Enabling the genomic revolution in Africa

H3Africa is developing capacity for health-related genomics research in Africa

By The H3Africa Consortium*†

Our understanding of genome biology, genomics, and disease, and even human history, has advanced tremendously with the completion of the Human Genome Project. Technological advances coupled with significant cost reductions in genomic research have yielded novel insights into disease etiology, diagnosis, and therapy for some of the world’s most intractable and devastating diseases—including malaria, HIV/AIDS, tuberculosis, cancer, and diabetes. Yet, despite the burden of infectious diseases and, more recently, noncommunicable diseases (NCDs) in Africa, Africans have only participated minimally in genomics research. Of the thousands of genome-wide association studies (GWASs) that have been conducted globally, only seven (for HIV susceptibility, malaria, tuberculosis, and podoconiosis) have been conducted exclusively on African participants; four others (for prostate cancer, obsessive compulsive disorder, and anthropology) included some African participants (www.genome.gov/gwastudies/). As discussed in 2011 (www.h3afrika.org), if the dearth of genomics research involving Africans persists, the potential health and economic benefits emanating from genomic science may elude an entire continent.

The lack of large-scale genomics studies in Africa is the result of many deep-seated issues, including a shortage of African scientists with genomic research expertise, lack of biomedical research infrastructure, limited computational expertise and resources, lack of adequate support for biomedical research by African governments, and the participation of many African scientists in collaborative research at no more than the level of sample collection. Overcoming these limitations will, in part, depend on African

RESEARCH CAPACITY

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Yet, roughly a decade ago, newly proposed DNA-based taxonomy (11) promised to solve the species debate. A Barcode of Life Data Systems (BOLD) (12) quickly emerged, seeking to provide a reliable, cost-effective solution to the problem of species identification (12) and a standard screening threshold of sequence difference (10× average intraspecific difference) to speed the discovery of new animal species (13). Sometimes considered a “caricature of real taxonomy” (14), this approach failed to identify, perhaps not surprisingly, two American crow species and a number of members of the herring gull Larus argentatus species assemblage above the set threshold (13). Furthermore, despite past (3) and present (6) sequencing projects, carrion crows and hooded crows can also not be differentiated from one another by means of DNA-barcode approaches. By contrast, Poelstra et al. show that much more DNA sequencing data are needed, combined with RNA expression data, to reconstruct the evolution of a reproductive barrier that culminated in the speciation of these two crow taxa. Armed with this new very detailed genetic information, it is clear that none of the currently formulated species concepts fully apply to these two crow taxa (unless one is willing relax some stringency in the various definitions). Indeed, the genomes of German carrion crows are much more similar to those of hooded crows than to Spanish carrion crows. Put simply, apart from the few carrion crow type “speciation islands,” German carrion crows could be considered to represent hooded crows with a black (carrion crow) phenotype.

There is a clear need for additional population genomic studies using a more dense sampling, especially among the fully black carrion crows, before the complexity of reproductive isolation and speciation among these two taxa can be fully understood. The speciation genetics strategy already proved itself in unraveling the complexities of mimicry among many Heliconius butterfly taxa (7) and, as in the study of Poelstra et al., stresses the importance of using RNA-based information in addition to DNA. Only time will tell if, and when, German carrion crows will adopt the “hooded phenotype,” a fate that seems unavoidable. Until then, we can only applaud these crows for defeating Linnaeus’s curse.

REFERENCES

accelerated CKD progression and the de-
velopment of end-stage renal disease, that
is two to five times normal, respectively (2, 
3). These variants also confer 29 times the
risk of HIV-associated nephropathy (HIVAN) 
(4). Despite these renal outcomes, the preva-
ience of the risk genotype is 13% among AA 
and virtually absent among those of non-
African ancestry. The prevailing hypothesis 
is that APOL1 renal risk variants evolved in 
sub-Saharan Africa about 10,000 years ago 
to confer protection against the regionally 
endemic trypanosome parasite, the cause of 
African sleeping sickness. Recent stud-
ies led by African scientists showed that the 
frequency of the risk variants, as well as the 
prevalence of CKD and HIVAN in carriers of 
the risk variant, are much higher in West 
Africa (Yoruba, 28%; Igbo, 23%; the major 
ancestral populations of AA) where the try-
panosome parasite is endemic as compared 
with the non-endemic region of Ethiopia 
(1%) (3–7). The association between CKD 
and APOL1 [a component of high-density 
lipoprotein (HDL) cholesterol] is shedding 
light on the complicated protective rela-
tion between HDL cholesterol and CKD in 
global populations (8). In another example, 
African scientists participating in H3Africa 
have used genomic tools to understand how
genes interact with life style (barefoot farm-
ing practices) to increase susceptibility to 
odoconiosis, a neglected tropical disease in 
Ethiopia and Cameroon (9).

A key challenge to building critical mass 
for genomic research in Africa is the reten-
tion of scientific leadership capable of de-
veloping and maintaining sustainable research 
programs. The dearth of research-intensive 
institutions on the continent, coupled with 
a shortage of funded positions, continues 
to drive Africa’s talented scientists to coun-
tries where they have better opportunities to 
develop their potential and pursue their in-
terests. Furthermore, the African continent 
lacks a strong history of collaborative sci-
entific endeavor (10), as African researchers 
have turned to their well-resourced counter-
parts from Europe, North America, and Asia, 
rather than to their neighbors, to achieve 
scientific excellence and strong publication 
records. Consequently, African scientists have 
not adequately developed the necessary infra-
structure and large-scale biomedical research 
culture required to promote research in Af-
rica. H3Africa has begun building a strong 
foundation for genomic research based on 
collaboration among African scientists. Per-
haps more important, H3Africa is facilitating

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the implementation of the norms and standards for project oversight, goal orientation, and timely dissemination of discoveries and training of the next generation of biomedical researchers across Africa. The consortium is also addressing the use of standardized protocols with detailed attention to community engagement and ethics approval (see below), protocols and policies for sharing biospecimens and data, and publication policies for large collaborative groups.

Approaches to these issues are facilitated by frequent interactions among consortium members to share experiences in developing genomic research programs, to support and promote interactions among the collaborative projects, and to jointly tackle ethical and policy concerns. An important example is data harmonization. By standardizing phenotype measurement and how collected responses are coded to facilitate data merging, statistical power for discovery of genetic variants and for modeling gene-by-environment interactions can be greatly increased.

Implementation of multinational and multiinstitutional genomics research projects in Africa faces additional challenges. Many local ethics review committees have little experience in genomics studies that require broad consent for long-term storage and sharing of biospecimens and data, and some have balked at the concept of global sharing of biospecimens and data with no immediate local benefit, viewing it as another form of exploitation. Several African countries have restrictive legislative policies that hamper sharing across national boundaries. Cultural beliefs and practices regarding donating any body part, including blood, need to be addressed. The growing international debate about return of individual genomic results is also an issue in Africa (11). Finally, there are huge disparities across Africa that span rural communities adhering to long-established cultural beliefs and practices on the one hand to sophisticated “citizens of the world” residing in major cities on the other. These communities share genetic heritage, but require different approaches to engagement and informed consent. Thus, H3Africa includes a grant program that supports empirical research on innovative approaches to informed consent; community engagement; and the ethical, legal, social, and cultural factors unique to the African research environment.

The H3Africa Consortium has developed an approach that attempts to balance (i) protection of the ability of African scientists to be the first to analyze and publish findings about their main research questions, given their limited resources and capacity to deal with data as quickly as scientists in developed countries with (ii) the benefit of global access to H3Africa data and biospecimens. To reach these not completely compatible ends, the H3Africa Consortium has agreed that data will be made initially available to the consortium members via H3ABioNet until submission to the European Genome-phenome Archive, from which they will be publicly accessible (through an independent Data and Biospecimen Access Committee).

As is common in genomics, there will be a short lag (12 months) between data submission and publication; this is somewhat longer than the norm (6 to 9 months) to provide resource-challenged African investigators a bit more time to analyze and submit their manuscripts for peer review.

Similar considerations went into development of the policy for the release of biospecimens collected in H3Africa. The biospecimens will be stored in an African biorepository (with backup elsewhere on the continent), and from there shared globally for further research. Data and biospecimen sharing does, however, raise the often contentious issues of ownership and commercialization rights. The H3Africa Consortium is addressing this issue while embracing an ethos that promotes research for the global common good. Resources generated by H3Africa are expected to be useful in future genomic research not only in Africa but also globally.

H3ABioNet has also embarked on a program of training and accreditation of its bioinformatics nodes to carry out specific data analysis techniques, i.e., of GWAS or next-generation sequencing data. Part of the training involves a series of workshops, often held at the nodes, to prepare for an accreditation exercise. The accreditation involves giving the nodes raw data sets to analyze, with their results being assessed by an international accreditation committee. One of the major challenges in holding training courses or even just joining working-group Skype calls, is poor Internet connectivity. H3ABioNet is using creative approaches to overcome these issues by seeking low latency alternatives and using portable devices that host data and tools and run independently of the network.

There are several criteria for success that have been defined to assess the accomplishments of the H3Africa initiative (see the table). Each of the component grants has a set of specific, yearly milestones, progress toward which is assessed on an annual basis by the funders (with input from an Independent Experts Committee of outside scientists. Both Wellcome Trust and the NIH will also critically evaluate the progress of H3Africa through peer review toward the end of the initial funding period. Accomplishments of both individual grants and the overall program will be considered in each funder decision process to determine whether continued support is justified.

The efforts of the African scientific community and their international colleagues will not in themselves be sufficient. It is essential that national governments and regional political and economic organizations support sustained funding of all research fields, including genomics and research infrastructure development. In fact, H3Africa has been useful in leveraging additional funding from local sources, as demonstrated by support from the South African Department of Science and Technology to enhance data collection in an H3Africa project of cardiometabolic disease genomics, an early promise of potential long-term success.

**Measures of success for the 5-year H3Africa program**

- Publication in high-impact journals with African lead and senior authors
- Increased availability of funding for biomedical and genomics research in Africa
- Effective operation of a pan-African bioinformatics network
- Regular data release
- Establishment of one or more full-scale biorepositories
- Effective release of samples within and outside of the African continent
- Contribution to the ongoing efforts to reverse African “brain drain”
- Extension of funding for a second 5 years

**REFERENCES AND NOTES**


**SUPPLEMENTARY MATERIALS**

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