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H3Africa Biorepository Program: Supporting Genomics Research on African Populations by Sharing High-Quality Biospecimens

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Introduction

THE ESTABLISHMENT OF Human Heredity and Health THE ESTABLISHMENT OF TIGHTON has catalyzed in Africa (H3Africa, www.h3africa.org) has catalyzed collaborative research across national boundaries, building on existing infrastructure and resources to grow a pool of African scientists leading genomic research activities that address diseases of pan-African and international relevance such as kidney disease, rheumatic heart disease, AIDS, and tuberculosis (as discussed in the H3Africa marker article¹). H3Africa is perhaps the largest funded initiative collating the efforts of African scientists across national boundaries to share ideas, knowledge, experiences, and resources; to develop standardized tools and processes for genomic research in Africa; and to support the developing careers of young African scientists. African researchers are increasingly enabled to implement their own research with appropriate oversight, documentation, data generation, and analysis that meets international standards. H3Africa scientists are now publishing discoveries that have the potential to impact the fast-growing field of genomic medicine, a field in which African scientists have been significantly underrepresented. For example, APOL1 variants associated with nephropathy in African Americans were also found to be a high risk for developing HIV-associated nephropathy in South-African blacks² and among Nigerians of the Yoruba ethnicity with nondiabetic forms of chronic kidney disease.³ Other African investigators have shown association between variants in HLA class II loci with podoconiosis (a noncommunicable disease),4 which is currently being further studied by a H3Africa investigator.

H3Africa Consortium

The National Institutes of Health and the Wellcome Trust have invested over \$76 million in the H3Africa consortium

since 2011 when they first sent out an announcement requesting for applications from African institutions led by African scientists on genomic research on diseases of importance to the African continent. A second opportunity for African Institutions to submit genome research applications was again announced in 2016, expanding the areas of genomic research to include HIV/AIDS. A number of the funded projects address infections (such as tuberculosis, trypanosomiasis, fevers, and respiratory diseases); a number of projects are on noncommunicable diseases of significant importance (such as diabetes, rheumatic heart disease, cardiovascular diseases, stroke, cancers, and kidney diseases). The announcement included opportunities to build capacity through the establishment of regional biorepositories and a bioinformatics network to store and distribute high-quality biological specimens and data gathered from the 25 research projects across 27 African countries involving over 500 investigators and about 75,000 study participants (Fig. 1). Most of the grant applications had to involve multiple sites; the bigger Center grants were multicountry in nature encouraging collaborations across multiple African countries. Due to the nature of genomic research where the results may not have an immediate clinical relevance or intervention for an individual or community, it is critical that clear communication strategies are developed to mitigate stigma or other undesirable consequences. In addition, terms like "genes," "database," and "biorepositories" are difficult to convey to the general population and in different African languages. As a result, the H3Africa consortium has funded projects focused on establishing a coherent communication strategy for the research community, the lay audience, and leaders and encouraging high ethical standards for all projects and collaborations. Training and mentoring in all aspects of genomic research for the next generation of young African scientists remains the cornerstone of this unprecedented investment in Africa

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Morocco

Tunisia

Egypt

Senegal

Mali

Senegal

Niger

Guinea

Sudan

Nigeria

Sudan

Cameroon

Democratic

Republic of

Congo

Tanzania

Alawii

NIH Primary Award Institution

WT Primary Award Institution

Collaborating Institution

Other collaborating Institution

South Africa

FunoED AND COLLABORATING SITES

WWW. h3africa.org

FIG. 1. Distribution of H3Africa projects. Color images available online at www.liebertpub.com/bio

to sustain it through a pool of trained clinicians, laboratorians, bioinformaticians, and social behavioral researchers. H3Africa truly demonstrates the African proverb that says "If you want to go quickly, go alone; if you want to go far, go together."

H3Africa Biorepositories

The H3Africa Biorepositories play a critical role in supporting the collection and storage of African specimens that are linked to diseases relevant to African populations. Realizing that biorepositories in Africa have historically been underfunded and many are therefore operating below internationally accepted standards, ^{2,5} the H3Africa approach was to begin by promoting best practices using internationally accepted guidelines such as the International Society for Biological and Environmental Repositories (ISBER). This was achieved mainly through evaluation, training, and mentoring by well-established biorepository consultants through an iterative process to ensure continuous quality improvement both in the biorepository and at the end-user interface.

Three regional H3Africa biorepositories were established in the West, East, and South Africa (Fig. 2) to support H3A projects within their region and ensure access to high quality samples and data using best practices that respect the cultural and societal norms of study participants. The three biorepositories use Laboratory Information Systems (LIMS), which automate sample tracking. This complies with ISBER guidelines for efficient storage, retrieval, and chain-of-custody maintenance while allow-

ing them to support different H3Africa projects as outlined in Figure 1.

H3Africa biorepositories continue to work together to share resources and knowledge across large pan-African collaborations even outside of H3Africa, as exemplified by the engagement with the African Society of Laboratory Medicine (ASLM) and the Bridging Biobanking and Biomedical (B3Africa) group supporting research across Europe and Africa forming important synergies and collaborations, highly desirable for sustainability. While the H3Africa biorepositories have joined the wave of accreditation of laboratories that swept through Africa in recent years as a result of the step-wise accreditation program established by ASLM, the B3Africa has engaged H3Africa biorepositories in testing simple LIMS and bioinformatics tool kits developed for less resourced settings.

How Do the H3Africa Biorepositories function? The Blue Print

The three regional H3Africa biorepositories function through a number of collective processes published in detail elsewhere (Croxton et al.⁶) and outlined briefly below:

- First, the H3Africa biorepository working group made of members of the three biorepositories meets biweekly to address biorepository-specific practices
- Second, biorepository members participate in other working groups and contribute to issues surrounding ethics of research and biorepository operation; data manage-

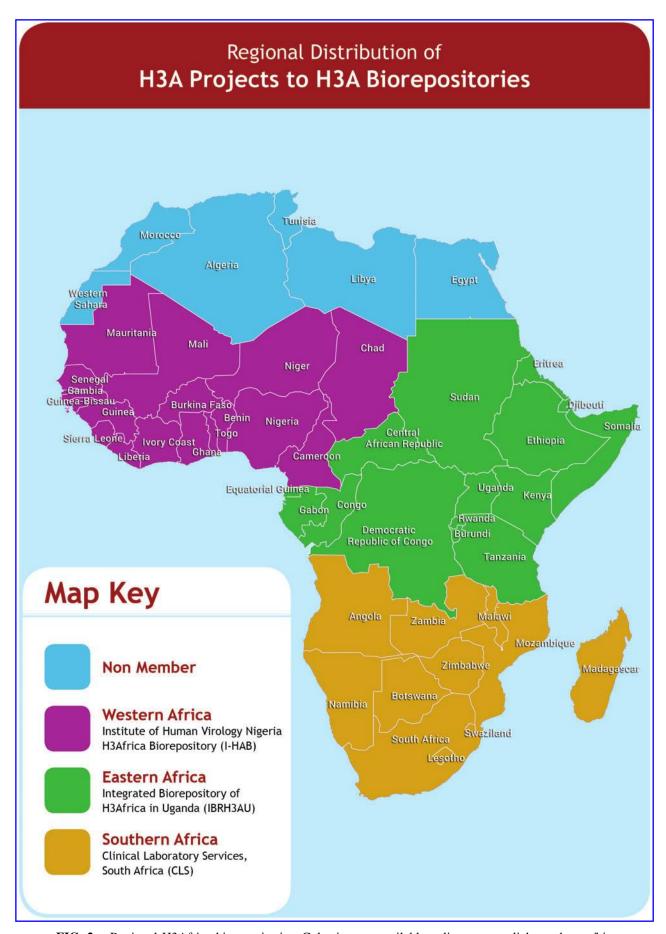


FIG. 2. Regional H3Africa biorepositories. Color images available online at www.liebertpub.com/bio

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ment and bioinformatics; and governance of the H3Africa consortium.

- Third, consortium-wide topics are discussed during the biannual consortium face-to-face meetings that engage the whole consortium, experts, and invited external groups.
- Fourth, through the Consortium-wide policy guidelines that inform the activities of the biorepositories within the consortium. The Biospecimens Deposit Guidelines describe the regulatory requirements, instructions, and required documentation for submitting H3Africa biospecimens to H3Africa biorepositories for sharing with authorized researchers.
- Fifth, the principles governing access to biospecimens stored at H3Africa biorepositories are codified in the H3Africa Data and Biospecimen Access Guidelines discussed in detailed in an accompanying article.
- Sixth, all H3Africa biorepositories have quality assurance measures to optimize biospecimen integrity.
- Seventh, H3Africa biorepositories have identified best practices for shipment of different biological samples and have used the consortium's collective bargaining power to engage major shipping couriers in addressing the challenges of shipment of biological material across the continent while maintaining integrity of biological samples at affordable pricing.

These processes are critical for sharing and standardizing experiences across the continent. The networks formed are important for the sustainability of these biorepositories and for the introduction of new tools and information that would improve efficiencies.

Successes and Challenges

H3Africa has been successful in establishing ISBERcompliant regional biorepositories that conform to the cultural and societal norms of study participants in Africa and have the capacity to process, store, and distribute biological specimens using internationally accepted standards. Significant progress has been made in standardizing Material Transfer Agreements (MTAs) and considering the ethical concerns related to biobanking across the African continent. More importantly, templates and processes developed by H3Africa could be used and adapted by the wider scientific community. The robust and continuous interaction and synergy among the H3Africa groups (biorepositories, clinical sites, project leads, ethics groups, H3ABioNet, expert committee, NIH and Wellcome Trust (WT) staff members, the local communities, government agencies, and shipping couriers) are unprecedented with great dividends in terms of sustained discussions and progress in tackling sensitive issues surrounding sharing of biological samples and data to improve Africa's participation in, and contribution to, genomic science (see also Beiswanger et al.⁷ and Croxton et al.⁶ in this issue).

Despite these successes, more needs to be done in streamlining more efficient processes. For example, while some countries are efficient in approving MTAs quickly within 1–2 months, others take much longer, up to 6 months. More needs to be done to optimize sample collection and processing at clinical research sites, to deal with issues of interrupted power supplies and few trained staff. Although H3Africa biorepositories have successfully

piloted less expensive ways of shipping high-quality DNA samples at controlled ambient temperature, the cost of shipping other biological samples requiring cold chain maintenance is still prohibitively high, sometimes $10 \times \text{more}$ due to high cost of dry ice and its replenishment during transportation.

Nonetheless, the landscape for biorepositories in Africa has changed drastically in the last 2-3 years with the H3Africa investment: the infrastructures are better; companies have come to the table to do business with H3Africa due to its increased bargaining power and visibility; government ethical and regulatory structures are responding to the special needs of conducting genomic research through consultations and generation of national guidelines; researchers within the continent and internationally are becoming more aware of these resources in Africa that will mitigate the need to ship samples out of the continent which is very unpopular; and African Institutions are beginning to see the need to invest in biorepositories based on the visibility and added funding such structures attract. The future is promising: there is heightened awareness of the need for quality biorepositories, and other African investigators and projects are already reaching out to H3Africa to utilize and build on this resource.

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Author Disclosure Statement

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