Pediatric HIV BioBank: A New Role of the Spanish HIV BioBank in Pediatric HIV Research

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Abstract

The vulnerability of children has long raised ethical concerns resulting in the lack of inclusion of children in research studies. This has impeded the development of relevant medical therapies specific for children. In response to these circumstances, international policies have begun to recognize the need to carry out research focused on children. Translational HIV infection research is highly dependent on many factors including the availability, quality, and traceability of samples and their associated data under a strict system of quality management. The primary objective of the Pediatric HIV BioBank is to contribute to the furthering of scientific knowledge about vertical HIV infection. To achieve this aim, the BioBank processes, stores, and provides distinct samples from HIV/AIDS children to research projects free of charge. Strict compliance to ethical norms is always guaranteed. At present the Pediatric HIV BioBank has 429 vials containing different sample types from 243 vertically HIV-infected children. The Pediatric HIV BioBank represents a novel approach to HIV research that might be of general interest not only for basic and clinical research teams working with HIV, but also for those groups trying to establish large networks focused on researching specific clinical problems. It also represents a model to stimulate cooperative research on specific clinical problems. The main objective of this article is to show the structure and function of the Pediatric HIV BioBank that allow it to efficiently provide samples to different research projects in Spain and in other countries.

Past abuses have raised ethical concerns about the inclusion of children in research, which has prompted their exclusion from different studies.1 This has hampered the development of relevant medical therapies for children and forced researchers to rely on the extrapolation of data derived from adult-oriented studies resulting in inexact conclusions when applied to children. In response to these circumstances, international policies have begun to recognize the need to include children in research.5

Sample types stored in individual laboratories that, in some way, “function as tissue and biological fluid banks” have played an essential role in HIV/AIDS pediatric research. However, biobanking is a new discipline, which needs to continuously evolve according to the ongoing development of new techniques and scientific goals. Therefore, biobanks are identified as a biomedical scientific/infrastructural development and represent a political/legal/ethical enterprise with the goal of being integrated into the preexisting form of regulation, medicine, law, and society.3

The Pediatric HIV BioBank belongs to the Spanish Research HIV BioBank,4,5 a part of the RED RIS,6 organized by the Laboratorio de Inmunobiología Molecular of the Hospital General Universitario Gregorio Marañón. A single hospital is responsible for the preservation and storage of these HIV samples. The human resources, infrastructure, and material of the HIV BioBank have been funded by public research grants [Ministry of Science and Innovation and Foundation for HIV Research and Prevention (FIPSE)].

The Pediatric HIV BioBank receives samples from the pediatric HIV-infected children cohort (CoRISpe) among 33 hospitals spread across Spain. CoRISpe is an open prospective multicenter cohort of Spanish HIV-infected children, mainly infected by vertical transmission (ages ranging from newborn to 18 years old).

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vertically HIV-infected children that are included in the CoRISpe for the objective of carrying out research. These samples are deposited, processed, and cryopreserved by the BioBank. The HIV BioBank has been set up according to a system of quality management based on the rules written in UNE-EN-ISO 9001:2008.

It is assigned to a scientific and ethics committee that assists the BioBank director with her responsibilities. An independent ethics committee reviews the agreements made between the different cohorts with respect to the patients’ informed consent.

For the Pediatric HIV BioBank to receive samples, the BioBank director and the coordinator of the CoRISpe Cohort must sign a “Deposit Agreement” that outlines how the hospital must send the samples and how they are to be processed and stored.

The hospital personnel must coordinate with the BioBank to set the date for the sample shipment to the BioBank. The BioBank is responsible for sending the courier service to the hospital to collect the samples and deliver them to the BioBank.

To donate samples, the parents or a legal representative of an HIV-infected child must sign an informed consent form in which the risks and discomforts associated with obtaining the samples and the research objective for obtaining the samples are clearly explained. Moreover, the Declaration of Helsinki states that although parents or a legal representative of a child sign the consent, a child is required to give her or his assent to the participation in the study if she or he is able to do so. The informed assent is a document similar to the informed consent but written in a way understood by a child. If a child can read, she or he must sign the assent. If after having read the assent, a child decides not to participate in the study, this decision must be respected.

The evaluation of whether a child can give assent should not be based solely on age, but on other factors such as developmental stage, intellectual capacities (especially in children with special needs and/or learning difficulties), and life/disease experience. This needs to be made after discussion between the parents/legal representative and the pediatrician, but the parents will normally know the child best and hence are usually in a position to decide whether the child has understood the information as much as possible.

The informed consent and assent form must go to the Ethics and Clinical Research Committee and are stored in the clinical history of the HIV individual. Throughout this process the official law on protection of personal data is in effect. As a general rule, the consent can be cancelled at any time. If an HIV-infected child or her or his parents or a legal representative decides that the child does not want her or his sample to be used for research, the sample will be destroyed. In all cases, the sample bears a numeric code that can be used to remove the associated patient’s data. CoRISpe is in charge of compiling and watching over the clinical and demographic information associated with the samples since the information stored in the BioBank is just the sample number, the patient code, the name of the hospital that sends each sample, and the date of extraction. The patient code and the sample number allow the samples stored in the BioBank to be connected with the data available in the cohort.

All the BioBank samples belong to prospective longitudinal studies, thus the pediatricians check the progressing maturation of the child and the child’s ability to provide assent. The HIV-infected children have a follow-up visit every 3 months. They donate samples to the HIV BioBank once a year. Thus, children grow up during the project, which means they mature and develop the capacity to make independent decisions. Because of that, it is important to realize that consent is a dynamic, continuous process, and should therefore not only be obtained prior to enrolling a child in the Pediatric HIV BioBank but should be maintained during the donation of samples on a continuous basis.

Once the samples have been deposited, they are processed to obtain the distinct components (blood, serum, plasma, solid or liquid tissue, DNA, RNA, pellet cells, PBMCs for physiological studies) through standardized techniques, which are cryopreserved in the Pediatric BioBank. The establishment of a regulated specimen storage facility guarantees the availability, quality, and traceability under a strict system of quality management.

To ensure that the information kept by the Pediatric BioBank on the stored samples is correct, periodic checks and comparisons of data between the BioBank, the cohorts, and the hospitals are carried out.

Access to the Pediatric HIV BioBank samples can be applied for by anyone researcher who is a member of the AIDS Network, or anyone in collaboration with a member as long as the project is scientifically, technologically, and ethically viable. To receive samples, a researcher must complete a sample release application. This application must be submitted and evaluated by the members of the Scientific Committee. If the project is approved, the researcher signs a “Release Agreement” with the director of the BioBank and with the coordinators of the CoRISpe cohort. Once the samples have been released, the principal researcher is required to send a scientific report containing their results once a year, so that the BioBank can keep up-to-date records on all the projects.

The HIV BioBank does not charge any fee for providing samples to other research groups apart from the cost of transporting the samples.

The Pediatric HIV BioBank began in September 2008 and, presently, the HIV BioBank has more than 429 vials containing different sample types (blood, serum, plasma, solid or liquid tissue, DNA, RNA, pellet cells, PBMCs for physiological studies) from 243 HIV-infected children.

The number of samples stored in the Pediatric HIV BioBank is a relevant aspect required to support the needs of personalized medicine. In Spain there are approximately 850 HIV-infected children and our objective is to incorporate samples from the majority of the vertically HIV-infected children in the Pediatric HIV BioBank. It is thought that by next year we will have at least a basal sample for the 850 vertically HIV-infected children and 400 follow-up samples stored in the Pediatric HIV BioBank. The large quantity of available samples will allow researchers to conduct studies with greater scientific and statistical significance. The excellent traceability of the samples of the CoRISpe cohort allows investigators to study well-characterized HIV-infected children in distinct stages of the disease and to correctly carry out studies on the evolution of the infection in a group of children over a long time period. However, it should not be forgotten that these mul-
disciplinary tasks can be fully achieved only because of the generosity of the children donors, who rightfully expect progress to be made in pediatric HIV infection using their donations. Therefore, the sharing of data and samples for good research needs to be an obligation for those involved in decisions on the access to donor samples. The manager of the sample resource as well as others involved in controlling the access to the samples in the HIV BioBank are merely the caretakers of the samples and must act in the best interests of the donors.

Therefore, to exploit the full potential of the HIV BioBank, networking between individual biobanks is indispensable. As a requirement for international cooperation, it is necessary not only to define common standards for sample quality and data formats, but also to consider the differences in ethical, legal, and social environments in the different countries of partner biobanks. Moreover, BioBank management and governance need to cover a variety of aspects such as compliance with biosafety and biosecurity regulations, as well as keeping a balance between sample usage and accrual. The HIV BioBank has been created to offer an important resource for global research in vertical HIV infection. Its success is measured as much in publications as in technical and scientific advances achieved via the use of these samples.

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