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Perspective

Translation of genomic epidemiology of infectious pathogens: Enhancing African genomics hubs for outbreaks



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ABSTRACT

Background: Deadly emerging infectious pathogens pose an unprecedented challenge to health systems and economies, especially across Africa, where health care infrastructure is weak, and poverty rates remain high. Genomic technologies are vital for enhancing the understanding and development of intervention approaches against these pathogens, including Ebola and the novel coronavirus disease 2019 (COVID-19).

Discussion: Africa has contributed few genomes of severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) to the global pool in growing open access repositories. To bridge this gap, the Africa Centre for Disease Control and Prevention (ACDC) is coordinating continent-wide initiatives to establish genomic hubs in selected well-resourced African centres of excellence. This will allow for standardisation and efficient and rapid data generation and curation. However, the strategy to ensure capacity for high-throughput genomics at selected hubs should not overshadow the deployment of portable, field-friendly and technically less demanding genomics technologies in all affected countries. This will enhance small-scale local genomic surveillance in outbreaks, leaving validation and large-scale approaches to be taken at central genomic hubs.

Conclusion: The ACDC needs to scale-up its campaign for government support across African Union countries to ensure the sustainable financing of its strategy for increased pathogen genomic intelligence and other interventions in current and inevitable future epidemics in Africa.

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Brief introduction of COVID-19 situation

The novel coronavirus disease 2019 (COVID-19), a viral outbreak caused by the severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2), first arose in Wuhan, China, in December 2019, and it was declared a Public Health Emergency of International Concern on January 30, 2020 (WHO, 2020b). Seven months into the COVID-19 pandemic, the number of cumulative cases continues to steadily increase. As of August 3, 2020, 17,660,523 cases had been detected, with 680,894 total deaths globally. Africa has borne 4.5% of global morbidity and 2.0% of fatalities (WHO, 2020a).

Costly investments required for COVID-19 intervention

COVID-19 has placed an unparalleled burden on the health systems and economies of all affected countries, with a projected serious impact on African countries that are already saddled with weak health care provision and economic systems. Apart from the immediate economic losses, there are considerable costs associated with the containment of the pandemic, from laboratory testing to personal protective equipment, treatment and personnel costs. Mass testing is being advocated, and this requires molecular techniques, the current gold standard for COVID-19 detection, as recommended by the World Health Organisation (WHO) (WHO/Africa, 2020). However, these polymerase chain reaction-based tests do not provide information on the origin of an infection, possible mutations in the virus or transmission links in clusters of infection. Monitoring the evolution of the virus and transmission networks is essential for containment strategies, and this requires obtaining genomic data by sequencing viral isolates from infected

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persons. The use of high-throughput next-generation sequencing tools can provide additional data to refine strategies to fight against COVID-19. Examination of the nucleic acid sequences of a virus enables detailed understanding of its genetic content, evolution and diversity both within and between local communities. The information obtained from sequencing is also essential in the design of effective vaccines, drugs, efficacy monitoring and transmission studies. As the virus continues to evolve in African populations, African countries and the Africa Centre for Disease Control and Prevention (ACDC) must facilitate investment in costly laboratory technologies that will ensure that the strains of SARS-CoV-2 circulating in Africa are included in the design of new interventions.

African SARS-CoV-2 genomes in publicly available sequence databases

While SARS-CoV-2 sequence data are an integral part of the information used for making decisions on other continents (Lu et al., 2020; Zhu et al., 2020), Africa has yet to integrate this information into our decision making for managing COVID-19 outbreaks within the continent. This is primarily due to limited skillsets and infrastructural deficiencies (Devex, 2020). To the present, only 900 SARS-CoV-2 genome sequences from 14 African countries have been uploaded out of a total of 62,267 whole-genome sequences in GISAID (GISAID, 2020), an online database for the rapid sharing of viral genomes and clinical and epidemiological data. Africa has recorded approximately 642,387 cases and close to 10,789 deaths from COVID-19 (WHO, 2020a). On a global scale, this significantly outweighs the available African SARS-CoV-2 genomes, putting the continent at disadvantage in global genetic epidemiology studies of SARS-CoV-2 and in consideration for the design of vaccines that could provide broad potency against all virus strains circulating in the continent. The above narrative could be different if each country appreciated the need for genetic data and deliberately empowered at least one molecular laboratory involved in COVID-19 detection and diagnostics with sequencing technologies. The transition to sequencing viral genomes could adopt cost-effective, easily deployable and portable sequencing platforms with less restricted access to reagents and readily available protocol-sharing global networks.

During an epidemic or a pandemic, most countries close their land borders and airspace to restrict movement and curb the spread of the infection. If viral sequencing platforms are not available in a country, it must rely on shipping samples to laboratories elsewhere to generate sequences. Doing so allows real-time contributions to global sequencing challenging and unrealistic. Therefore, while ACDC aims for a coordinated, centralised approach to high-throughput next-generation sequencing using platforms such as the Next-seq and Hi-Seq, the generation of moderate-quality data using Miseq, capillary electrophoresis and Nanopore technology should be prioritised. This model has been tested in the United Kingdom with reported success (GenomicsEngland, 2017).

Biomedical research challenges impeding epidemic response in Africa

A lack of concerted financial commitment, skilled personnel and advanced infrastructure are top amongst the many hurdles facing biomedical science research in Africa (Omoleke et al., 2018; Gilbert et al., 2020). Unlike in the global North, African capacities are heterogeneous, with wide differences between most sub-Saharan African countries and South Africa, for example. Moreover, research activities are little coordinated across borders, disallowing meaningful continental approaches. This is largely driven by lack of political will and buy-in by various African governments,

which continue to consider investments in advanced scientific technologies as low priority despite the large burden of infectious diseases. The cost of acquiring and maintaining new technologies such as Next Generation sequencing platforms remain relatively high and outweighs other interventions. For instance, sequencing the genome of a virus or other pathogen can cost tens to several hundreds of dollars, depending on the sequencing platform used, the number of samples available and the depth of data required (Weymann et al., 2017). At the moment, direct budgeting and investment by African governments in medical research remains minimal, despite the pledge signed by all countries in the African Union to commit 2% GDP to investment in research, under the auspices of the ACDC designated body for coordinating disease control across the continent. Beyond data-generating platforms, there is also an acute shortage of expertise in genetic and genomic data analysis and interpretation for translation into public health interventions. This lack of trained human capacity has resulted in heavy reliance on research collaborators and donor funding from the global North for limited quality and few valid data outputs. Hence, the benefit of using genetic epidemiology data in real-time to inform policy is currently largely unrealistic.

Example institutions in Africa with impactful genomics platforms

Despite the challenges within the continent, there are a small number of medical research centres or institutions in Africa that are changing the narrative. These have been largely funded by external donors, including the NIH, World Bank, Wellcome Trust and the African Academy of Science. Taking West Africa as an example, the following institutions have established genomics platforms with evidence of data generation in publications or deposition in open access repositories: The Medical Research Council Unit, The Gambia at London School of Hygiene and Tropical Medicine (MRCG-LSHTM); West African Centre for Cell Biology and Infectious Disease Pathogens (WACCBIP), University of Ghana; Institute Pasteur Dakar, Senegal; Malaria Research and Training Center (MRTC), Mali; The African Center of Excellence in Genomics of Infectious Pathogens (ACEGIP), Nigeria. In Central Africa, genomics centres are almost entirely absent, with the exception of Institut National de Recherche Biomédicale DRC. Eastern and Southern Sub-Saharan Africa have many more institutions, including a large number of public, private and commercial platforms in South Africa. These institutions, supported by funders, are investing significantly in infrastructural and human capacity development. They provide platforms for teaching and research and are building momentum for advanced molecular bioscience research in West and Central Africa.

Emerging coordination and networking of genomics and testing hubs

The ACDC has taken up a coordinated continental perspective to define strategies that can address some of the challenges impeding the derivation of full benefits from currently available technologies that will facilitate interventions against SARS-CoV-2 and future emerging pathogens (ACDC, 2020). The larger goal is to set up centralised genomics laboratory hubs, coordinated by the Pathogen Genomics Intelligence Institute (ACDC, 2020). The main goal is to strengthen and link health systems with these institutions for the effective surveillance, detection, tracking and monitoring of outbreaks before they occur across the continent. To substantiate their efforts, Illumina, a leading genomics company, has donated \$1.4 million in equipment, software and reagents to the region through the ACDC (Devex, 2020).

Recently, the African Union Commission/ACDC formally launched the Partnership to Accelerate COVID-19 Testing (PACT) on June 4, 2020. The goals of PACT are to improve testing for COVID-19, enhance the

training of health workers across the continent, establish a central procurement system at ACDC and deploy one million community health workers to perform contact tracing of confirmed cases at the community level (ACDC, 2020). As this initiative is coming in the middle of an ongoing outbreak, the impact of its interventions might not be manifest in the short term. However, the ACDC, as a new institution, could take advantage of the experience of already established centres such as the European and American CDCs to put into place regulation and structures that will facilitate and sustain cross-border collaborative platforms for more robust epidemic preparedness, readiness and response across the continent in the near future.

Conclusion and recommendations

Despite the efforts of ACDC to promote centralised genomic hubs, a situational analysis of continental needs and priority areas in epidemic preparedness and genomic intelligence is necessary. The current state of institutions, infrastructure and human resources for data generation, management and analysis needs urgent attention. To respond to epidemics such as COVID-19, genomic data generation for real-time decision making could be enhanced by the adoption and decentralised application of small, portable and easily operated experimental tools such as the Oxford Nanopore technology-MinION sequencer, Illumina MiniSeq or the BGI-DNBSeq across all countries. These easily deployable, user-friendly field-based technologies were instrumental in the sequencing of the Ebola virus (EBOV) during the last outbreak in West and Central Africa (Arias et al., 2016; Hoenen et al., 2016; Quick et al., 2016). The data generated were useful for strategizing and ensuring the efficacy of interventions, including tracking and stopping the spread of EBOV and evaluating vaccine efficacy.

Already established genomics hubs strategically located in the west, east, south and north of the continent could collate samples from each country for validation and high-throughput production of data because they have the requisite technical expertise and infrastructure. In this regard, standardised operating procedures, quality-assured operations and data curation strategies can be assured and disseminated as well. This can provide a benchmark for future comparative data analysis.

To build on its current gains, the ACDC should engage in a massive campaign for stronger political commitment African Union member states to support funding for genomics as a tool for the surveillance and monitoring of disease outbreaks. Better engagement approaches will enable government buy-in and ensure the financial strength and sustainability of established genomics institutions for rapid containment of emerging infectious disease epidemics.

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