Biobanks in Healthcare

From the Collection of Biological Samples to Digital Health

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Paul Hofman

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Series Editor
Nicole Arrighi

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First published 2024 in Great Britain and the United States by ISTE Ltd and John Wiley & Sons, Inc.

ISTE Ltd
27-37 St George's Road
London SW19 4EU
UK

www.iste.co.uk

John Wiley & Sons, Inc.
111 River Street
Hoboken, NJ 07030
USA

www.wiley.com

Library of Congress Control Number: 2024943915

British Library Cataloguing-in-Publication Data
A CIP record for this book is available from the British Library
ISBN 978-1-78630-023-2

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Foreword

If we go back as far as possible in the history of humanity, it is possible that the first gesture of the first researcher was to collect objects taken from nature. Gathering, classifying and preserving these objects in order to observe and study them were probably at the origin of the first scientific approach of our ancestor, gifted with consciousness and abstraction, and the irrepressible desire to know the world. More recently, in the 17th-century curiosity cabinets, it was a question of enthralling the visitor, but also of affirming one's rank and power. European kings understood this well when they created museums and other royal gardens that brought together collections of extraordinary animals and plants taken from the confines of their kingdom. These collections were at the origin of the change in our knowledge of life sciences. Just think of Buffon's monumental *Natural History* during the Enlightenment!

Human biological collections were established with the advent of hospitals in the 19th century, which became not only places of charity but also establishments for care and for the transmission of knowledge. In order to describe and try to understand diseases or congenital anomalies, it was necessary to collect, preserve and classify affected organs and fragments of biological tissues. Thus, the famous anatomical collections of Jean-Martin Charcot at the Salpêtrière Hospital, of Marc-Antoine Petit, the first surgeon-major of the Hôtel-Dieu Hospital in Lyon, and of the medical schools of Montpellier and Strasbourg, were created. This period also gave birth to anatomopathology, the study and classification of the macroscopic and microscopic lesions of injured tissues, with Jean-Baptiste Morgagni in Padua, Rudolf Virchow in Berlin and Jean Lobstein in Strasbourg. Significant collections were thus accumulated over decades in accordance to

the passions of these physician-researchers; collections that most often ended up in the dark basements of hospitals some time after the disappearance of their creators, closely followed by that of the notebook blackened with cabalistic annotations understandable only by its author.

At the dawn of the 21st century, with the development of high-throughput analysis techniques, access to quality biological samples became a major issue. Indeed, it quickly became apparent that the growing industrialization of research in biology and health required that biological objects be of impeccable quality and provided with reliable annotations for analysis. The first databases resulting from the exploitation of human samples were often marred by errors and generated erroneous scientific information. Another major issue was that of economic value. The development of biotechnologies, the rise of biological drugs and the identification of biomarkers associated with molecular classifications of tissue lesions made it essential to have orderly access to human biological samples, which had become precious and rare.

France was a pioneer at the international level in organizing and defining the missions of biological resource centers, or biobanks, new biology–health infrastructures designed to collect, store and make available human biological samples. It was also the first country to establish a standard for the operation of biobanks, which was recently converted into an ISO standard, and to establish ethical rules for access to biological samples from the human body, which are included in the Public Health Code. The normative progress has been considerable, the scientific production improved and the services rendered to the advancement of medicine indisputable. Functional biobanks today are those that combine quality assurance of biological samples and their annotations, technical and scientific expertise, transparency of governance, innovation, training and integration into the local, national and international research community.

More than 20 years after their creation, the biobanking project is not yet complete [CLÉ 19]. The business model is still unstable due to the lack of a real national strategy to structure and finance a national network of biobanks based on independent peer evaluations. In many cases, stocks are thus increasing indefinitely, in the hope of a hypothetical valorization. Moreover, access to epidemiological, bioclinical and genomic data associated

with collections remains difficult, in the absence of harmonization of hospital information systems and a real willingness to share these data. Despite important advances at the European level, the legislative and regulatory framework is slow to adapt to the evolution of biobanks and the constitution of large cohorts that involve the storage of biological samples and associated data for future research.

Biobanks are at a crossroads. Like all essential infrastructures in biology and health, they must adapt to advances in research and technology. In the digital era and with the production of Big Data by practically all laboratories that have access to very high-throughput and low-cost technological platforms, biobanks are becoming the guarantors of the reproducibility of experiments and of the overall quality of research in biology and health. They are expanding their scope of intervention, automating processes and exploring new analysis techniques with precious samples, while preserving them for future generations. They are diversifying their storage capacities; in addition to information on biological objects, epidemiological, clinical, biological, genomic and imaging data are being included in their computer bases. Biobanks, by their very nature, are interface infrastructures, which erase the artificial divide between care and research activities. A striking example is their central role in medical genomics, which relies on the intensive deployment of digital technology to produce information that is simultaneously useful for patient care and for researchers studying disease.

This book reviews the current state of biobanking. It explores new avenues, in particular the change linked to the massive deployment of digital health and precision medicine. The authors show that the future of biology and health requires the deployment of biobanks in fields that have yet to be explored, at the forefront of the extraordinary adventure of 21st-century research.

Bruno CLÉMENT
Director of research at Inserm
Institute of Nutrition, Metabolisms and Cancer
CRB Santé Biological Resource Center of Rennes University Hospital

Acknowledgments

This book is the result of collegial research that contributed to the creation of the Master of Science in Biobanking and Complex Data Management at Côte d'Azur University. The authors would like to thank all the experts from the various European and North American countries who have contributed to and continue to enrich the training program for future biobank managers.

Dr. Bruno Clément has given us the honor of writing the foreword to this book. He is the director of the Inserm U991 unit "Liver, Metabolism and Cancer" at the Pontchaillou Hospital of the Rennes University Hospital. Always extremely involved in action in favor of innovations in biotechnology, he strongly participated in the creation of the national project for biobanks and has played an essential role in the IBISA infrastructures (platforms of resources in biology, health and agronomy open to the scientific community).

Dr. Robert Hewitt, founder of the Biosample Hub and co-founder of the European, Middle Eastern and African Society for Biopreservation and Biobanking (ESBB), played a central role in the construction of the course by sharing his expertise in biobank management and his experience in the industry. We would like to thank him for his presence at the inauguration of the defense juries for the Master of Science in Biobanking and Complex Data Management at Côte d'Azur University.

Dr. Marius Ilié is a pathologist and a professor in the Faculty of Medicine of Nice and a member of the biobank scientific council of the laboratory of clinical and experimental pathology at Pasteur University Hospital in Nice.

Through his expertise in sample management, he has contributed to numerous publications in biomedical research. He is a member of IRCAN team 4 (Inserm U1081/UMR CNRS 7284).

Dr. Élodie Long-Mira is a physician of molecular and clinical pathologies. Her research activities at the laboratory of clinical and experimental pathology of the Pasteur University Hospital in Nice are focused on lung cancer and melanoma. She is a lecturer at the Faculty of Medicine in Nice and teaches embryology and histology. She is a member of IRCAN team 4 (Inserm U1081/UMR CNRS 7284) and in charge of the melanoma collection at the Nice biobank.

Dr. Giorgio Stanta is Professor of Pathology at the University of Trieste. His major interest is in the application of molecular analysis to formalin-fixed and paraffin-embedded tissue samples. He has demonstrated the importance of pre-analytical conditions and standardization of genomic and proteomic methods. He is an expert of the BBMRI-ERIC network and coordinates the European group IMPACTS Archive Tissues: Improving Molecular Medicine Research and Clinical Practice[1].

Dr. Georges Dagher was the Director of the French Biobank Infrastructure and Director of Research at Inserm (France). In addition to his clinical research activities, he has contributed to the OECD guidelines on good practices for biological resource centers, human biobanks and genetic databases. He participated in the development of the French standard NF S96-900 and its transformation into an international ISO standard for biobanks.

Dr. Kurt Zatloukal is Director of the Austrian Biobanking and Biomolecular Resources Research Infrastructure (BBMRI). He is a pathologist and professor at the Medical University of Graz (Austria) and heads the Christian Doppler Laboratory for biospecimen research and biobanking technologies. As coordinator of the preparatory phase of the BBMRI infrastructure, he is involved in the development of new European standards in the pre-analytical phase of molecular diagnosis of tissue samples.

1 www.impactsnetwork.eu.

Taycir Skhiri is project manager of the FHU OncoAge (University Hospital Federation Oncoage, www.oncoage.org) the goal of which is to share research results and develop innovative solutions in the FHU OncoAge. Converting and applying the results of research requires the transmission of knowledge that meets, among other things, the demand for the professionalization of biobanks.

Dr. Kevin Washetine is a quality engineer in the clinical and experimental pathology laboratory of the Pasteur University Hospital in Nice. He coordinates the implementation of quality procedures. His work has enabled the laboratory to obtain and maintain certification according to the NFS 96-900 standard (quality of biological resource centers) from AFNOR and accreditation by COFRAC according to the ISO 15189 standard for pathology and molecular biology activities.

Zeineb Messaoudi is a quality engineer at the clinical and experimental pathology laboratory of the Pasteur University Hospital in Nice. She is implementing the transition from the NFS 96-900 standard to the international standard for biobanks ISO 20387 (quality management system for all biobanking activities).

Dr. Laurent Counillon is Director of the EUR Life University Research School, the infrastructure that, among other things, pilots the IDEX Masters of Science (initiatives of excellence launched by the French government). These interdisciplinary programs, taught at Côte d'Azur University in English, focus on creating programs of excellence with international visibility.

Dr. Sophie Raisin-Tani is a professor at Côte d'Azur University. Her involvement from the beginning of the project has accelerated the sharing of resources and the opening of the project to the international scene, increasing its attractiveness to students and biobank managers invited to participate in the teaching.

We wish to thank all the members of FHU OncoAge who, thanks to their multiple translational research activities, actively contribute to the influence of the Nice University Hospital biobank (BB-0033-00025).

Introduction

Biobanks in 2022: Why and How?

Research is based on several foundations: fundamental concepts, cellular and animal models, validation of discoveries obtained in laboratories through a "translational" approach and then, depending on the sector of interest, clinical or applied research or research carried out *in silico* using databases. Depending on the research topics, it is necessary to achieve a continuum between the discovery of new cellular mechanisms and an application in the living world, whether it is the plant, microbial or animal and human world.

One of the unavoidable links between basic research and its various applications is the use of different biological resources, whether they come from plants, microbes, animals or healthy or sick human beings [ALD 19, VAU 19]. From time immemorial, researchers have needed to analyze these different biological resources to validate their hypotheses or observations made with cellular models. Several purposes have progressively emerged, such as better understanding of developmental biology or of the mechanisms of cell death, growth or transformation. One of the most successful examples of the use of biological resources is the discovery of biomarkers of human diseases, which can be biomarkers for diagnostic, prognostic or predictive purposes in a therapeutic response [BAR 20, HEW 11]. While the these biological resources were initially used in a poorly controlled manner and without any real established rules, several reflection policies have gradually led to the establishment of a controlled and rigorous operation. Thus, the notion of a *collection* was born, associated with the need to control use and the necessary storage spaces. In recent decades, these different collections have been associated with the creation of *biological resource centers* (BRCs), still