

The Role of Biobanks in the Fight against COVID-19 Pandemic: The Portuguese Response



O Papel dos Biobancos na Luta contra a Pandemia de COVID-19: A Resposta Portuguesa

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INTRODUCTION

The World Health Organisation (WHO) declared COVID-19 as a pandemic on the 11th of March 2020. Soon after, the Coronavirus Global Response¹ was initiated to kick-start the rapid development and deployment of affordable diagnostics, and vaccines against COVID-19. Fundamental preventive measures were developed worldwide to mitigate the spreading of COVID-19, and in Portugal these measures² included early lockdown, the use of face masks and social distancing. However, these measures have led to ongoing dramatic economical, healthcare, and societal consequences.³⁻⁶ In comparison with COVID-19, the swine flu H1N1 pandemic in 2009⁷ was spread even more rapidly. However, it was associated with a much lower infection fatality rate and was less driven by clustering effects and mass gatherings than COVID-19.⁸

As the pandemic emerged all over the world, more research was critically required to better understand the mechanisms of SARS-CoV-2 infection and transmission, to improve treatment protocols and characterization of long-term phenotypes and individual susceptibility. Biobanks have been instrumental in collecting, processing, storing and providing high quality samples and clinical data from symptomatic and asymptomatic patients^{9,10} which are necessary for COVID-19 diagnostic testing and vaccine development, which followed a rigorous legal and ethical framework that have fully respected the privacy of the participat-

ing patients. Such collections have been vital to understand pathogen characteristics associated with virulence, replication and transmission dynamics of the SARS-CoV-2 virus. The knowledge obtained during past outbreaks of other infectious diseases has helped some countries to develop a better strategy for biobanking during the COVID-19 pandemic.¹¹

In this perspective article, we aim to shed light on the Portuguese biobanks experience during the COVID-19 pandemic.

Sample types and biosafety recommendations

All COVID-19 samples should be handled with precaution in accordance with the recommendations and guidelines outlined by the World Health Organization, Public Health England, and the European Centre for Disease Control and Prevention.¹² According to these guidelines, safety measures must be taken when collecting, handling, and storing COVID-19 samples. The handling and processing of these samples should be carried out in laboratories able to handle samples with biosafety level 2 (BSL-2) or higher due to the associated infection risk. The content of the active virus load varies depending on the type of sample collected, for example, samples collected from the upper and lower respiratory tract are considered highly infectious in comparison with whole blood samples and its derivatives.¹³

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A more comprehensive review of the biosafety measures is described in detail by Naeem *et al.*¹⁴

The most common COVID-19 sample types are listed in Table 1 -Type of sample and clinical data collection

The Portuguese response

The National Biobank Infrastructure, Biobanco.pt, created in 2019, is composed of eleven biobanks across Portugal, which are directly linked with hospitals and academic research institutes. Here, we only report on the biobanks that had initiated a COVID-19 collection since the beginning of the pandemic as highlighted in Table 2 - Biobanco.pt members and their respective COVID-19 collections.

The Portuguese biobanks responded to the pandemic by being actively involved with the collection, processing, and storage of COVID-19 samples and worked rapidly to adapt their informed consent to comply with the requirements imposed by the pandemic and their future use in medical research.

Each biobank listed in Table 2 has its own informed consent that was adapted for the COVID-19 collection. The informed consent along with the collection protocol were approved by the institutional ethics committee associated with each biobank and data management and confidentiality were conducted in compliance with the National Commission for Data Protection (CNPD).

COVID-19 challenges: ethical and legal issues for current and future research

The International Society for Biological and Environmental Repositories (ISBER) has defined informed consent as “a process by which a biobank participant freely and voluntarily confirms his/her willingness to participate in the biobank, after having been informed of all aspects of the research or future unspecified research that are relevant to the decision to participate”. Informed consent is documented by means of a written, signed and dated consent

form.¹⁵ In this context, biobanks can either seek consent for a specific study/line of research or often they opt to obtain consent to collect biospecimens and relative data for future research studies. Typically, sample collection involves minimal physical risk to the participants. The actual risk, however, lies in the potential misuse of collected data and the breach of privacy and/or confidentiality of the participants.

In addition to maintaining the quality of the collected samples, it is equally important to uphold ethical, legal and societal issues (ELSI). In this respect, public health ethics, personal data protection, data sharing, consent protection as well as compliance issues within international data sharing procedures have gained urgency in COVID-19 research. In 2020, the Biobanking and Biomolecular Resources Research Infrastructure – European Research Infrastructure Consortium (BBMRI-ERIC) ELSI Services & Research department held a webinar to discuss consent given by COVID-19 patients. It was noted that when consent is directly pursued by healthcare providers at the time of data collection, the consent may be viewed as invalid by the General Data Protection Regulation (GDPR) due to the vulnerability of the patients at that time and due to the imbalance between the data controller and the data subject as it is explained within the European Data Protection Board (EDPB) “Guidelines on Consent” document.⁹ The EDPB has suggested that consent to non-interventional type research would be legitimate if there was no pressure or threat of disadvantage. However, there is no mention made by the EDPB if the obtained consent may be affected by the severity of the patient’s condition as it may be unfeasible to obtain the consent of a critically ill patient. Thus, broad consent¹⁶ in these circumstances, may be used to avoid the strict requirements of study-specific consents. The organizational model adopted in Portuguese biobanks during the pandemic, was similar to that of other European countries, where the informed consent followed international standards.¹⁷

Table 1 – Type of sample and clinical data collection (adapted from^{18,19})

Sample type	Function	Testing type	Data extraction	Storage temperature until testing	SOP
Sputum (from the lower respiratory tract)	Determination of active pathogens i.e. viral presence and load	Nucleic Acid Amplification Tests (NAAT)	Confirms current SARS-CoV2 infection	2 - 8 °C	Adopted from PHE, WHO, and CDC
Nasopharyngeal & oropharyngeal swabs (from the upper respiratory tract)					
Whole blood, Faeces, Urine, Saliva	Detection of IgM and IgG anti SARS-CoV2 antibodies	Serology: Antibody based immunoassay	Overall infection/ immunity rates in a community	2 - 8 °C	
Serum					

PHE (Public Health England): Guidance and standard operating procedure COVID-19 virus testing in NHS laboratories, 2020.

WHO (World Health Organisation): Laboratory testing for coronavirus disease (COVID-19) in suspected human cases Interim guidance 19 March 2020. (<https://apps.who.int/iris/handle/10665/331501>).

CDC (Centre for Disease Control and Prevention): CDC’s Diagnostic Test for COVID-19. (<https://www.cdc.gov/coronavirus/2019-ncov/lab/virus-requests>)

Table 2 – Biobanco.pt members and their respective COVID-19 collections

Biobank	Affiliation	Number of samples	Type of samples	Observations
Biobanco-iMM/CAMIL	Instituto de Medicina Molecular, Faculty of Medicine, University of Lisbon	1966 2066 1083 1601	Serum Plasma Dry Pellets PBMCs	Donors were selected from hospitalized and recovered patients, and samples were obtained from additional groups, according to various criteria in accordance with the disease evolution (severe, mild, moderate, and asymptomatic); samples were also obtained from donors who had tested positive for the virus and recovered from the disease (recovered group). COVID collection was active between 2020 and 2021
Comprehensive Health Biobank (CHAIN)	Comprehensive Health Research Centre, NOVA Medical School, NOVA University of Lisbon	1645 237 95 625	Serum PBMCs Nasopharyngeal, oropharyngeal swabs,	Investigative study to determine the seroprevalence of SARS-CoV-2 antibodies among NOVA university employees and to assess the community's mental health. Task Force COVID-19 took the initiative to create a bank of nasopharyngeal and oropharyngeal exudate samples that aims to boost the investigation of infectious diseases in particular in the area of COVID-19 through the validation of new diagnostic and prognostic tools for this disease. The detection of the presence of coronavirus in the respiratory system is evaluated by performing Polymerase Chain Reaction tests, in Real Time (RT PCR). The samples were collected between May 2020 August 2021.
AZORBIO biobank	Specialized Service of Epidemiology and Molecular Biology (SEEBMO), Santo Espírito Hospital, Terceira Island (HSEIT), Azores	1200 15 (patients)	Nasopharyngeal, oropharyngeal swabs, bronchoalveolar lavage. Serum, plasma and DNA	The AZORBIO biobank initiated, in early March 2020, a collection of SARS-CoV-2 positive samples, mainly from nasopharyngeal and oropharyngeal swabs. A collection of positive SARS-CoV-2 samples available for sequencing and other research studies.
Champalimaud Foundation Biobank (CFB)	Champalimaud Foundation	9084 2688	Serum Nasopharyngeal swabs	Collections made throughout the different waves of COVID-19 in Portugal and included: the first serological screening in high-risk professionals in the Loulé area, in collaboration with the Algarve Medical Center (ABC), to assess the incidence of SARS-CoV-2 exposure. Another serological study in collaboration with the "Ordem dos Enfermeiros", which involved nurses and medical auxiliary staff of Hospital Santo António in Porto, Hospital de Santa Maria in Lisbon and the Champalimaud Clinical Centre (CCC) and other health professionals of the Hospital D. Estefânia in Lisbon. After promoting vaccination of all health professionals in the CCC, 4-weeks post-vaccination serological specimens were collected. all the SARS-Cov-2 PCR positive specimens have been stored, as well as all the pre-and post- SARS-Cov-2 PCR negative specimens of the same patient.
Minho BioMedical Biobank (MinhoMedBiobank)	School of Medicine, ICVS, University of Minho	600 patients 156 patients 20 769	Serum Plasma and PBMC Oropharyngeal swabs	Specific informed consents for the oropharyngeal swabs that were only used for COVID 19 diagnosis but broad consent for the blood that was collected and for their possible derivatives such as serum, plasma, DNA, RNA and cells. Samples were collected during the 1 st and 2 nd wave of the pandemic in Portugal
NeuroBiobank CHUPorto (NBC)	Centro Hospitalar Universitário do Porto (CHUPorto)	469 469 300	Plasma DNA Orospharyngeal swabs	A prospective study (a cohort of 750 patients with different degrees of disease severity, ranging from asymptomatic to critical illness) on the acute and long-term neurological manifestations of consecutive COVID-19 patients from the first pandemic wave (March-July 2020). A dedicated biobank includes samples for genetic testing and fluid biomarker assessment collected one year after infection (January-July 2021) and Oropharyngeal swabs collected during the infection acute phase.

PBMCs: peripheral blood mononuclear cells

DISCUSSION AND CONCLUSION

The demand for high quality COVID-19 collections has continued throughout the pandemic, which in turn has shed light on the importance of biobanks in maintaining these collections and their central role in the advancement of research. However, prior to the pandemic, biobanks, in general, suffered from a lack of collections exposure with some collections not being used for years. Therefore, collaborations and sample/data sharing are of utmost importance so that researchers can advance their research. The importance of using the recommended standard operating procedures when collecting, processing, and storing these valuable sample should also be highlighted. Creating a national database for the COVID-19 collections is vital to increase collaborations and sample/data sharing within Portugal, which is not a member of the BBMRI-ERIC yet. Joining BBMRI-ERIC has many advantages such as easy access to high quality samples/ clinical data from biobanks around Europe, harmonized guidelines for data and sample collection and access to knowledge on ethical, legal, and societal issues.

Through biobanks, access to high quality collections will undoubtedly provide a basis for future research regarding the effectiveness of novel vaccines, which could, for example, include a detailed characterization of the immune profile (response) induced by a particular disease such as COVID-19, and the effect that a vaccine has on such profile, in a large cohort of healthy controls and patient samples. This is of obvious interest to the vast community of researchers interested in immune responses, vaccine efficacy and biomarkers.

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AUTHOR CONTRIBUTIONS

SA, SD: conceived the content of the article, wrote, reviewed and edited the manuscript.

AA, MC, JMF, IF, BP, AC, JBA, AMR, AG, AD, IT, AL, CF, FM, JCS, RS, PP, MC, LM, HC: helped to draft and review the manuscript.

All authors read and approved the final manuscript.

COMPETING INTERESTS

None.

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ETHICAL CONSIDERATIONS

Ethical committees of participating biobanks/hospital approved the collections and patients provided informed consent.

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