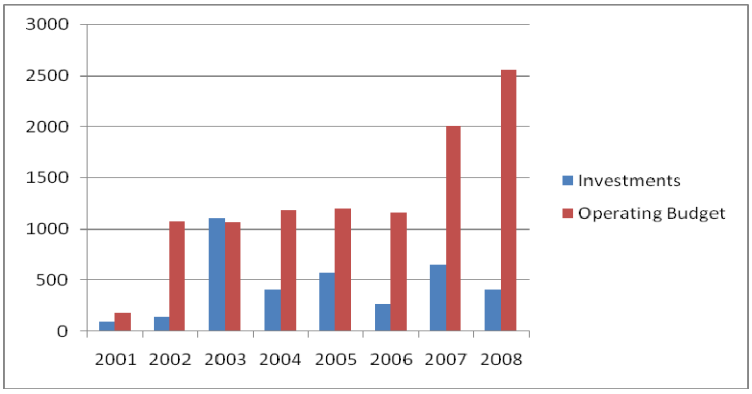

Fig. 5: Development of the operating budget and investments of the division for Biophysics & Cryotechnology.

Major projects, in which this department was involved, will be shown in chapter 4.5. The quantitative output of the R&D work done can be seen in Fig. 6, in which the number of new publications and patents listed per year are shown. Next to the number of publications four persons finished their PhD work in the past eight years. Especially the number of patents is very important to measure the economical impact, as already three spin-offs use this knowledge saved by these patents for their business. This impact is described later in chapter 7 of this case study.

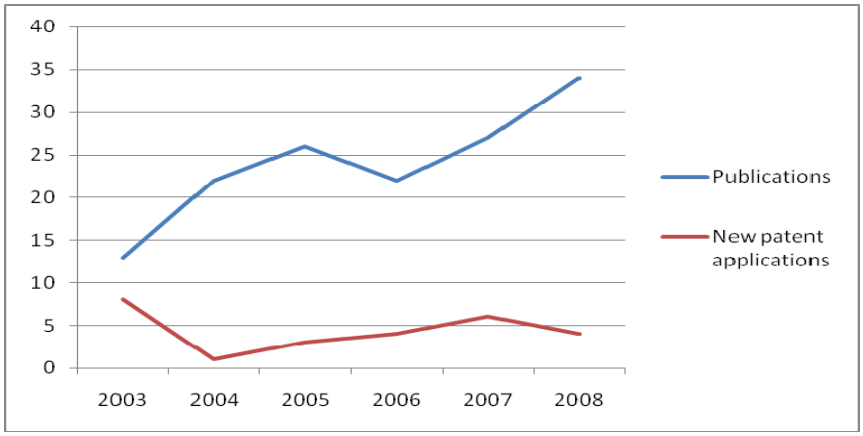

Fig. 6: Development of the numbers of publications and patents of the division Biophysics & Cryotechnology.

4.3. Global HIV Vaccine Research Cryorepository - GHRC

On the basis of the experience gained by running the EuroCryo biobank and offering cutting edge biobank technology, the Bill & Melinda Gates foundation awarded the IBMT by commissioning to build up a cryorepository for the global HIV vaccine research of the CAVD consortium[16] in 2007. The GHRC group is an R&D group of the department Cell Biology & Applied Virology with their own biobank capacity under the surveillance of the cryobank group at IBMT.

[16] CAVD: Collaboration for AIDS Vaccine Discovery.

4.3.1 Goal of GHRC

The goal of the Global HIV Vaccine Research Cryorepository (GHRC) is to establish the first large-scale centralized biobank (also termed "central cryostorage facility") for low-temperature storage of HIV-1 related specimens and reagents providing standardized access to these important samples. Additionally, clinical samples from selected primary sites relevant to potential vaccine trial sites will be collected and offered by the HIV cryobank.

The GHRC network develops novel procedures for optimized sample processing, cryopreservation and storage of clinical specimens from regional centers, or for reagents generated elsewhere in the CAVD consortium. In addition, it provides training and capacity building for regional centers and technology transfer to the CAVD consortium. The participants generated key information about these reagents, as well as all new technology developed by this network is made available for HIV/AIDS vaccine development throughout the whole Global HIV/AIDS Vaccine Enterprise. This will help to insure that the vaccine candidates will be genetically, immunologically and biologically relevant.

After a successful construction phase in the first three years, in August 2009 the Bill and Melinda Gates Foundation commissioned the IBMT for the second project phase for two more years.

4.3.2 GHRC Services

GHRC provides three kinds of services to the scientific community which are correlated to the biobank.

HIV Cryobank
The HIV cryobank stores all kind of samples, also infected samples in a special storage place adhering to the regulations of a S3/L3 laboratory. E.g., the samples come as a back-up from the vaccine research groups. Others are collected by the GHRC group, which could be e.g., blood samples from early infected persons from all over the world in cooperation with primary sites.

Pseudovirus production
For the CAVD consortium pseudo-viruses are produced which are necessary for testing new vaccines. For this production, a big stock of different pseudoviruses is needed, which is stored in the GHRC biobank.

Research & Development
The GHRC-Group will continue its research in the two already mentioned areas and will look for new areas of research. As the GHRC group is part of the Fraunhofer Society, this group will at this point enter the Fraunhofer business model of being a contract research institution.

4.3.3 Investment and Running Costs

The GHRC project started in 2007 with the construction of an S3/L3 laboratory and storage place. This investment in building capacity and equipment cost about 3.3 Mio €, which had been financed by the Saarland's government administration and the Fraunhofer Society. The operating costs of this

group of about 1.7 Mio € per year are financed by the Bill & Melinda Gates foundation. All services offered by the GHRC group are free of charge for members of the CAVD consortium. The costs of all included partners like other universities and primary sites are also about one Mio. € per year.

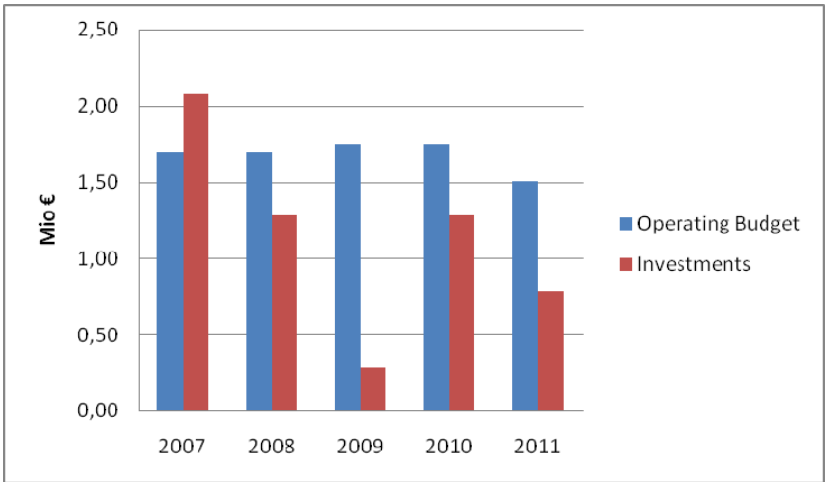

Fig. 7: Budget of the GHRC-group divided into operating budget und investments financed by the Bill and Melinda Gates foundation as well as other project partners.

4.3.4 Results

Since its beginning, the GHRC group published 15 scientific (peer-reviewed) articles and stored about 215 kinds of samples in their biobank. The challenge was to investigate the corrected storage protocol of each of these samples in this short period of time. Today the group is developing a fully automated pseudovirus production to enhance the quality of their products.

4.4. Departments of Fraunhofer-IBMT using the Fraunhofer-Bioarchive

4.4.1 Department Biohybrid Systems

The department Biohybrid Systems is representing a collaborating network in the R&D field of biotechnology, biohybrid micro- and nanotechnology. An interdisciplinary acting team of molecular and cellular biologists, pharmacists, biophysicists and engineers develop novel modules for automation, parallelization and synchronization of analytical processes in life sciences at the interface of biotechnology, microsystems and sensor systems. The groups Cell Based Sensors & Biomonitoring and Molecular Cell & Tissue Engineering with its resources Experimental Cytogenetics and Biocompatibility realize the development of cell and tissue based biosensors, drug delivery systems, microimplants, transplants and gene therapies for implementation in neuroscience, cardio-vascular and cancer research. The department focuses on biomolecular R&D, consulting and the interface of a biotechnological network providing novel, innovative, biohybrid modules (biohybrid technology; e.g., screening and diagnostic modules). All used cells lines are stored in the Fraunhofer-Bioarchive.

4.4.2. Department: Telematics & Intelligent Health Systems

The Department of Telematics & Intelligent Health Systems provides solutions for electronic communication in health care, personal care and the networked medical research. For the

networked clinical research the department develops the electronic infrastructure and respective tools. Examples are its GRID-enabled, ontology-based management system for multicenter clinical trials ObTIMa, which facilitates the integration of study data. This project will be presented in the next chapter 4.5. One of the major goals of this department in the past eight years was the development of the EuroCryoDB, an innovative sample logistics system for biobanks.

4.5. Major R&D-projects with the participation of the Fraunhofer-Bioarchive

In this chapter an overview of major R&D-projects in the past five years are given which were enabled by IBMT's own biobank.

- CellPROM

The main focus of the research project CellPROM was in developing new technologies for the automated and defined differentiation of stem cells. Funded by the EC with 16.7 M €, 27 partners of 12 European countries successfully collaborated for 4 years in the field of converging nano- and bio technology. Appropriate reference cell models have been identified as one main pillar of the project in order to reach quantitative and comparable results. They have to provide highly significant differentiation results and high usability to be established at laboratories with different expertise and equipment.

The role of the Fraunhofer IBMT (3.4 M€ EC funding) was scientific coordination and technological integration and more than 20 scientists made profound contributions to the project. Among other activities, the administration and distribution of cryopreserved cellular samples among the partners has been managed centrally by the IBMT together with EuroCryo. The glandular stem cells as isolated by Fraunhofer EMB in Lübeck and characterized together with IBMT have been one of the key cell models. Cells have been proliferated based on specific material transfer agreements among the partners and reference samples have been collected at EuroCryo enabling complete traceability.

Technologically the cell bank standards have been important boundary conditions for the CellPROM development. The prototypes have been realized to comply with the interfaces and standard substrates of the cryobank. Software interfaces with the data structures of EuroCryo are foreseen and can be implemented on demand for successive research projects and in the framework of collaborations with industry.

- ACGT- Advancing Clinico Genomic Trials on Cancer

ACGT is a European Union co-funded project aiming at developing open-source, semantic and grid-based technologies in support of post genomic clinical trials in cancer research. It addresses clinicians', bio-researchers' as well as software developers' needs, providing an open platform where novel and powerful services can be offered and used by practitioners in the field.[17] IBMT's job in this project was with their biobank experience to develop Biomedical data analysis and knowledge discovery (cellular level) Data Mining as well as a knowledge discovery-information systems.

In this EU-project 25 partners were involved and the project had a volume of 10 Mio € for a period of four years. The Department of Telematics & Intelligent Health Systems employed four persons in this project and received a budget of 650.000,- € for their work.

[17] http://eu-acgt.org/.

- CRYSTAL

The aim of CRYSTAL is to develop tools and procedures to enable cryopreservation of different stem cell types for generation of sufficient numbers of high-quality cells suitable for safe human stem cell therapy. To this end, CRYSTAL will carry out focused research on methods, tools and protocols required for optimal cryopreservation and banking of stem cells. Five stem cell research laboratories providing four different sources of adult (from cord blood, bone marrow and placenta) and human embryonic stem cells have teamed with two partners specializing in applied banking and fundamental cryobiological research. Thus CRYSTAL is in a position to resolve existing problems in an integrated, systematic approach and to provide standardized, reproducible methods and tools to advance therapeutic stem cell research in Europe.[18]

The Fraunhofer technology enables the study of critical thermodynamical parameters which are important in banking methodology. These technologies are realized and evaluated in the IBMT-owned cryo research bank. Optimization of cryopreservation protocols are only possible if crystallization and phase transitions while freezing and thawing are fully explored. This will be obtained by using cryomicroscopy and electron microscopy-based methods. First experiments with a new, massively parallelized bio-imaging-system and the technique of surface based freezing already achieved promising results.

CRYSTAL started in February 2007 and will deliver a set of validated and optimized protocols within three years. It is funded with 2.400.000 € from the Community´s Sixth Framework Programme of the European Commission, thereof 251.971,91 € for IBMT.

- µAirjet

This project used the concept of encapsulated-cell therapy for the production of long-term functional transplants by using alginate. This biomaterial is used for immuno isolation of allogeneic and xenogeneic cells and tissues. In this case for Langerhans islets for diabetic therapies. The goal was to get a clinical application for this disease, which requires validated technology for long-term cryopreservation of encapsulated cells to maintaining a product inventory in order to meet end-user demands. As shown here these demands could be met by the development of novel, validated technologies for production of transplantation-grade alginate and microcapsule engineering and storage.

In this project six partners were involved during the period of four years. The total budget for all partners was up to 3 Mio €.

- Staphylococcus: Infection Biology and Epidemiology of Staphylococci and Staphylococcal Diseases in sub-Saharan Africa

Staphylococcus aureus continues to be a major pathogen causing invasive disease with high associated morbidity and mortality. The pathogen has acquired resistance against virtually all antimicrobials available, and in the recent years, the worldwide emergence of multiresistant S. aureus clones in hospitals and communities has spurred significant concern for local and global health initiatives. In contrast to the 'classical' tropical diseases, however, almost nothing is known on the strain phylogeny and prevalence, disease type, and associated morbidity and mortality of infections due to S. aureus in most African countries. This project organized by four sub-Saharan African and five German groups thus focuses on a registry of S. aureus community-acquired disease, on the isolation and characterization of clinical isolates with advanced methods for typing and

[18] www.crystal-eu.org.

virulence factor expression, and on GLP-conform long-term isolate handling and scientific database exchange.
All strains of ascertained cases will be processed, stored, frozen, shipped, and analyzed according to Good Laboratory Practice procedures in accordance with respective Ethic regulations of the African countries and of Germany. Long-term specimen deposition and handling will be performed by the Fraunhofer-Bioarchive and the GHRC group in the biosafety level (BSL) 3 facility.
The total budget of this German Research Foundation project (DFG) is for all partners about 1.5 Mio € for a period of three years. The facilities in Saarland gets about 250.000,- € of this budget.

- µCryoLab
It is the goal of the project µCryoLab to develop a system platform for the cryo-storage of cell aggregates for medical diagnostics and analytics. Cryo-storage means freezing, storing (< -130° C) and controlled defrosting of cells while preserving their vitality as well as their functionality. The platform will be mainly used for development of drugs against diabetes and tumor banking. In this project five academic and six industrial partners were involved. Project costs: € 3.9 million. Duration: from September 2006 to August 2009

- CRIP
In 2007, the Central Research Infrastructure for molecular Pathology (CRIP; www.crip.fraunhofer.de) was transferred to IBMT. CRIP had been founded 2006 in public-private partnership with an overall funding of 1 Mio. € from the former Förderverein Humangenomforschung, BMBF and seven pharmaceutical companies[19]. Being well-known for its competence in biobanking and cryo-biology, IBMT was able to acquire the CRIP consortium comprising Charité Universitätsmedizin Berlin, Medizinische Universität Graz and Klinikum rechts der Isar / TU Munich. CRIP partners rank amongst Europe's six largest human tissue banks and expect to cross-fertilize leading expertise in pathology and in cryo-preservation of healthy and diseased human biospecimens by collaborating with IBMT.

With the acquisition of CRIP and the participation in BBMRI (see below), IBMT made the strategic decision to support and co-develop biobanking infrastructures (like CRIP and BBMRI) as basis necessary for further R & D in medicine and biology.

- BBMRI
IBMT participates in the preparation for the construction of a pan-European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) for biomedical and biological research in Europe and worldwide. This infrastructure builds on existing infrastructures, resources and technologies, specifically complemented with innovative components and properly embedded into European ethical, legal and social frameworks. This infrastructure is part of the ESFRI program of the European Commission. [20] In this context this case study is performed.

[19] Altana, Bayer, Boehringer Ingelheim, Merck, Sanofi-Aventis, Schering, Roche.
[20] www.bbmri.eu.

5 Industry and Partners to run a biobank

To run a biobank like the EuroCryo Saar biobank or the GHRC biobank, investments in building and equipment have to be done. Later on, operating costs occur. Both are part of the chapter one describing direct effects on the economy. This chapter will describe the partners which are necessary to run a biobank in the construction phase and in the operational phase.

5.1 Construction Phase

For the EuroCryo Saar biobank an old building was reconstructed and adapted to the needs of a biobank. This first part of process cost about 1.5 Mio €, which was mainly financed by the Saarland administration. For this process mainly engineers, architects and different construction companies were involved. This part is equivalent to any construction done.
The second part is in regards to the investments of equipment. The main equipment are the cryotanks with all the supply equipment. For this part, IBMT invested 500 T€ for both. Next, investments in laboratories are necessary. The EuroCryo Saar lab equipments cost about 300 T€.

5.2 Operational Phase

The main things needed to run a biobank are energy in form of liquid nitrogen and electricity. The bigger a biobank gets, the cheaper the costs per sample are, since the biobank gets a quantity discount. The same thing is true for lab material, if a bigger quantity is needed.
The operating costs of EuroCryo Saar are about 100 T€ per year. In this amount, all maintenance services are included. Additionally, the laboratory costs for five persons have to be added.

If a biobank wants to offer their storing services at a cheap price, they should be interested in achieving a fixed cost degression by the biobank size and the variety of services offered in their laboratories. The more material the biobank needs the bigger the discounts get. This major impact biobanks get with the importance they get today, that the equipment and material needed gets cheaper as bigger the biobank market gets.

This study tried to point out, the effect of these equipment investments to the manufacturer as well as the operating supplier or the size of this industry. The problem is that all partners to run a biobank are integrated in big multinational companies like, e.g., Linde AG or AirLiquide AG. The part of the return of these companies made by the biobanks couldn't be analyzed, so that no direct effect could be measured. But the fact that these companies engage themselves in this market is a sign, that the market is interesting for them and they see a future need of the equipment offered by them.

5.3 Infrastructure development of the biobank environment

In 2009, the Fraunhofer-IBMT achieved by the Ministry of Economy of the Saarland administration and the EU a grant of 12 Mio € for the development of the location Sulzbach. The used square meter will rise from 2.500 m2 to 6.000 m2 in 2013 (see Fig. 8). The supplementary space will be used for new laboratories and storage space as well as for biotech-companies, like e.g. Diagnostic Laboratories or a research company which works with stem cells. The construction starts in the beginning of 2010.

Fig. 8: Floorplan of the Sulzbach-location. On the right hand site the already used space with the HIV-Kryobank and the EuroCryo Biobank is indicated (green background). On the left hand site the new space is indicated with the pink background.

6 Spin-offs from the biobank

This is a documentation about the Spin-offs, which are the results of the IBMT basic research in the cryotechnology sector. All three Spin-offs mentioned together represent the entire storage process for the new storage generation.

a) Askion

Askion was formally a company of the AGFA Gevaert AG and produced analog photolab equipment (until 1995) and after 1996 equipment for digital printing systems. In 2005, Askion was founded and they started to develop and produce devices in the following three areas:

- Medical Equipment and Bioanalytics
- Photolab Equipment
- Optoelectronic Modules and Subassemblies

Part of the Medical Equipment section was the idea for Askion to start in the cryo-technology sector. In 2006 a cooperation between Askion and the Fraunhofer-IBMT started. They licensed two patent families from IBMT to produce cryo-workbenches and hoodsystems. Both products will be available since summer of 2009.

b) Perma Cryo Technology

Perma Cryo Technology was founded in 2007 to produce cryovials with memory chips and RFID for supplementary identification of a sample, which is another Fraunhofer IBMT development. All GHRC-samples are being stored in these cryovials. Perma Cryo Technology is supported by a

venture capital company, who financed most of the necessary investment in a clean room and automatic production line. A certification for the cryovial as a medical device is expected for the second half-year.

c) Soventec

Soventec is a software engineering company located in Schleswig. This company started in 1999 as engineering company Marquardt & Diercks. At this time, they started a cooperation with Evotec AG and Evotec Technologies GmbH in Hamburg to develop LIMS-Systems (Laboratory Information Management System; LIMS). In 2006 they started a software project in cooperation with the IBMT and Evotec Technologies GmbH in the area of AIDS research. The idea of this software project started in 2003 in a cooperation between Evotec Technologies GmbH and IBMT. Since 2008, Soventec sets new strategic focuses on Life Sciences and they started to distribute the software "ChameleonLab", which is the result of this cooperation between IBMT and Soventec. ChameleonLab is a Laboratory Information Management System (LIMS), which guides a sample through the lab process and documents automatically all accruing data.

d) Possible future spin-off

It is planned to found a commercial biobank by the end of 2009. This biobank will use Fraunhofer-IBMT storage capacity to provide a complete storage service.

Since all three existing spin-offs were founded recently, an economic evaluation of the effect of these spin-offs is not yet possible. The fact that three companies feel motivated by an interesting market is a strong indicator for the biobank's effect on economy.

7 Conclusion

The description of the Fraunhofer-Bioarchive with the units GHRC and EuroCryo biobank demonstrate that a biobank can't be evaluated as a simple unit, but always has to be seen in combination with the research done in cooperation with this biobank. The biobank itself is only a tool for the medical and pharmaceutical research or for the storage of samples for therapeutic purposes like stem cells or tissue. Without the research done in cooperation with a biobank it would be useless. The value of a biobank is based on the kind of samples stored for a specific R&D or therapeutic purpose. To identify the impact of a biobank this has to be seen as the most important effect.
In this specific case, the economical impact could be shown in a rising number of employees in the biobank and the connected R&D groups as well as in the three spin-offs raised from the research done. The public investment in this biobank had a positive response for the Saar region, since the output of IBMT measured in patent, publication, education and spin-offs is high. The operational budget of the division Biophysics and Cryotechnology, one the main user of the Fraunhofer-Bioarchive, grew from 200 T € in the year 2001 up to 3.5 Mio € in the year 2009. The expectations of the public hand in this flied of biobanking is very high, as they will invest 12 Mio € in the infrastructure of the Sulzbach location in the next three years. And as over 20 patents of the Fraunhofer cryotechnology-family are licensed to companies, also the industry has positive expectation in the biobank sector.

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