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Chapter

Neglected Tropical Diseases Pathogen and Human Genetic Interaction in the Genomic Era: Opportunities for (Sub-Saharan) African Scientists to Get on Board

Issiaka Soulama

Abstract

The worldwide prevalence of the neglected tropical diseases (NTD) shows the diseases are affecting more than 1 billion. The burden of the Neglected tropical diseases cost to developing, the burden of the diseases cost to developing economies billions of dollars every year. The genomic research in the last decades providing a full sequence (some currently in the sequencing pipeline) of genomes of many of the organisms including those which are responsible of neglected tropical diseases, may help in the management of such diseases. With the human genome being sequenced, the understanding of the genomic interaction between human and NTD pathogen enable scientists to develop new strategies to prevent and treat these devastating diseases. In this context of genomic era, African scientists may interestingly play an insider role in order to be part of the history of the elimination of these diseases. However, a critical mass of African scientists in genomic area constitutes the first step toward this long way in struggle against NTD. Although the challenge is enormous, it is very important to recognize that some African countries and institutions are fully committed to develop and strengthen African leadership in genomic area, while some are conspicuously absent from this debate. Joining African competences and leadership through collaborative activities and moving forward remains the next challenge to really impact the control and elimination of the NTD.

Keywords: NTD, genomic, scientists, elimination, Africa

1. Introduction

The neglected tropical diseases (NTDs) are known as a group of bacterial, parasitic, viral, and fungal infections strongly associated with poverty with an increase overlapping in tropical areas. They occurred particularly in areas affected by socioeconomic progress and unfortunately combined with other factors such as limited access to safe water and sanitation, chronic hunger, and also in areas where vector-transmitted diseases are more frequent. According to the World Bank Study, Sub-Saharan Africa population represents the major focus for the NTDs [1] and as mentioned from the 2010 Global Burden of Disease Study, NTDs accounted

for more than 26 million [2]. Most of the NTDs are well known as ancient diseases resulting in humanity concerns for centuries [3]. From the 2020 Roadmap, 20 NTDs were identified as following: Buruli ulcer, Chagas disease, cysticercosis/taeniasis, dengue fever, dracunculiasis (guinea worm disease), echinococcosis, food-borne trematodiasis, human African trypanosomiasis (HAT) (sleeping sickness), leishmaniasis, leprosy, lymphatic filariasis, onchocerciasis (river blindness), rabies, schistosomiasis, soil-transmitted helminthiasis (ascariasis, hookworm, and trichuriasis), trachoma, and yaws [4]. The World Health Organization classified the NTDs into two main groups: in one hand the preventive chemotherapy and transmission control (PCT) NTDs including prominently lymphatic filariasis, onchocerciasis, schistosomiasis, and soil-transmitted helminthiasis while the innovative and intensified disease management (IDM) on the other hand is constituted with Buruli ulcer, Chagas disease, human African trypanosomiasis, and leishmaniasis disease that are currently lack suitable tools for large scale use [5]. NTDs remain as a public health problem for poor populations living in tropical environments and difficult-to-access areas with more than 40% of impacted people living in the WHO African Region. The challenge is as much as important to justify the development of a specific program at WHO AFRO which mission is to provide technical orientation, support and guidance to Member States in the WHO African region. The development of genomic represents an opportunity that can contribute to the accelerated prevention, control, elimination, and eradication of NTDs and neglected zoonoses.

2. Geographical distribution and global burden of the NTDs

The concept, the burden, and the geographical repartition of the NTDs (**Figure 1**) justify the need of a global advocacy including the health policy-makers and ultimately the opportunity for tackling the NTDs with the same urgency and the commitment as for HIV/AIDS, tuberculosis, and malaria [6].

As previously well described by Hotez [6–8], the NTDs are characterized by the following important elements:

- Described as the most common infections of people living in sub-Saharan Africa, Asia, and Latin America and the Caribbean where the poverty is known as the component.
- NTDs affect about 1.4 billion people who live below the World Bank poverty figure of US\$1.25 per day.
- Unfortunately, the NTDs result in chronic infections lasting years or even decades resulting in a great impact on the affected people family revenue.
- The chronicity of The NTDs affect child growth and intellectual and cognitive developments, impair pregnancy outcomes, and decrease worker productivity and then the billions of affected people cannot escape poverty.
- Among the consequence, the NTDs also cause blindness and disfigurement that are psychologically devastating and result in social stigma.
- This high level of morbidity, economic impairment, and stigma does not necessarily translate into large numbers of deaths; overall, the NTDs cause high-morbidity but low-mortality conditions.

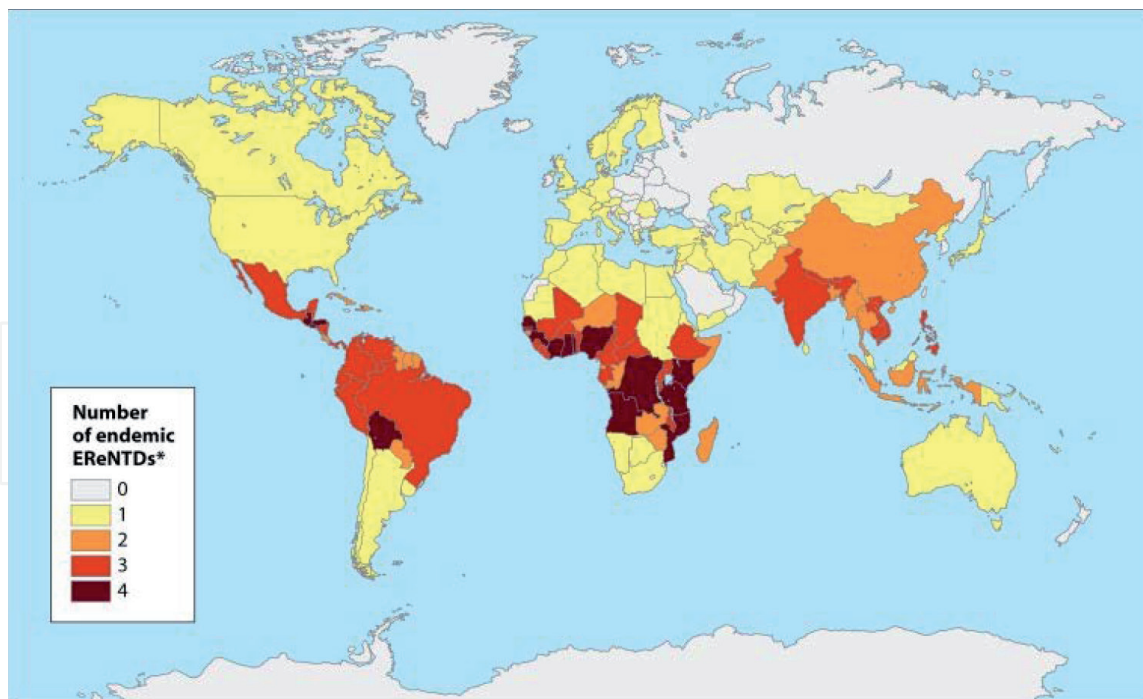


Figure 1. Global intensity map of EReNTD regions of endemicity. Data are from the World Health Organization (2013).

Regarding the chronicity of the disease but also as diseases afflicting humankind for centuries, NTDs are considered as “non-emerging” disease in contrast to emerging infections such as HIV/AIDS, SARS, and avian influenza.

Moreover, based on the previous studies, it is well documented that there is a geographic overlap among seven of the NTDs (ascariasis, trichuriasis, hookworm infection, schistosomiasis, LF, onchocerciasis, and trachoma). This is especially observed in sub-Saharan Africa where those NTDs present a very high prevalence. However, the overlapping of the NTDs in this part of the world allow to target these conditions simultaneously by combining the drugs in an integrated concept so named “rapid-impact package” [7, 9], as the drugs can be easily and quickly deployed by a contingent of community drug distributors. The rapid-impact package strategy if well implemented should ultimately contribute to the interruption of the diseases transmission such LF, onchocerciasis, and trachoma [9].

3. Impact of NTDs on public health

Although the NTDs are known to severely impact everyone, the diseases affect women and girls disproportionately for the following reasons:

Biological and physiological factors of women and girls lead to increased vulnerability of this specific category to particular pathologies—for example, female genital schistosomiasis and severe helminth-related anemia in pregnant women.

Socio-cultural factors are suspected in increasing risk to NTDs. A specific notified example is the water-based domestic activities carried out in two-third Sub-Saharan Africa by women or girls which increases risk of diseases such as schistosomiasis, whereas child-care and caregiving increases risk of trachoma and blindness. In fact, research suggested that women account for 80% of disability-adjusted life years linked to trachoma-related blindness.

NTDs that cause disfigurement and disability (such as lymphatic filariasis) can have a disproportionately negative impact on employability and marriageability



Figure 2.
A woman washing dishes in a canal. Image credit Anouk Gouvras.

of affected women, making them dependent on family members and potentially leading to stigmatization and social exclusion.

Indirect impact of NTDs can also disproportionately affect women and girls as caregivers, having to give up their jobs or drop out of school in order to take care of a sick family member (**Figure 2**).

4. Global mobilization and role of scientific commitment against neglected tropical disease

The worldwide burden of NTDs lead to a global mobilization with a development of a strategic work plan 2014–2020, which has been developed with the following objectives: scale up access to NTD-related interventions; enhance planning for results, resource mobilization, and financial sustainability of national NTD programs; strengthen advocacy, coordination, and national ownership; and enhance monitoring, evaluation, surveillance, and research [10] (WHO, 2012): Roadmap: accelerating work to overcome the global impact of neglected tropical diseases.

The 2020 roadmap against NTD recommend further research including the need for newer and safer drugs, vector control, personal hygiene, and the development of vaccines. In the implementation of the roadmap, there are several initiative including control programs or research initiatives bringing their resources and competences. Then, a more macro approach may be necessary to promote greater effectiveness in addressing the underlining social, human health, zoonotic, and environmental challenges to prevent morbidity, and mortality from these diseases. One such approach that is growing worldwide in recognition is the “One Health” initiative, a commitment of interdisciplinary and multistakeholder involved locally, nationally, and globally in areas of human and animal health, agriculture, and the environment [1–15]. However, these one health approaches should be sensitive

to resource-poor settings and should leverage partners and broader global public health networks as it is represented in **Figure 3**.

Although there are many NGOs and partners committed in NTDs control, scientific commitment is quite negligible in designing strategies and implementation. However, very few of them are from Africa where most of the NTD are present. Although African scientist's mobilization and commitment are well practical in some of the NTD control, very few inputs is observed in the genetic and genomic area. Indeed, the control and the elimination of certain NTD will be rapidly and successfully carried out with the contribution of the understanding of human and pathogen genomic interaction. Interestingly genomic constitute the new insight generating from genetic studies that can provide explanations and may even allow predictions to be made, in the context of a range of biological problems including the field of inherited human disorders. The development of the genetic in the last decade leads ineluctably to the "genomic" era. Then, importantly, with the improvement of sequencing technologies and the enormous reduction in the cost of sequencing, biologists are facing with a "data avalanche." The development of the next generation whole exome or genome sequencing may bring to the scientific community large possibility of tools to elucidate genetic perturbation occurring in many diseases including the neglected tropical diseases. Consequently, genomic data analysis may also be useful for the dissection of the genetic mechanisms underlying complex polygenic diseases or in understanding how some modifiers genes can influence the age of onset or clinical severity of a given disease



Figure 3. Proposed United Nations "One Health" framework. FAO, Food and Agriculture Organization; OIE, World Organisation for Animal Health; TDR, WHO Special Programme for Research and Training in Tropical Diseases; UNDP, United Nations Development Programme; UNEP, United Nations Environment Programme; UNFPA, United Nations Population Fund; UNICEF, United Nations Children's Fund; WHO, World Health Organization; WMO, World Meteorological Organization.

entity. Interestingly, while we are acquiring new research capabilities, we are also encountering new problems with the analysis of genomic data such as genomic data presentation, format, sharing, and reanalysis.

5. Programs and strategies ongoing in the field of genomic supporting the eradication of neglected tropical disease

The number of emerging infectious diseases is increasing annually despite the numerous of effort going on. In parallel to the wide incidence of the infectious disease including neglected tropical disease, characterizing novel or re-emerging infections is aided by the availability of pathogen genomes. This also helps to develop new approaches. Indeed, recently an *in silico* approach for discovering new filarial drug targets was developed in which comparative sequence analysis and functional genomics data from the related model nematode *Caenorhabditis elegans* are combined into subtractive filters that can be used to identify potentially essential nematode genes and generate a pool of pre-validated candidate targets [15–17]. Different techniques such as the RNA interference (RNAi) experiments and other functional studies serve as potential genomic tools to examine gene function from NTDs pathogen. Interestingly, sequencing of pathogen genomes, can contribute to describing nearly every aspect of transmission dynamics when some of the following information, date, location, clinical manifestation, or others data regarding the samples origin are including. The analyses of these data can positively affect the clinical management of the disease or the public health practice such as policies for surveillance, prevention, and treatment. The combination of genomic and epidemiological data represents consequently a perfect tool to address answers to epidemiological questions and reduce incidence and prevalence. How can genomic approaches support neglected tropical disease eradication particularly by analogy with how conservation genomics is supporting efforts to prevent extinctions. They are genomic approaches of capacity building programs in Africa as described through the next paragraphs that are contributing to reach this goal demonstrating the opportunity behind this cutting-edge method for African scientists.

6. Genomic training programs in Africa

Genomics remain one excellent component in the long way of NTD control and elimination. In order to tackle neglected tropical disease and move forward with elimination steps, the development of competent resources constitute one of the important challenge particularly in Sub-Saharan Africa, where the NTD present the highest prevalence. There are few institute in Africa taking the opportunity of genomic era that are focused and committed to the development of scientists with excellent competence and capacity in genomic. The global effort required to apply genomic science and associated technologies to improve the understanding of health and disease in diverse populations is undeniable today. In fact, identify individuals and populations who are at risk for developing specific diseases such as NTDs, and to better understand underlying genetic and environmental contributions to risk could greatly contribute in finding sustainable responses. And the large diversity of African continent that constitute genetic complexity represents an enormous opportunity to utilize such approaches to benefit African populations and to inform global health.

The most involved institution in the training of human resources in genomic are Pan African based in South Africa and Nord Africa. Few are developing in west Africa mainly in Nigeria, Ghana and recently introduced in Mali.

6.1 H3Africa

The Human Heredity and Health in Africa (H3Africa) constitute one of the largest consortium with the objectives to facilitate fundamental research into diseases on the African continent, while also developing infrastructure, resources, training, and ethical guidelines to support a sustainable African research enterprise. By his constitution, H3Africa is led by African scientists, for the African people. Today, H3Africa initiative consists of 48 African projects that include different data set from population-based genomic studies of common, non-communicable disorders such as heart and renal disease to communicable diseases such as tuberculosis. Those studies are designed by African scientists with the objective to identify hereditary and environmental contributions to health and disease. While H3Africa is working mainly in developing African scientist's capacity, the consortium is also committed to support many crucial capacity building elements, such as ethical, legal, and social implications research; training and capacity building for bioinformatics; capacity for biobanking; and coordination and networking (**Figure 4**).

As a continental consortium, today H3Africa constitutes as one of the most important supporting institutions to African researchers and also contributing to the establishment of effective collaborations among African researchers. Through these different collaborations, the consortium is able to generate specific and large data set in relation to the global health. The consortium is supporting different initiative in Africa such the West African Center of Excellence for Global Health Bioinformatics Research Training in Mali, the Eastern Africa Network for Bioinformatics Training (EANBIT), the Collaborative African Genomics Network” (CAfGEN) and the Integrated approach to the identification of genetic determinants of susceptibility to trypanosomiasis (TrypanoGEN) in Uganda.

H3Africa is also collaborating with the African Center of Excellence for Genomics of Infectious Diseases (ACEGID) at Redeemer's University in partnership with academic, clinical, and research institutions in Nigeria, Sierra-Leone, and Senegal to develop African research capacity in genomics by building a critical mass of well-trained scientists.

In order to boost the genomic concept and interest African scientists to this revolutionary scientific area, a group of stakeholders from the H3BiotNet (Pan African Bioinformatics Network for H3Africa) and the African Society of Human Genetic

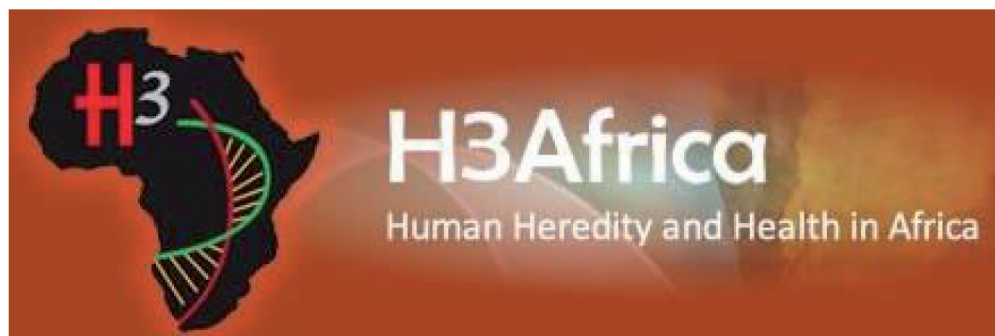


Figure 4.
H3Africa, A Pan African network to study genomic and environmental determinants of common diseases of African population.

launched in 2016 in Dakar in Senegal, the African Genomic Medicine Training initiative called AGMT.

The African Genomic Medicine Training Initiative (AGMT) was initiated by a Working Group made up of volunteers from across the globe with a clear vision to “*increased effectiveness of Health Care in Africa through the application of Genomic Medicine*”. This initiative includes several mission:

Design and develop Genomic Medicine training for African-based healthcare professionals.

Develop competency-based Genomic Medicine curriculum for healthcare workers in Africa.

Develop and implement flagship training courses based on the collaboratively developed curricula.

The first iteration was run in 2017 with 19 classrooms in 11 countries, 1 online class, and 225 students registered.

The second iteration is running from March to July 2019 as a professional development course.

The purpose of this Professional Development Course is to provide genomics and genetics education to nurses based in Africa emphasizing the practical application of content into learners’ current settings and roles. In addition to contributing increasing knowledge in the genetics of African health issues, this second iteration of the AGMT initiative aim to develop skills in Genetic counseling, Community engagement/Ethical conduct in research, and patient care and development of health promotion material. Therefore, this course seeks to support improved Genetics & Genomics knowledge, attitudes and skills for genomic medicine in Africa.

6.2 Genomics Africa

Genomic Africa is a training program organized by the Kwazulu-Natal Research Innovation and Sequencing Platform (KRISP) with the aim of “*Bringing genomic technologies to Africa to fight our great challenges: loss of biodiversity, famine, migration and diseases.*”

As a Flagship program of the South African Medical Research Council (SAMRC), KRIS develops collaboration with DIPLOMICS ASSOCIATED LABORATORIES which is a South African Research Infrastructure Roadmap (SARIR) program of the Department of Science and Technology (DST). To reach his mention, different training programs are developed and run each year at KRISP Genomics Africa targeting several diseases including tropical neglected disease as well as the development of new technologies to help in Africa including Microbiome and Metagenomics Sequencing with Illumina and Nanopore.

There are others genomic training initiatives developed and running in Africa, and even not targeting specifically neglected tropical disease are greatly contributing to human resources strengthening. By helping strengthen human capacity in genomic area, they may help answering how African scientists are prepared to tackle the NTDs in the context of genomic era.

6.3 DELGEME

The Developing Excellence in Leadership and Genetics Training for Malaria Elimination in sub-Saharan Africa (DELGEME) is a new training programme sponsored by the Wellcome Trust Developing Excellence in Leadership, Training

and Science Africa (DELTA Africa) initiative in partnership with the Department of International Development (DFID) and the Alliance for Accelerating Excellence in Science in Africa (AESA). Led by the University of Science Techniques and Technologies of Bamako Mali (USTTB), this genetic and genomic training program is partnering with the Medical Research Council (MRC) Unit in The Gambia, The United States Army Medical Research Directorate (USAMRD-K)/KEMRI Kenya, The Noguchi Memorial Institute for Medical Research (NMIMR)-Navrongo Health Research Centre, Ghana, The National Institute of Medical Research (NIMR) Tanzania, Université des Sciences de la Santé of Libreville, Gabon, Bernhard-Nocht Institute for Tropical Medicine (BNITM) Germany/Kumasi Centre for Collaborative Research (KCCR) Ghana, and the University of Oxford/Wellcome Trust Sanger Institute UK. In collaboration with MalariaGEN (www.malariagen.net) and the Plasmodium Diversity Network, The DELGEME program aims to enrich the pool of African Scientists working in African institutions with relevant expertise to leverage big genetics and genomics data in the drive for malaria elimination in sub-Saharan Africa (**Figure 5**).

In order to reach this objective DELGEME aim to:

To train, retain, and develop Graduates, Doctoral, and Post-doctoral fellows on genomics and bioinformatics across malaria endemic countries.

To develop programs to enhance the understanding and dissemination of genetic data relevant to malaria interventions and eradication program.

Short-term training will be delivered for various trainees including public health officers on genetics, clinical studies, ethics, grant writing, grant management, leadership development, etc.

Formal long-term curricula (big data science, biostatistics, health informatics, genomics, cell biology, molecular biology, and bioinformatics) will be designed and implemented with contribution and oversight from a wide range of local and International Faculty and relevant advisory boards.

6.4 Others genomic training institutions/programs in Africa

Interestingly from last year, genomic education is progressively taking off in Africa. Indeed, many genomic training programs at the countries or regional level are entering in operational phase. Many of them are mainly supported by H3ABioNet which organizes a variety of high quality courses and training events covering various aspects of bioinformatics from general introductory topics to more



Figure 5.
The Developing Excellence in Leadership and Genetics Training for Malaria Elimination in sub-Saharan Africa (DELGEME) program.

specialized ones such Next Generation Sequencing and Genome Wide Association Studies analyses. Indeed, H3ABioNet is comprised of 28 Nodes distributed among 17 countries, 16 of which are African.

7. Conclusions

Genomic is a rapidly evolving medical field relying on technological advances and with a direct effect on disease treatment, control, and elimination including such neglected tropical disease. Nevertheless, in Africa, the introduction, the development, and the application of genomic are variously appreciated. Interestingly, there are institutions greatly introduced in genomic era and they are working to spread the knowledge to the rest of the African continent as pioneers with support from some North European and American institutions. Hence, even there is still limit critical mass of African scientists well trained in this new scientific domain to contribute to the diseases control and elimination in general and neglected tropical disease in particular, there is room of hope since there is positive signal within the continent. However, this provided the strongest possible argument in favor of working together in south-south collaboration way on steps to bridge this genomic divide. The challenge exists but still remain surmountable.

Conflict of interest

There is no conflict of interest.

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Author details

Issiaka Soulama

National Centre for Training and Malaria Research, Ouagadougou, Burkina Faso

*Address all correspondence to: soulamacnrfp@gmail.com

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