Genetics for Africa – Strategies & Opportunities

Human genetic research for Africa: Workshop Report

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International Centre for Genetic Engineering and Biotechnology
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Cover photo: Children in Ngarenairobi, Tanzania; Dr Bernie Jones

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Executive Summary

The Genetics for Africa – Strategies and Opportunities planning grant aims to investigate the extent to which genetic research in and for Africa has a direct relevance to social and economic development, and the extent to which improved communication can assist in public understanding, acceptance and uptake of the research outcomes and to more appropriate regulation.

The project is investigating these matters through three workshops, on new plant breeding technologies, animal and human genetics research respectively.

The third workshop, on human genetic research for Africa, was held on 25th and 26th February 2016 at the International Centre for Genetic Engineering and Biotechnology in Cape Town, South Africa.

The first and most important issue emerging is that in this field humans are both the subjects and beneficiaries of research. Understanding of the principles of genetics and how they relate to health and heredity and to medical research is therefore doubly important, so that people can properly consent to the research being carried out on them and understand the risks and consequences of participating in that research and what the research might uncover, as well as being able to appreciate and take up the results of that research as eventual customers, patients or members of the general public.

Engagement, consent and public appreciation are complicated by issues of language (many indigenous languages may lack the concepts necessary to easily explain the issues and risks), education and literacy levels, the challenges of maintaining long-term engagement with communities in which research is being carried out, and the lack of genetic counsellors and professionals trained to communicate in the field of medical genetics. In addition ethical and societal issues come into play, especially from inability of large sectors of the population to access healthcare other that via medical research, which skews the principles behind informed consent and may increase pressure to participate in studies.

The research potential for human genetics in the continent, however, is huge. There is a high burden of disease in the African continent, and a large number of diseases – communicable and non-communicable – that have a disproportionate impact on Africa (sickle cell disease, ebola, and HIV/AIDS, for example). Many of these diseases lend themselves to genetic treatment, characterisation or diagnosis, and modern technology is making it possible to bring the benefits of medical genetics to the general population, rather than this being an expensive science whose benefits are reserved for the few who could afford it.

With effective (genetic) diagnosis, for example, 70% of birth defects could be prevented or ameliorated. But this would need to rely not only on widespread availability of genetic testing resources and the expertise to administer the tests, but also expertise in genetic counselling and ability through the public health systems to act on the results of the genetic tests. Such expertise, capacity and infrastructure are not widely available in Africa at the moment.

And the recent Ebola outbreak showed how appropriate introduction and use of modern genetic technology (in particular the ability to

rapidly sequence virus samples from diseased individuals) can significantly assist the management of public health emergencies, by lending rapid insights into patterns of transmission of communicable diseases and, more importantly, highlight atypical cases that may demonstrate gaps in the understanding of a disease outbreak.

The origin of humans in Africa – which is in itself an important and still under-researched and locally under-appreciated area – means that African populations have a greater genetic diversity than in other regions of the world, making research more complicated, expensive and – in some cases – means that commonly used global research tools and diagnostics are unsuitable for use on the genomes of African populations. Of the most commonly used GWAS SNP arrays, for example, 40% of the data points are unsuitable for Africa.

Health and medical research facilities are widespread in the continent, and even work on issues and conditions which are genetic at heart. But research infrastructure and capacity is often poor, and awareness and expertise in medical genetics, even in the research community of the continent, is still suboptimal. Medical doctors in Cameroon as recently as 2006 were unaware that genetic testing for sickle cell disease and Down's syndrome were possible.

Human genetic research and genetic education and training is insufficiently-well funded on the continent, there is a lack of international collaboration, a lack of research infrastructure on the continent, and there are structural issues (such as poor broadband connectivity, regional cloud storage and data processing capacity, material transfer agreements) that further restrict research.

Whilst there are initiatives, like H3Africa and the African Society for Human Genetics, that are trying to carry out relevant research, build the capacity of their own research collaborations and develop processes and resources to help them carry out and communicate that research, address the issues of local capacity and share their resources across the continent, they are still small and represent a tiny fraction of the research community across the continent.

Meeting participants made the point quite sharply that very visible international collaborations, like H3Africa, can even have a masking effect in that the outside research and funding community erroneously believes that they represent all of the research capacity and diversity of the continent, and other less visible and less well connected research institutions suffer even more from being overlooked. And whilst H3Africa activities seem to be aiming towards broader dissemination of their resources, principles and communications tools in subsequent phases of the projects, it is a highly ambitious proposition that these small individual research initiatives can effect change across the entire continent.

There is an urgent need for better public engagement and awareness-raising in the area of genetics, to build the capacity of the research and policymaking community in genetics and genomics, and to facilitate more international collaboration in order to translate the rich potential of the African human genome and research into realisable benefits for the population.

Medical and research professionals have shown a degree of enthusiasm for better communicating their science and knowledge, and the example of sickle-cell disease (where

despite a lack of understanding of formal genetics, many communities in Africa have a basic awareness of the issues of risk, inheritance and how the disease can be carried as a recessive trait) shows that existing knowledge of common conditions can act as an entry-point to public awareness and education initiatives in genetics and genetic research.

Long-term community engagement, use of local languages, and the broader use of the arts and public media (cartoons, local radio) have all been identified as effective in increasing the power of public outreach efforts. But it is still a challenge for medical research professionals to dedicate sufficient time to both communicating and carrying out their research, especially when the communication challenge is so broad and has so many different potential audiences – research subjects, specific local communities, the general public, ethics committees and regulators, national decision-makers and health professionals to name but a few.

And to ensure that initiatives like H3Africa do not have the unintended effect of masking other good research on the continent, it is important to enhance the public visibility of the other human genetic research establishments across the continent, so that they too can begin to benefit from enhanced international dialogue and collaboration, and – by networking them more effectively across the continent – they can share common resources and tools to build capacity and enhance public benefit from human genetic research across Africa.

“An entire continent could be left out of the promise of genomic medicine, if Africa is not included in future genomics studies”

Session 1: Introduction

Genetics for Africa – Strategies & Opportunities (G4ASO)

Dr Bernie Jones, Co-leader, G4ASO

The Genetics for Africa – Strategies & Opportunities (G4ASO) planning grant was developed in response to the feedback received to Biosciences for Farming in Africa (B4FA), a three-year project that focused on communication and dialog activities on crop genetic improvement for agricultural productivity. The B4FA media fellowship trained 160 media professionals from four Sub-Saharan African countries: Ghana, Nigeria, Tanzania and Uganda, and established a lively network of media and research professionals. However, many participants felt strongly that keeping the focus solely on plant genetics was artificial, since genetic research on animal and insects is also critical for increasing the productivity and profitability of agricultural systems. In addition, human genetics research is thriving in the continent and is very important not only for addressing major health challenges specific to Africa, but also for deepening understanding of the evolution of mankind, since the continent is the cradle of our species. Those with a particular interest in the science involved could see that the principles of genetics and genetic research applied equally to crop, animal and human investigations, but were frustrated that there was no opportunity under the project to further investigate the work being done in the animal and human fields.

B4FA also drew attention to the fact that despite the richness in indigenous research projects addressing important national priorities, little of this research is generally known to the general public or even to members of the scientific community working in other fields or outside the country. Increasing the visibility of the range of research activities in the continent would facilitate streamlining of priorities, reducing duplication, encourage collaborations and help to prioritise national and international funding for increased impact.

G4ASO aims to answer three key questions:

1. **Where** – which African countries should be the focus of future genetics communication?
2. **Who** is active in genetics research in the continent? And what are motivations?
3. **Which** areas of genetics should be showcased?

A follow-on initiative on communication and outreach activities focused on genetics in Sub-Sahara Africa would therefore have three main objectives: 1) Cover genetic research more widely, including in animals and humans; 2) Promote public outreach in more African countries; 3) Uncover and celebrate African research and researchers.

The workshop on human genetics covered in this publication was the third and final in a series of three focused two-day planning workshops organised for each topic (plants, animals and human genetics). The first, held in July 2015 in Cambridge, United Kingdom, reviewed recent advances and applications of the new plant breeding technologies (NPBTs) and epigenetics. The second workshop was held in Nairobi, Kenya, in September 2015, and reviewed existing initiatives in animal, fish and insect genetics.

The B4FA experience

Dr Claudia Canales, Co-leader G4ASO

Biosciences for Farming in Africa (B4FA) was a three-year initiative intended to develop a model for promoting dialogue and communication in the field of crop genetic improvement, in order to help increase the uptake and impact of national research initiatives particular by smallholder farmers in the relevant countries. The project focused its activities in four target countries: Ghana, Nigeria, Uganda and Tanzania. The underlying premise is that just by adopting currently available knowledge and technologies, farm productivity in a smallholder setting could increase by up to a factor of four. Communication of research and outreach with the aim of enhancing uptake therefore has very important implications for livelihoods and overall development outcomes.

B4FA consisted of three main activities:

1. Production and dissemination of two publications: Insights and Viewpoints. These are collections of personal accounts by global opinion leaders with experience in African countries about the potential benefits, concerns, applications and consequences of new genetic technologies for farming in Africa. In addition, a dedicated website, www.b4fa.org, was developed to explain the science that underpins plant genetics and plant breeding with a clear focus on African crops, as well as to serve as a platform to more widely disseminate the publications of the B4FA media fellows.
2. Media Fellowships for the effective communication of genetics formed the second pillar of B4FA activity. Due to a lack of focus on science reporting as a skill and profession in Africa, and a scarcity of funding for research outreach activities, the technical knowledge and understanding of science by journalists and editors in Africa is generally low. B4FA ran a series of long-term, professional development Media Fellowships based around genetics, crop improvement and modern agricultural bioscience. The best Fellows from all the programmes were further engaged in a final series of science reporting masterclasses in the four countries involved. A total of 160 journalists and editors from print, radio and television were enrolled in the Fellowships, selected by competitive application in a programme that offered technical training combined with field-visits, mentoring and support. The Fellowship also offered opportunities for long-term networking amongst the Fellows, and between them and the agricultural research community of their country. B4FA Fellows attended, by competitive application, field trips to 50 research institutions and commercial and experimental facilities in their own countries, and to nine international conferences in the UK, the USA (World Food Prize conference and AAAS), Kenya, Ghana (the FARA African Agricultural Science Week), and Ethiopia (the African Science Academies' Annual Conference). As a result, more than 1,000 print, online and broadcast pieces were published during the three years. Many fellows are still actively reporting on the topic.
3. Studies to strengthen agricultural extension services or their alternatives,

which are critical for ensuring that new advances and technologies are known and used by farmers. These studies were carried out in collaboration with the National Institute of Agricultural Botany (NIAB), UK; Reading University, UK; Makerere University, Uganda and the NGO Farm Africa in Tanzania.

The ICGEB Cape Town Component

Iqbal Parker, Director ICGEB Cape Town

The International Centre for Genetic Engineering and Biotechnology (ICGEB) was established as a Centre of Excellence for Research and Training that specifically addresses the needs of developing countries and economies in transition. ICGEB is made of three Components (Trieste, New Delhi and Cape Town) and a network of Affiliated Centres. Despite its extended global membership (ICGEB is composed of 61 Member States and 24 Affiliated Member States) few African countries are represented, although the situation is improving and a number of countries in the continent are in the process of joining ICGEB or have expressed an interest in doing so.

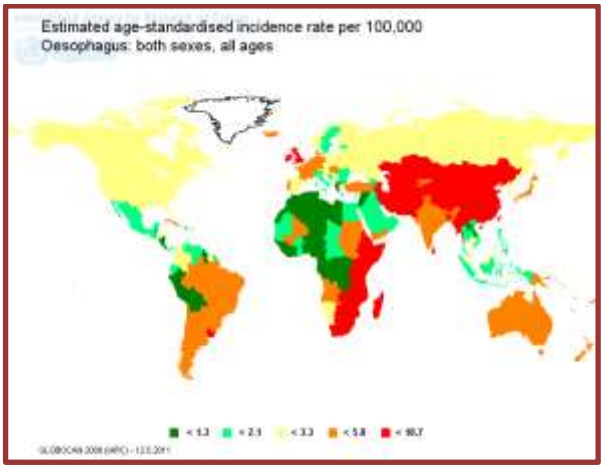
Of the three Components that make up ICGEB, the Trieste component is primarily engaged in basic research, while the New Delhi component, with 400,000 employees and 40 large research groups, is focused on infectious diseases and agriculture. The ICGEB Cape Town Component was established in 2007 to specifically address the needs of African countries since it became apparent that they were not benefitting from the funding and research opportunities at the New Delhi Centre. ICGEB Cape Town is entirely funded by the South African Ministry of Science and Technology, and its main objective is to train students and post-doctoral researchers from Member Countries in basic and applied research skills. One of the requirements for receiving ICGEB training fellowships is the commitment by the recipients to return to their country of origin and participate in building the national research capacity.

ICGEB also awards research grants for initiatives in Member Countries, funds pre- and post-doctoral fellowships, and also sponsors courses and workshops, such as the Biosafety Unit, and genetic modification training held four times a year. While the CT Component also hosts a number of European fellows, funded by their own countries, South African nationals are only eligible for ICGEB fellowships to work in other Member States. There are four research groups in ICGEB Cape Town: Cancer Molecular and Cell Biology (Prof Iqbal Parker); Cytokines and Disease (Prof Frank Brombacher); Cellular Immunology (Dr Jeffrey Dorfman); Cancer Genomics (Dr Luiz Zerbini); and a Biosafety Unit (Dr Dennis N Obonyo).

Genetics is a central pillar to many key strategic priorities in African countries: in the numan and animal health sectors with respects to communicable and non-communicable diseases (CD and NCD, respectively); for agriculture and food security; for the preservation of the environment in terms of indigenous resources and genetic diversity; and to further our understanding of human evolution, in particular Africa's particular role as the origin of the human species.

Although some of these issues receive particularly prominent international attention and funding, a number of the

challenges in the African continent deserve much more attention than they currently receive. In the area of non-communicable diseases, cancer kills more people than HIV and malaria combined but receives disproportionately little support.



Global distribution of oesophageal cancer

For example, in oesophageal cancer the most prevalent global cases – squamous-cell carcinomas of the oesophagus (SCCO) – occur mostly in developing countries, while adenocarcinoma (which affects the junction between the stomach and the oesophagus) is largely limited to developed countries. While there is a very high incidence of SSCO in a belt of countries in Eastern Africa, the disease is nearly absent from West Africa. The observed distribution of SCCO may represent a founder effect in a southern migrating population in the East of the continent, or perhaps a specific gene-environment interaction. African populations have a very high level of genetic diversity that is still poorly understood, as is the interrelation of specific genetic factors with the environment and disease. But further genetic research into this area is likely to prove invaluable in understanding the distribution of the disease, and therefore ultimately assist in developing effective treatments.

Addressing the question of whether the general public in the African continent is aware that humans originated from Africa, and whether this was a source of pride, Dr Parker responded that whilst the importance of the African centre of human origin is well appreciated in academic circles, this was generally not communicated to the public or in schools in a way that could be well-understood or appreciated, in lay language. He commented that the huge genetic variability in African human populations, whilst it represented a tremendous genetic research resource, also represents a research challenge since that very diversity, both between and within ethnic groups, is still not well understood by the scientific community and potentially makes research more complicated and expensive.

In response of future priorities for the Cape Town ICGEB component, NCD and their relationship with CD are high on the list. While genetic research for agriculture is important, this area is generally funded through different other institutions, at least in South Africa.

The H3Africa Initiative

Dr Michelle Skelton, H3Africa Coordinator, University of Cape Town

Human Heredity and Health in Africa (H3Africa) aims to facilitate the study of genomics and environmental determinants of common diseases with the goal of improving the health of African populations. The objectives of the initiative have a heavy capacity-building focus, including:

- increasing the number of African scientists who are internationally competitive in genomics and population-based research
- Establishing collaborative networks of African investigators pursuing genomics-based disease-oriented projects; train the next generation of researchers and increase the number of African countries that are internationally competitive
- Create/expand infrastructure for genomics research, including bioinformatics and biorepositories
- Establish programs within research initiatives; retain African scientists; and run courses on genomics, genetics, epidemiology, bioinformatics, statistical genetics
- Address ethical, legal and societal Issues
- Improve governance

Principally funded by the US National Institutes of Health (NIH) and the UK's Wellcome Trust, the H3Africa initiative had its origin in a white paper published in 2011[1], designed to stimulate and solicit input and guidance from senior members of the African research community on research priorities for the continent; how best to bring together the best researchers from across the continent into a collaborative structure and network; build infrastructure; and enhance training and research capacity-building objectives. The inaugural meeting of H3Africa was held in Addis Ababa, Ethiopia, in 2012. Subjects prioritised by the initiative and under active investigation by members of the H3Africa consortium include sickle cell disease, ethical issues, the microbiome, trypanosomes, schizophrenia, heart disease, kidney disease and diabetes.

*The **microbiome** is the aggregation of the genomes of all the microorganisms (such as bacteria and fungi, but not micro-animals) that live on and within humans, including on the skin and in the gastrointestinal tract. It has been shown that this microbiome, and the microbiota with which it is associated, can affect response to and progress of disease in the host organism (humans).*

The largest single H3Africa investment is the H3Africa BioNet – a pan-African bio-informatics network composed of 32 research groups in 15 countries in the continent. It offers training courses throughout Africa and provides assistance with tools for data submission and storage (such as eBioKit and NetMap) that help researchers overcome particular issues associated with research, energy and telecommunications infrastructure in Africa, such fluctuations in internet bandwidth (or indeed intermittent connectivity).

H3Africa also has 3 biorepositories funded by the South African National Institutes of Health (NIH) in South Africa, Nigeria and Uganda, which are already operational.

Consortium documents are developed and shared among members of H3Africa to serve as a resource for the rest of the network. Some examples consist of guidelines for data sharing, access and release; community engagement guidelines; policy publications; guidelines for informed consent; and guidelines published by the Data and Bioaccess Committee.

The development of ethics and governance guidelines constitute a very important aspect

[1] h3africa.org/images/PDF/h3africa_whitepaper.pdf

of H3Africa, aiming to ensure that community engagement occurs in the early phases of projects and that all research participants give full informed consent for the research uses for which access to their biosamples and data is required, including potential secondary uses.

The next phase of this work will be to reach out to members outside the consortium to improve the governance of the broader scientific community across the continent, though this be challenging. mGenAfrica, a mobile phone application currently under development, is a tool designed to improve this wider community engagement.

In the Q&A there was discussion about the importance of establishing the original motivation for community engagement. Although this should primarily be aimed at informing and protecting research participants, there is a risk of it being regarded as an exercise to mainly benefit the research community ("what needs to be done to allow us to get the research done").

In response to the question of whether there are sensitivities related to outsiders funding genetic research in African countries and then taking away samples and results, Dr Skelton responded that this is indeed a very difficult topic. Although material transfer agreements are in place, several African countries are currently developing legislations aimed at preventing samples being sent abroad. This poses challenges in itself however, since high-throughput sequencing facilities tend to be located outside Africa and, in bioinformatics for example, there are no cloud-based server farms in the African continent, so loss of control of samples and data is a live issue.

Dealing with illiteracy in dispossessed communities poses another challenge, as does the fact that the genetic research profession uses a large number of technical terms. Maintaining community engagement over a long period of time, the use of local languages (sometimes with the help of interpreters) and the use of local concepts ins metaphors or descriptive terms all help communication. Local radio is also an important medium to promote broad engagement and encourage informed debates on the topic.

H3Africa is currently in its first phase of funding (of five years) which is likely to be extended to a second 5-year funding phase. The point was made, however, that although it represents some of the most internationally visible human genetics research in Africa, not all the human genetics research institutions in Africa form part of the H3 consortium, and managing that "excluded community" is an ongoing strategic challenge.

South Africa's Strategic Health Innovation Partnerships programme

Rizwana Mia, South African Medical Research Council

Under the South African government's mandate to drive the country to being a knowledge-based economy, the Department of Health is exploring solutions for innovative patient treatment in a more cost effective way, in addition to finding a way to address the issue of genetic sovereignty.

The vision of the South African Medical Research Council (SAMRC) is *"building a healthy nation through research and innovation"*, with the mission to *"improve the*

nation's health and quality of life by conducting and funding relevant and responsive health research, development, innovation and research translation". The Strategic Health Innovation Partnership (SHIP) is a new funding opportunity created by SAMRC to develop new and improved vaccines, treatments, diagnostics and prevention strategies to solve the country's most serious health challenges. It is based on the global Product Development Partnership (PDP) model, but applied in the African context, and has the objective to improve the alignment of health research and innovation with the most important health problems in South Africa. SHIP will be implemented through partnerships of a multi-disciplinary nature across public and private institutions to bring together different strengths towards a common goal. As a mechanism to bring government, private and academic funding together, SHIP also enables multiple partners to provide funding for health innovations.

SHIP receives funding from government departments such as the Department of Health, and the Department of Science and Technology, in addition to contributions from international partners such as the Bill & Melinda Gates Foundation, Medicines for Malaria Venture, with a total budget for 2015-2017 of R780 million (approx. 55 million USD).

What does SHIP do?

- Seek, manage and fund multi-disciplinary and multi-institutional product research, and development and innovation projects from prototype to proof of concept
- Develop local and international partnerships to increase the likelihood of success and reduce costs to market
- Develop pathways to facilitate movement of new products and services from the laboratory to the marketplace
- Facilitate the transfer of research outputs into improved health outcomes and/or social benefits
- Enhance the capacity of South African science in improving the health of the nation

Despite the very high burden of disease in the African continent, most of the commercially available medicines have been tailored to the non-African population. The realisation that the people of Africa have the highest degree of genetic variation in the world has spurred the interest of the pharmaceutical sector. There is a need to manage the disease burden and ensure effective treatment is administered.

The continent is currently facing a quadruple disease burden: maternal, newborn and child diseases, and non-communicable diseases are 2-3 times higher than in other developing countries. The incidence of HIV and TB are also vastly higher than the global averages (23 times for HIV and 7 times for TB). High levels of violence (the continent has twice the global average for injuries, and 5 times the global level for homicide) place additional pressure on the health system.

In 2009, 100,000 cases of cancer were reported in South Africa, and this figure is considered a gross underestimation. Cancer is a molecular disease with a genetic etiology (cause) that differs from individual to individual, and hence has spurred interest in exploring personalised medicine. The SAMRC Precision Medicine Programme proposes the customization of healthcare, with medical decisions, practices, and/or products being

tailored to the individual patient. Although still in development, the programme aims to:

- Create a central database of next generation sequencing data to become the proprietary knowledge of the South African genetic diversity
- Help inform patient treatment strategy
- Establish a central biobank database by coordinating the various sample repositories present around the country and enable controlled access
- Establish a functional personalized medicine platform in a coordinated way including cutting edge technology and all relevant role players.

In the discussions following the presentation it emerged that there was no cross-cutting focus on outreach and communications in this programme, and that therefore such activities would be dependant largely on the individual on the project and partnership in question.

Also discussed was the fact that patients in Africa often seek treatment at very advanced stages of disease, due to the financial burden inherent in treatment (for many people treatment is financially out of reach). Therefore a priority for African countries should be prevention.

Lack of quality data is also a challenge to both medical treatment and research. For example, a serious problem is that there are no up to date statistics available for cancer incidence across Africa, meaning the the disease is poorly characterised and understood. The same sort of concerted effort devoted to mapping HIV incidence for surveillance and for the administration of retroviral treatments is badly needed for NCDs.

NCDs, which are largely genetically-determined, are neglected in Africa with insufficient funds devoted to their research. Much more is needed, from surveillance, basic science through to developing and implementing prevention measures. The funding of diagnostics should have priority over development of treatments.

"For decades knowledge of genetics has had a large role in the healthcare of a few patients and a small role in the healthcare of many. We have recently entered a transition period in which specific genetic knowledge is becoming critical to the delivery of health care for everyone"

– Guttmacher and Collins (2002)
New Engl J Med 347: 1512-1520

Session 2: Medical genetic research

The Genetic Basis of Disease

Dr Zane Lombard, University of Witwatersrand

Opening with the adjacent quote from Guttmacher and Collins, Dr Lombard suggested that genetic diseases are fairly common: each year 7.6 million children are born with a congenital disease, and the majority (90%) of these are born in low and middle-income countries. This number does not include complex diseases that affect individuals later in their life and that represent important burdens, such as cancer and diabetes.

The distribution of genetic disease varies among populations with some diseases being more common in specific groups. This may be due to chance/genetic drift; founder effects/isolation of given populations (such as Ashkenazi Jewish and Afrikaner). Very little research has been carried out on founder populations, an important topic that deserved further investigation. Diseases may also remain in populations because of heterozygote advantage or selection, where the presence of one copy of the disease allele is advantageous to the individual even though two copies would lead to development of the disease (such as sickle cell anaemia, a disease with particular African prevalence, where presence of one copy of the disease allele confers the genetic advantage of partial resistance to malaria although two copies would lead to development of the disease).

This information will also be useful to develop new tools in an effort to understand the molecular basis of complex diseases. It is important to shift the focus from rare single gene disorders to common complex disorders, as this will enable moving from treatment-focused health provision to predictive medicine and prevention.

Efforts to understand the molecular mechanisms in common complex diseases, as well as the roles of lifestyle and other environmental factors, needs to build on insights and strategies developed in the study of single gene diseases. Risk factors are important from a public health perspective. In addition, sick individuals who are outliers in the spectrum of genetic and environmental factors linked to disease may have to be identified and perhaps treated different. The scope of analysis is greater, and new tools and customization of existing tools will be required. Africa, as the site of human origin and due to the demographic history of the continent, represents a huge opportunity to fine-map risk genetic loci.

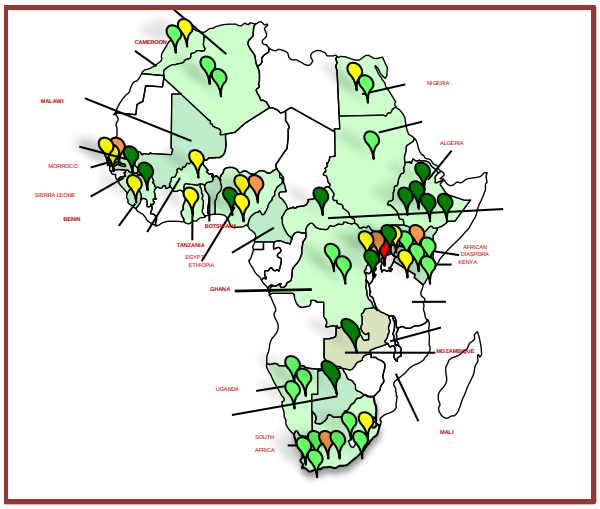
Dr Lombard then introduced the Southern Africa Society for Human Genetics (SASHG), which was established in 2011 to serve the human genetics community of the region, including students, researchers and genetic counsellors. One of SASHG's ultimate aims is to improve the quality of life through an understanding of human genetics and genetic diversity, which is often acknowledged but not sufficiently understood. It also pursues the development of capacity for genomic research in Southern Africa so that all the stages of research can take place within a country, including sequencing but especially analysis, in order to establish a sustainable resource for genomic research and to translate information and knowledge into improvements in human health.

SASHG mission is to:

- Advance the practice and science of human genetics in Southern Africa
- Facilitate contact between those persons engaged in clinical practice, investigative sciences and research in human genetics
- Arrange conferences and symposia on human genetics
- Initiate and maintain contact with similar organisations in other parts of the world

Illustrating the importance of this mission, 70% of birth defects could be prevented or ameliorated if diagnosed early. Medical genetics is the branch of medicine that involves the diagnosis and management of hereditary disorders. It is relevant to assist in family planning and reproductive choices; for community education; genetic counselling and for prenatal diagnosis when appropriate. Such genetic testing and counselling is not widely available in Africa however.

Furthermore, recent literature in genetic testing has highlighted that direct-to-costumer genetics testing of apparently healthy individuals has important ethical and societal considerations. In particular, with respect to how the information will be used at the secondary analysis point. These considerations are true the world over, but recent market availability of such tests in Africa where public awareness of genetics is lower and where less counselling is available, makes these concerns more immediate.



Map of origin of genome sequences for the African CHIP

GWAS *– genome-wide association study – is a research method to examine multiple common genetic variations in different individuals to test whether any of those variants is associated with a particular trait (eg development/susceptibility to a major disease). 100's of thousands of these variations (SNP, or single nucleotide polymorphisms) can be tested for simultaneously using SNP chips – physical microarrays of molecular probes to detect the presence (or absence) of the different polymorphisms in a given sample.*

SASHG is engaged in developing new genomic tools for Africa. The African Custom CHIP Consortium was formed after recognition that currently available GWAS arrays are not suited to studying African populations: of 2.5 million data points on the arrays, 1 million are inappropriate to human genomes on the continent. This poor fit makes genomic studies in Africa much more expensive and difficult than in the EU and US.

The main aim of the consortium is to design a cost-effective GWAS chip with content appropriate for use in genomics studies of individuals from the African continent. Data for the new chip arrays has been collected from 3500 whole genome sequences across the African continent (see map). The new tool should be available for researchers to use later in 2016.

A further medical condition discussed in the Q&A was pre-eclampsia, where a marked difference in incidence can be observed between sub-Saharan African and European countries. This difference is known to have a genetic component, although socio-economic factors and access to healthcare also play a deciding role.

In terms of issues related to genetic testing, there was a feeling among participants that the 'African genome' is still not properly understood. This makes it difficult to establish whether variations detected are medically relevant, and highlights the need for appropriate genetic counselling and medical genetics.

On genetic testing generally, and pre-natal testing of foetuses in particular, there was agreement that awareness in the general population was still low – if tests are performed, this tends to be done more reactively after a baby is born, for validation if the baby displays symptoms of a disease. Participants felt there was a need to change this approach.

Genetic Medicine in Africa: problems, promises and prospects

Prof Ambroise Wonkam, University of Cape Town

A number of predictions about the anticipated progress and benefits of genomic research were made by V McKusick in 2003:

- 2010: Predictive genetics tests available for 25 conditions, although access remains inequitable
- 2020: Gene based drugs for diabetes, HTA, cancer and other diseases
- 2030: Genomic sequencing of an individual is routine
- 2040: Genomics-based health care is the norm

Importantly, the prediction was that sensitive ethical issues and worldwide inequities would persist, resulting in international tension. Indeed, this prediction was borne out with tensions originated in the United States with the company Myriad Genetics[2]. This controversy centred around Myriad's patenting of several human genes, including some relating to breast and ovarian cancer. After a protracted legal process, the US Supreme Court finally ruled in 2013 that "a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated", and therefore held Myriad's patents to be invalid. It did however note that manipulation of a gene to create something not found in nature could still be eligible for patent protection.

The problems of carrying out genomic studies in African countries include the following:

- High cost of implementing research findings
- Current intellectual property regime
- Limited biotechnology and information management capacity
- Lack of technology infrastructure in many African countries

[2] Gold, E. R., & Carbone, J. (2010). Myriad Genetics: In the eye of the policy storm. *Genetics in Medicine: Official Journal of the American College of Medical Genetics*, *12*(4 Suppl), S39–S70. http://doi.org/10.1097/GIM.0b013e3181d72661

- Low level of public and professional understanding of genomics in African countries

In addition, even in those research institutes where the infrastructure for carrying out genomic research is available, such as the University of Cape Town, the infrastructure and capacity for analysing large data sets is often absent. In other countries, facilities are even worse, and international collaboration is rare. Taking the particular example of Cameroon, where Dr Wonkam has worked extensively: before 2009 only a handful of institutions and researchers were part on international collaborative efforts.

A study assessing the knowledge of and attitudes toward genetics among members of the medical profession in Cameroon as recently as 2006 revealed very poor knowledge of the possibility of genetic testing for DNA diagnosis of sickle cell disease (SCD) and for Down's Syndrome, although they all agreed on the importance of genetic counselling.

SCD affects over 237,000 babies born each year in Africa, representing 76% of the global burden of disease. Only one treatment is available commercially. The use of genetics in prevention and care of SCD has several levels: primary prevention, which includes prenatal diagnosis and even parental testing; secondary prevention with guidance with genetic modifiers (such as fetal haemoglobin HbF); and therapy, including transplantation of stem cells and/or bone marrow, and gene therapy (reactivation of HbF levels).

In terms of primary prevention, the initiation of Prenatal Genetic Diagnosis (PND) represented the first medical genetic service in Cameroon. However, the possibility of diagnosis of foetuses raises ethical concerns, in particular with respect to the decision of whether to terminate a pregnancy. African countries have very strict rules on abortion, and only three countries permit terminations on medical grounds. Medical professionals differ in their attitudes towards abortion in Africa as anywhere, but since in African countries they are often also the only source of genetic counselling, this signals the potential for value-based conflicts. The preliminary PND experience in Cameroon also emphasized the need of collaborative effort to overcome the lack of human, technical and structural resources in the country.

Interestingly in some other African countries, there is more widespread understanding and acceptance of genetic testing regarding SCD – for example in certain areas of Nigeria, where local Chiefs mandate pre-marital testing of prospective couples to try to avoid marriages where there is a risk of offspring developing the disease (ie where both parents are carriers). Curiously, this acceptance and action on genetic in respect to SCD in these communities does not seem to translate into broader appreciation of genetics and genetic principles.

SCD is a complex disease and occurs as a result of the interaction of multiple genes and the environment. Secondary prevention and care of SCD can be also provided using the guidance of genetic modifiers. Genetic variation in a number of genes is known to affect the severity of disease and hospitalisation rates. This requires moving from single gene analysis to the study of the effect of modifiers in whole genome sequencing.

A literature review of the distribution of haemoglobin S haplotypes (collections of alleles that tend to be inherited together) was consistent with known historical migrations of African populations, and may also suggest a single evolutionary origin of the SCD mutation, in Ethiopia (the place where the four known haplotypes co-exist). Fine-scale mapping of cis- (beta-globin cluster) and long-range HbS haplotypes indicates a maximum of two independent origins of SCD. Further investigations on this topic are required, as it has important implications for diagnosis and disease and for improving our understanding of the migration of African populations.

Genetics can also play a role in the prevention and care of SCD. Genetic treatment has successfully been demonstrated in mice but this is not yet feasible in humans. Efforts are now focusing on using our understanding of the role of genetic modifiers of the disease to change the phenotype (i.e. the incidence of disease). A number of modifiers with the ability to induce fetal haemoglobin without affecting the neurological development of the fetus for the treatment of SCD have recently been identified and their potential contribution to treatments is being investigated in accepted disease models (umbilical cord stem cells and K562 erythroleukemeia cells).

Therapeutics specific to the African population need to be developed. Nevertheless, given the relatively widespread incidence and public awareness of SCD, this disease and its treatment/diagnosis provides a possible entry-point into the practice and public appreciation of medical genetics and genetic science more broadly on the continent.

As an example of action and engagement with other genetically determined conditions, a collaboration between medical professionals from Cameroon, Switzerland and France investigated and treated 179 patients with genital malformation. Surgical treatment was accompanied by genetic sequencing of the patients. Although still rare, the condition – which has genetic causes – has prevalence around 10 times higher in Cameroon compared to the rest of the world, but is still late- and under-diagnosed. The outcomes of the genetic research have allowed better genetic and incidence maps to be built and will help with future diagnosis and overcoming ethical and social problems associated with the disease and its treatment. This international medical and research collaboration also serves as a model for how the technical and resource gap can be addressed in sub-Saharan African countries.

A further difference in disease in African populations identified through genetics occurs with congenital hearing loss, where it

“Genetics alone cannot save Africa, but without genetics, Africa cannot be saved”

– Dr Ambroise Wonkam

has been shown that the genetic cause in African populations is different than in European and Asian populations.

Summarising his experience, Dr Wonkam felt that the H3Africa programme had planted the seed for capacity building in medical genetic science in Africa, but that this seed now needed to be nurtured, especially by African governments themselves. Further development of academic and industrial research partnerships between Africa, the industrialised world and other developing countries is a priority, as is the development and evolution of appropriate national frameworks within Africa to consider the ethical implications of genetic research and its application in nations' own unique social, cultural, economic and religious context.

And finally, in order to benefit fully from the genetic research they carry out, African countries must develop a critical mass of expertise in bioinformatics to be able to analyse and act on their own data. The Q&A discussed the rapid advances in this area. Mass sequencing of genomes can be done quickly and cheaply, but the challenge remains how to deal with large amounts of data optimally, including both its analysis and transmission (bearing in mind the data bandwidth limitations in many African countries).

mGenAfrica

Victoria Nembaware, H3Africa Training Coordinator, University of Cape Town

mGenAfrica is a communications platform developed following the realisation that H3Africa information, resources and outputs were being communicated only to the research groups directly involved in the project, and that a wider engagement with the research community (and general public) across Africa should be attempted, in particular to involve youths, excite them about genomics and promote medical genetics as a possible career choice. The target age group selected is 18-35, although other ages are not excluded.

Mobile phones were chosen as the medium for communication since most households across the continent will have at least one phone, potentially in communal use, and the penetration of the technology is still on the increase.

H3Africa trainees (typically early-stage researchers themselves) will contribute material by creating profiles; developing podcasts, quizzes and comics; and suggest translations of genomics terms into local languages. They have been requested to contribute at least 1 hour daily over a period of two weeks to generate this material. Users will then vote for winners among the contributors (for clarity/interest of their material) who will then receive a contribution towards their research funds.

The app aims to bring together the experience of individual projects and act as an aggregator. User feedback will also be encouraged through the use of comment sections. This initiative will also create a database of 270 fellows.

Lessons on how to improve communication can be learned from a previous initiative in South Africa, *MAMA SMS Service*, established to provide information and support to HIV-positive mothers, and to help women and understand how to prevent transmission of the disease to their babies. Online/SMS recruitment and communication was

established as a cheaper and more efficient way of communicating to an increased the number of subscribers.

mGenAfrica is currently under development. It will be the first Afro-centric mobile phone based intervention aimed at increasing public awareness in genomics and tightly linked to health promotion.

Sequencing Ebola – the contribution of genomics to controlling an outbreak

Dr Luke Meredith, Division of Virology, Department of Pathology, University of Cambridge, United Kingdom

The Ebola virus (EBVO) is in the *Filoviridae* family and the Ebolavirus genus contains five different species types. The symptoms of EVD occur most commonly 8-10 days after exposure, although in cases they can develop within a longer time frame (between 2-21 days after infection). The first stage of the disease is characterised by joint and muscle pain, sore throat, and fever. These lead to vomiting blood, diarrhoea and extreme fatigue in the second stage. In the third stage of infection, brain damage occurs, accompanied by bleeding from the nose, mouth and anus eventually resulting in multiple organ failure, massive internal bleeding and death in the fourth and final stage. Mortality rates are typically around 50%.

The Ebola virus disease (EVD) was first observed in 1972 in two simultaneous outbreaks in Nzara, Sudan and in Yambuku village, near the Ebola River in Congo. The most recent epidemic started in December 2013, with the first case of Ebola reported in Guinea and the first cases in Sierra Leone diagnosed in May 2014. In August 2014 the World Health Organization announced a state of emergency, with the establishment of steps to control the outbreak including closing the borders of the three countries and the introduction of a raft of screening programs in airports around the world.

In December 2014 *Public Health England* and the *UK Department for International Development* (*DFID)* established the Ebola Treatment Centres at Kerry Town, Makeni and Port Loko in Sierra Leone, and diagnostic facilities were set up at Makeni. By May 2015, 26,300 cases and 10,500 deaths had been reported across Sierra Leone, Guinea and Liberia. The outbreak was declared over in January 2016, although on the same day the announcement was made a new cluster of infections was reported in Sierra Leone.

In December of 2014 the need for a more reliable method of tracking the transmission of the virus through the country became apparent.

Since patient records were often non-existent, and in the face of manpower and skills shortages, genetic sequencing was determined to be the most effective way to track the progress of the virus through the country and to identify and confirm epidemiological links. This is particularly important during the final stages of an epidemic when “atypical” transmission occurs. In addition, sequencing information would enable those managing the outbreak and providing treatment to better understand the evolution of the virus and provide evidence of whether long-term transmission in humans was resulting in the adaptation of the virus to a new host. Finally, it would determine if repeated human-to-

human transmission compromised the efficiency of detection by diagnostic primer sets.

Establishing a sequencing facility required a number of challenges to be addressed. First, only 99 EBOV genomes were available at the time so assembling a pipeline for sequencing was going to be difficult. In addition, a sequencing effort would generate very large amounts (gigabytes) of data for analysis, and the limited access to data for field staff and the lack of local ICT infrastructure ruled out the possibility of sending data samples out of the country: the turnaround time on these would have been 3-6 months, a completely inappropriate timescale for an emergency situation.

The location for the sequencing facility needed to fulfil a number of requirements:

1) have a central location so as to be accessible by road from anywhere in Sierra Leone (in a maximum of 5 hours);
2) it should have reasonably stable power and water supplies;
3) appropriate and sufficient local expertise to staff the facility.

The Mateneh Ebola Treatment Centre in Makeni was chosen as the most appropriate location, and a sequencer was moved into this ebola treatment centre in the middle of an outbreak with financial support from the UK's Wellcome Trust.

The challenges encountered were mostly related to transport, communication, and procurement, rather than associated with the sequencer itself. Getting the equipment into the country took two months. The facility had to be established in a tent, which needed to be appropriately equipped. Temperature control was a particular challenge, since the machine would only function reliably below 25°C in the face of ambient temperatures in the tent of up to 50°C. Wildlife incursion and dust were also daily challenges.

These challenging conditions determined the choice of sequencer: the Ion Torrent Personal Genome Machine, coupled with the Ion Chef robot, was selected because of their reliability, ease of use and repair, small size and affordability. In addition, the workflow was straightforward, and sequencing turnaround could be as short as 24h from the arrival of the samples in the lab.

Over 1200 clinical samples were processed for sequencing, and more than 600 full genomes assembled: over 1/3 of all sequences from this epidemic and the largest dataset produce by any laboratory. Once the sequence data was obtained it was immediately entered in a publicly available database along with patient metadata from each case (age, sex, location, symptoms and date of infection/manifestation) in a decision to move joint research efforts forward as rapidly and effectively as possible. The analysis of the sequences indicated that, surprisingly, defined strains were circulating in each country, with shared ancestry relating back to Guinea strains.

Additional benefits of sequencing became apparent in the later stages of the outbreak with the atypical transmission of the virus. The number of cases and survivors in the outbreak was unprecedented, and these challenged a number of preconceptions about EVD. In particular they raised the question of whether patients with disease symptoms without any previous reported contacts represent undiagnosed survivors. Or whether, in a much more concerning

scenario, they might represent alternative transmission chains.

In one case an asymptomatic patient was diagnosed as an undiagnosed survivor of EVD, after her baby had died of the disease. Another case provided indication that the virus is also transmitted sexually. These cases raised important questions regarding quarantine durations, incubation times, alternative transmission routes and evolution of the virus.

After the emergency sequencing at Mateneh was no longer deemed necessary, the equipment was moved to create a more permanent facility at the University of Makeni: an Infectious Disease Research Laboratory. Local staff have now been trained and have the capacity to operating all the equipment in the facility, including the sequencer. Ongoing projects include:

- Screening for novel pathogens in the region that cause similar symptoms to EVD – lassa fever, yellow fever virus (YFV), dengue virus, rift valley fever (RVF), and Crimean-Congo haemorrhagic fever (CCHF).
- Screening for anti-microbial drug resistance in hepatitis-B and hepatitis-C positive patients by sequencing.
- Working with the London School of Hygiene and Tropical Medicine, Liverpool School of Tropical Medicine and regional hospitals in Sierra Leone on patient screening to allow for cataract surgery on patients in Freetown.
- Monitoring virus evolution and recurrence in EVD survivors, and also for the emergence of Zika virus.

Session 3: Other Approaches

Indigenous concepts of heritability and informed consent

Elonna Obiefuna, Institute of Human Virology, Abuja

The "Out of Africa" theory of human evolution makes Africa particularly interesting for genomics research, to help us understand human population ancestry. Africa is also important because it has a highly heterogeneous population and large variations in the environment, which may impact the expression and phenotype of specific human genes. In medical science, research on African populations can help understanding of the influence of genetic factors on the effectiveness (and any side effects) of drug treatments – an area known as a pharmacogenomics.

Although human genomics research has been conducted in Africa for many decades, large-scale genomics research initiatives such as the H3Africa project are recent.

Previous studies have sometimes found themselves at the receiving end of criticism for exploiting African populations, especially those with a low level of literacy (in particular rural, resource-poor populations) who have not had the benefit of good education, and who may not fully understand the nature of the studies (and therefore cannot give any meaningful consent) – especially when their native languages lack the vocabulary for concepts such as "genes" and "genomics".

The indigenous linguistic and cultural concepts of heritability and comprehension of informed consent (INDIGENE) study aims to explore linguistic and cultural concepts

among indigenous African participants through an H3Africa-funded cervical cancer research project, and to use the results to improve comprehension of informed consent. The study's objectives are:

1) to study the existing linguistic and cultural concepts of genomics including heritability and their relationship to non-communicable diseases in indigenous communities in Nigeria, and
2) to evaluate the impact of incorporation of cultural and linguistic concepts of heritability on the comprehension of informed consent in Nigeria.

In the first phase of the Indigene study, key informant interviews and focus group discussions were conducted to identify existing linguistic and cultural concepts of heritability that are used to understand common heritable traits and diseases in indigenous communities in Nigeria. 50 females and 50 males from diverse ethnic groups and religions living in villages around Abuja, Central Nigeria were gathered into 10 focus group discussions, and key informant interviews were carried out with 50 community and opinion leaders.

The extension of these linguistic and cultural concepts to improve comprehension of genomics research for cervical cancer in Nigeria is being evaluated. The approach is based on the premise that linguistic and cultural concepts of heritability exist in different indigenous cultures in Nigeria, and that these can be identified and usefully extended to enhance the comprehension of genomics research and consent forms in genomics research of a complex disease like cervical cancer.

Analysis of the qualitative data shows that participants were generally willing to discuss their culture and their beliefs about heritable traits, and volunteered several local words and concepts that are used to describe and discuss heritable traits and diseases in their local dialects. Heritability was, for example, often attributed to "blood" in terms of its essence rather than physical properties. In other cases the heritability of traits and the incidence of disease were believed to be the work of a Divinity. Recessive traits were attributed to a "female partner who is the weaker sex", situations where the woman has had multiple sexual partners, and/or specific environmental factors. Participants also believed that the possessor of "stronger blood" is often (but not always) the male partner.

Participants also identified several diseases that they thought were heritable, eg psychiatric illnesses, fevers, and malaria. Some of these diseases were attributed to "ancestral misfortune" – illnesses that run in families because of some historical events in the family. They also identified the presence of discrimination and stigmatization against families with heritable conditions.

These results indicate that the absence of specific words is not a barrier to comprehension, adoption or utilization of concepts. Concepts, words and phrases exist in local African languages that suggest awareness and knowledge of heritable characteristics. These can be harnessed to better explain genomics and improve comprehension of informed consent in the public.

Researchers felt there was a need for African scientists to engage communities through mass media and directly in order to

disseminate these new ideas and vocabulary. Further work is planned to make use of the phrases, local terms and ideas identified in the qualitative study to develop an informed consent document that will be tested among Nigerians for its effect on comprehension of informed consent. New consent documents will be developed and compared in a randomized trial to assess their relative effect on comprehension in comparison to current consent forms. The results and methods will be disseminated on an open source website so that other researchers in Africa can replicate them.

Enhancing youth literacy of Gene *x* Environment contributions to health

Dr Getnet Tadele, University of Addis Ababa

Podoconiosis, a non-filarial elephantiasis endemic in highland Ethiopia, is caused by the absorption of ultrafine silica particles from the soil through the skin of the feet when genetically susceptible individuals walk barefoot. The condition is entirely preventable if susceptible individuals begin wearing shoes at an early age and do so consistently. In Ethiopia, 11 million people are at risk through exposure to irritant soil, and an estimated one million people are affected by the condition nationwide.

Poor understanding of gene-environment contributions to health conditions can lead the public to conceive that genetics (or environment) alone determines health outcomes. This perception in turn can diminish public enthusiasm for the benefits of changing behaviours to reduce health risks. Podoconiosis offers an excellent and concrete context for identifying best practices in enhancing literacy among the youth in Ethiopia regarding gene x environment contributors to health, which could then be generalized to other conditions.

***Podoconiosis** is a type of elephantiasis – a disease of the lymph vessels of the lower limbs which causes the swelling of feet and legs leading to disfigurement and disability. The other main cause of elephantiasis is infection of the lymphatic system with roundworms of the filaroidea variety – hence the distinction between "filarial" and "non-filarial" elephantiasis.*

A study is currently being conducted to compare expert-generated, and youth-generated conceptual understandings (ie mental models) about how genes and environment co-contribute to health conditions, specifically podoconiosis, and identify knowledge gaps which can be addressed through genetic literacy-building activities.

200 affected and unaffected youth (between 15 and 24 years of age) of both genders have been enrolled in the project. Genetic literacy building activities will be undertaken with a test and a control group. The Wolaita zone of southern Ethiopia was selected as a study site due to the relatively high prevalence of the disease in this area.. The project will also explore optimal strategies and settings to conduct literacy-building activities to youth (with an emphasis on under-resourced and low literacy communities) living in highland Ethiopia to improve conceptual knowledge and promote positive attitudes about disease prevention. This work is innovative since little effort has been made to improve health communications about genomics in the developing world.

Results from the initial survey indicate that a number of unaffected youth believe that podoconiosis is inevitable if individuals have a hereditary predisposition (ie if the disease runs in the family). Others believe that some individuals are born with a "weak" body while others have a "strong" body, and this factor determines people's vulnerability to the disease. Wearing shoes and foot hygiene were perceived as important, but mainly for protection against incorrectly perceived environmental factors such as exposure to cold, dirt and insects/snakes bites. A number of participants believed that hereditary predisposition could be prevented through vaccination during pregnancy or at the time of delivery. The link between environmental factors and heredity factors was seldom understood correctly.

The next steps in the project involve a detailed comparison of the two different conceptual models, in order to identify the gaps and design the survey, and to help develop genetic literacy building activities.

Continental policy formulation processes and sustainability of political will

Prof Diran Makinde, NEPAD Agency African Biosafety Network of Expertise

The New Partnership for Africa's Development (NEPAD) is the technical arm of the African Union. NEPAD plays a role in promoting the role of science and technology as a multifunctional tool, with the mission to accelerate Africa's transition to an innovation-led, knowledge-based economy to fulfil the African Union's Objectives of the 2063 Agenda.

NEPAD's six main priorities are to:

1) eradicate hunger and ensure food and nutrition security;
2) prevent and control diseases;
3) improve communication;
4) protect Africa's territory;
5) build communities; and
6) create wealth.

NEPAD also has a policy advisory role, which focuses on strengthening capacity to improve institutional frameworks. It aims to help policy makers understand the importance of research in decision-making.

NEPAD has the following mandate:

- Facilitate and coordinate the implementation of Africa's priority programs and projects;
- Mobilize resources and partners in support of their implementation;
- Monitor and evaluate the progress made;
- Conduct and coordinate research and knowledge management; and
- Advocate the vision, mission, and core principles of the AU and the NPCA.

The research and innovation areas pertaining to the prevention and treatment of diseases include improving the understanding of endemic diseases (HIV/AIDS, malaria, ebola and haemoglobinopathy [3]), maternal and child health, and research into traditional African medicine.

The importance of political will and its sustainability is well illustrated by the case of Bt-cotton, a genetically modified (GM) crop,

[3] Haemoglobinopathy is a single-gene disorder that results in abnormal structure of one of the globin chains of the haemoglobin molecule.

in Burkina Faso. This technology is fully approved by regulatory authorities for cultivation by Burkinabe cotton growers and was widely planted in 2015, constituting approximately 50% of the cotton planted acreage in the country. The GM trait, Bollgard II®, has been introduced into local Burkinabe cotton varieties. Since the launch of first GM varieties in 2009, these have consistently delivered increased yield potential. Bt-cotton benefits to Burkinabe growers include 17% yield increase compared to conventional cotton, 60% reduction in insecticide use, and up to 50% increase in average farm income (INERA, Dec 2014).

Recently some changes have been observed related to the length of fibre (a key property determining the commercial attractiveness, and therefore market value of the crop), which farmers and activists have erroneously attributed to the fact that the varieties grown are GM. Fibre length depends on several parameters, including genetics, environment, soil fertility and timing of harvest. The variation in cotton fibre quality is a function of the interaction of environmental conditions and the genetic background of the varieties. This variation exists between all cotton varieties (conventional or GM) and is independent of the Bt trait.

The absence of awareness of this variation and interaction (and lack of dialogue with experts) in the farming and political community has caused a backlash against the technology which risks damaging the Burkinabe cotton industry.

Session 4: Outreach and human genetic research

Ethical Issues in Genomic Research – Rationale for Community Engagement

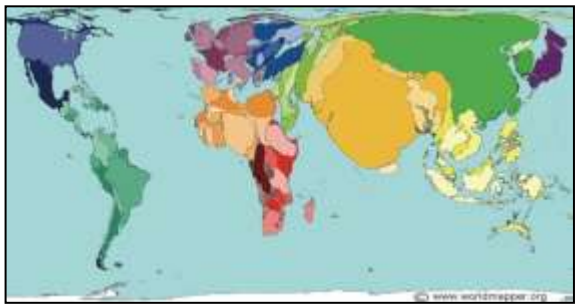
Prof Mogomotsi Matshaba, Baylor International Pediatric AIDS Initiative, Botswana

Botswana has a total population of just over 2.0 million people, a quarter of whom have been diagnosed with HIV/AIDS and are being treated with Highly Active Antiretroviral Therapy (HAART), which decreases the patient's total burden of HIV and maintains the function of the immune system.

HIV/AIDS does not only affect adults: close to 9000 children in Botswana are treated with HAART. The majority of the 2 million children infected by HIV in the world live in Sub-Saharan Africa. More than half a million children are infected every year, and 230,000 children die annually from the progression of the disease to AIDS.

HIV progression in children can be characterised as having an early start; usual start; or a very slow progression. Individuals who are HIV positive but have very low viral levels and no symptoms of disease are referred to as elite controllers, while children who develop symptomatic disease in the first three years of their lives are known as rapid progressors. Identification of the genetic factors that influence whether individuals develop as elite controllers or as fast progressors would be tremendously useful in treatment, and is therefore an important research question.

Disproportionate HIV disease burden in Africa



Population

HIV Prevalence

HIV is only one side of the story. Although tuberculosis (TB) is a global problem affecting a third of the total population (2 billion people), its distribution is also dramatically skewed: 95% of all TB cases and 98% of all TB deaths (1.4 million annually) occur in developing countries. The rate of TB incidence in most African countries is about 20 times higher than that in the United States. TB is also the leading cause of death in HIV-positive individuals. For HIV negative individuals, the lifetime risk of progressing from latent to active TB is 5-10%. However, for HIV infected individuals the annual risk of progressing from latent to active TB is 5-10%, and approximately 60-80% of adults with active TB are also co-infected with HIV-1.

Advanced genetic and genomic technologies have the potential of improving our understanding of the basis of health and disease, and may help in the development of novel treatments and therapies based on the identification of new genetic factors that module the incidence and severity of disease. Although these types of genomic studies are common in industrialised countries, they usually remain focused on non-African populations and they also exclude children, who are likely to differ in their route of disease acquisition and the clinical progression of the disease. Children are those who stand to benefit from and to contribute the most to these therapeutic advances.

The overall aim of the Collaborative African Genomics Network (CAfGEN) is to create a collaborative, multi-disciplinary, multi-institutional, inter- and intra-country network of African scientists, clinicians, and researchers who can use genomics approaches to study gene/pathogen interactions for HIV/AIDS, its co-morbidities, and other diseases among diverse paediatric African populations. It has 5 objectives:

1. Recruit well-phenotyped paediatric HIV and HIV-TB infected patients and create a DNA and RNA biorepository from blood and sputum samples that will be linked to a central clinical database.
2. Evaluate the roles of ‘established’ and novel HIV disease progression alleles in children by sequencing and allelotyping candidate genes and by using whole-exome sequencing in case-control genetic studies of long-term non-progressor status.
3. Use integrated studies of clinical outcomes, DNA and paired RNA analysis in HIV/TB co-infected children to identify

genes that contribute to the progression to active TB.

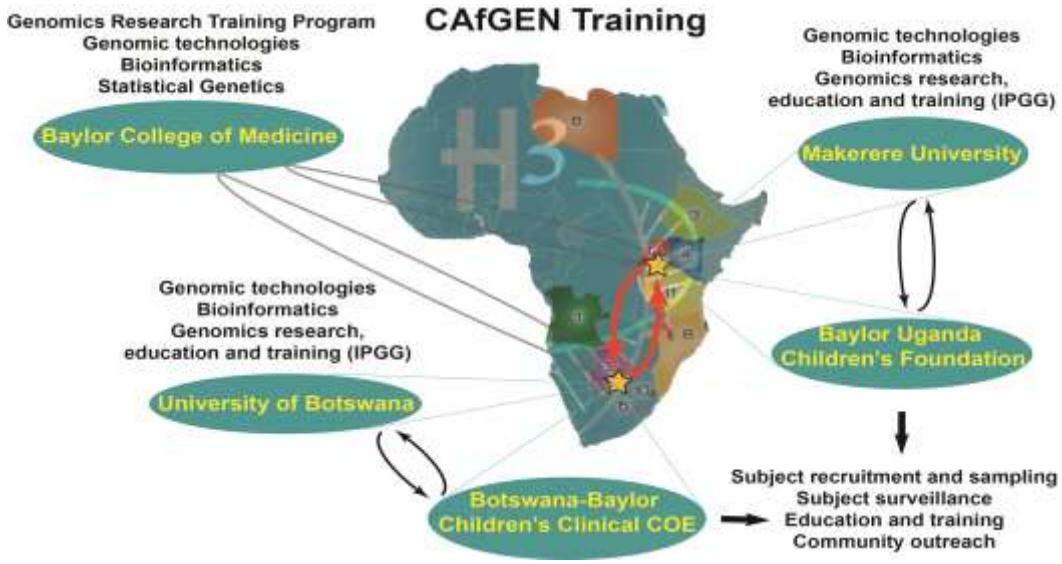
4. Enhance undergraduate, graduate and faculty education in genetics/genomics and provide opportunities for long- and short-term training of scientists and technicians from African universities.
5. Establish genetic and genomic technologies and supporting laboratory and physical infrastructure for large-scale genetic/genomic analyses of common diseases in Africa.

CAfGEN's Botswana and Uganda-based institutions have partnered with Baylor College of Medicine (BCM) in Houston, Texas, to provide access to cutting-edge genomics expertise and resources that will be transitioned to the Africa-based sites. Graduate-level trainees have been selected from the University of Botswana (UB) and Makerere University College of Health Sciences (MakCHS) for a 2-year Genomics Research Training Program (GRTP) at BCM where they will complete coursework and hands-on training in medical genomics and bioinformatics, as well as carry out mentored research with samples from Botswana and Uganda. Efforts are currently underway to procure an ABI 3500 capillary sequencer for UB and an Illumina MiSeq instrument for MakCHS.

This type of research also has important ethical considerations, which include the following:

- Benefiting from medical genomics will be expensive, which has the potential to exacerbate inequalities in health and health care
- There are limited incentives for for-profit entities (eg international pharmaceutical companies) to focus on health problems of developing countries.
- Traditional ethical processes (informed consent, confidentiality, etc) are different because of the nature of genetic information and the social, economic, political, and cultural contexts of developing countries

Genetic studies involve an additional level of complexity and ethical issues because the information collected is about families and can be highly predictive of future health. And interventions can raise eugenic concerns



because they may allow control of which kinds of children will be born. The fact that many countries lack trained bioethicists and the regulatory infrastructure to deal with these issues complicates matters further. More people are needed who are trained to handle genetic counselling (none exist at the moment in Botswana and Uganda, for example). Counselling should always accompany genetic testing, although there are still disagreements on how it should be provided (eg before or after all tests? only for positive tests? for all or only for specific genetic tests?).

Informed Consent is a process that in developing countries should meet international standards but be sensitive to local conditions and practices (for example, the need to involve community leaders without compromising individual consent). The process of obtaining informed consent is particularly important in this context because of:

- Complexity of the decision when there are no, or only limited, therapeutic options.
- Low educational levels in some developing countries.
- Medical care may only be available through research participation (which raises concerns over the exploitation of resource-poor subjects)
- Outside researchers in developing countries often have research agendas different from the health needs of the host country
- Use of information for purposes beyond those for which consent has been given

Community engagement and education are considered essential for both current and future genomics research and training.

Exploring Creative Engagement – Genome Adventures

Abraham Mamela, science communicator and writer

The Arts offer a unique and powerful form of communication and engagement. When exploring science communication and

"In today's multimedia society, the arts are the media, and therefore provide powerful and essential means of communication. The Arts provide unique symbol systems and metaphors that convey and inform life experiences – the arts are ways of knowing"

– Joan Bouza Koster
(2015: Growing Artists:
Teaching the arts to young children)

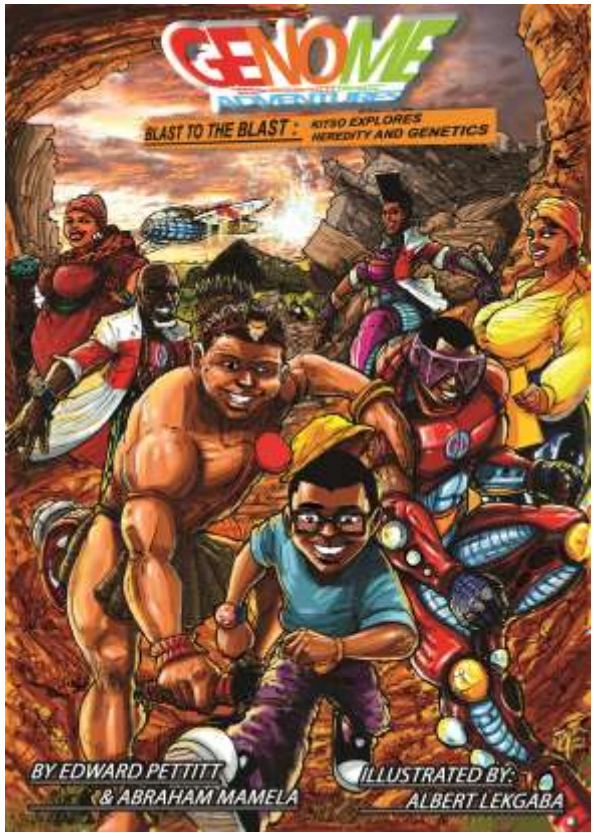
engagement through the arts, *"Art and science meet in wonder"* What is wonder? It is associated to new discoveries. Examples of engagement opportunities through the art include *The Great Sperm Race*[4]: an online game that tells a story of conception, or the use of comics to illustrate the effects of humans on climate change and environmental degradation.

Art in Global Health[5] has set up six artist residencies in six research centres to explore some of the more personal, philosophical, cultural and political dimensions of health research. This project, funded by the Wellcome Trust, aims to engage the public globally with the health research that the Trust funds - in Kenya, Malawi, South Africa, Thailand, Vietnam and the UK. It openly acknowledges the fact that the social relevance of scientific research is shaped by its cultural context.

The 'Genome Adventures' initiative aims to engage and sensitise the general public in Botswana on genomics and biomedical research through the use of comics. The team interacts with scientists and researchers in CAfGEN to understand their work and its potential social implications, to then relate the information in a way that the Botswana public will relate to in animated form. Although the primary target groups are youths, other stakeholders include policy makers, private sector and civil society groups. Comics were chose as the medium of communication because "a picture is worth a thousand words". In addition, comics stimulate the imagination, convey humour and appeal to younger generations.

The objectives of the project are to improve the understanding of biomedical science and research topics such as genomics and HIV/AIDS among 30 community stakeholder groups and with 15 cartoonists/journalists in Botswana; and to produce and disseminate 3,000 comic books on the topic of genomics and HIV/AIDS. The comics will be translated into Setswana, Luganda, Swahili, Hausa, French, Portuguese and Arabic to increase their reach and impact.

The storyline centres around a boy named Kitso who receives a letter inviting him to participate in a genomics study examining TB/HIV disease progression. As he grapples with the many unanswered questions in his mind and whether or not to participate, a



[4] www.channel4.com/programmes/the-great-sperm-race and www.silvergames.com/great-sperm-race for the joint Channel 4 and Wellcome Trust game.

[5] https://wellcomecollection.org/what-we-do/art-global-health

group of "Genome Adventure" superheroes arrive to help him understand what biomedical research and genomics are all about. The books were designed taking into account cultural preferences (including the African perspective of heredity) and embracing local languages and ethnic groups. Social media outlets are being used to disseminate the project.

Biobanking and public engagement

Dr Ciara Staunton, Stellenbosch University, South Africa

Community engagement (CE) is an essential component of biobanking research in Africa. A community needs to be aware of the implications of the research which is being carried out on them, and conversely, the research team needs to explore the local issues that may affect the impact of that research to develop governance policies that are informed by the community and its needs. There is therefore a need for education both of the community and of the research team.

Considerable work has been done on HIV and CE in Africa to develop best practises: the use of Community Advisory Boards (CABs) is now commonplace and South Africa has issued national guidelines on their use. However, H3Africa community engagement guidelines are the only ones that have been developed by and for Africans, with the aim to develop a CE model for biobank research that includes monitoring and evaluation, using the biobank at Tygerberg Hospital as a test case.

Educational tools that have been developed include pamphlets, a 15 min long video, an app and broader engagement activities. These include general information on medical and biobank research, the process of blood sampling, and on issues such as privacy, withdrawal of samples, and return of results. These materials are intended to inform communities, and to assist (but not to be a replacement for) the process of informed consent.

The video, *"I have a dream: a world without HIV"* was envisaged as the first step in engagement for the development of a HIV cure in South Africa[6]. The script was originally based on a 20-page document with the information provided by doctors on HIV, which underwent a large number of revisions and alterations in consultation with the community. To illustrate the iterative process that this stakeholder dialogue has involved, more than 25 drafts of the script have been produced.

Production of the video started by defining the parameters, medical research and biobanking research; developing a wish list of content; and creating a story line with 7 scenes.

Criticisms faced by the video included the suggestion that it was aiming to "sell" the research without including enough information (it is important to inform but not encourage). Important messages to convey concerned funding (it was important to explain that funds were needed for the shipping and the maintenance of cell lines, but that nobody profited from the process).

The initiative also found that it was difficult to communicate the message that taking part in the biobank research does not guarantee the development of a HIV cure, nor does it ensures access to a cure for the participants.

[6] https://youtu.be/oNfw9n5nBtU

Lessons learned include the importance of the process and of broad consultation to obtain consensus; and the need to pay attention to ethical considerations related to the content. The translation of technical terms also proved to be a challenge (language issues), as was the need to balance specificity with the provision of generic information.

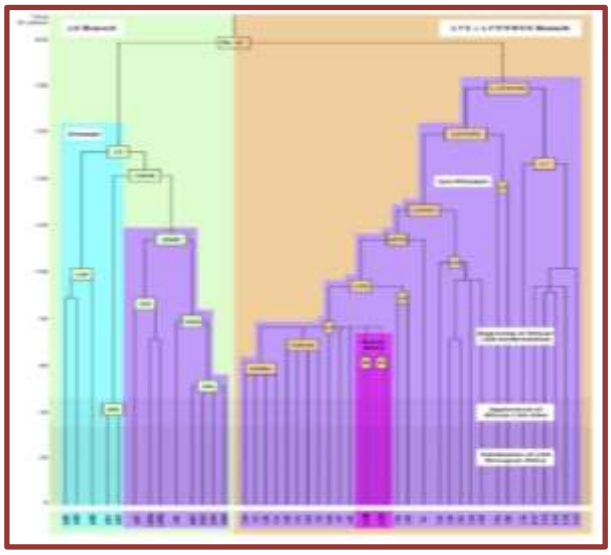
The project has experienced challenges in working with some members of the CAB over questions of payment (against the institute'/s policy, and risked establishing a poor precedent) and a lack of diversity in the membership. These experiences raise concerns about whether CABs are truly representing the interests of communities instead of focusing on making money, and whether research teams may be using them simply to "tick the boxes" in informed consent activities.

Human genetic research for Africa – improving outreach and public understanding

Prof Himla Soodyall, Division of Human Genetics, University of Witwatersrand

Outreach in scientific research on a human subject is important for a number of reasons. In a first instance it serves to communicate with relevant stakeholders, which include fellow peers and professionals, funders, members of ethics committees, university research offices, academic publishers and the media in all its forms. However, the same information needs to be communicated in a form that is suitable and accessible to the intended target of the message. In outreach it is important to set the communication objectives early, and to find ways of bridging gaps and creating synergies.

For example, it may help to ask oneself the following questions: "How do I approach an subject that is completely outside my area of expertise"? "How do I unpack and explain complicated concepts in my research?" "How do you communicate with other scientists to convey they are part of the bigger picture?" The communication of research to communities is a way of contributing to our society, and avoiding the "us and them" attitude is strongly recommended.

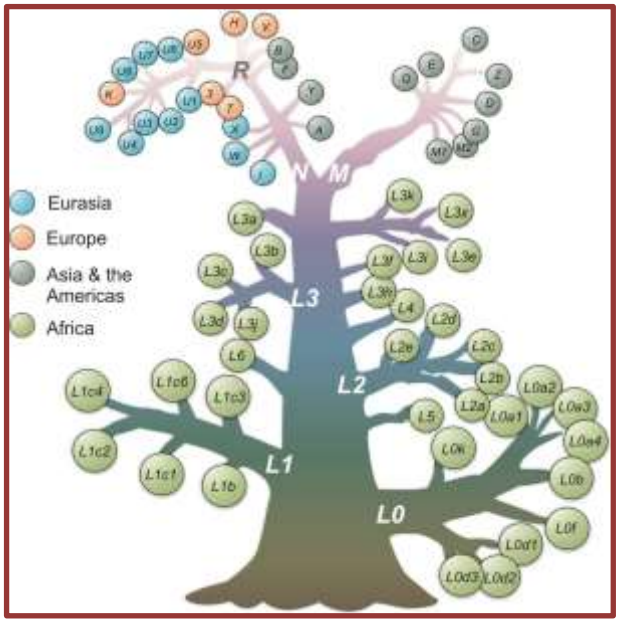


Evolutionary "family tree" of mitochondrial DNA

Since mitochondrial DNA (mtDNA) is inherited only through the mother and does not recombine, mutations in the DNA can be analysed to trace the ancestry and evolution of human populations. This analysis shows that only a very small proportion of the total variation in humans ever left Africa (deep pink branch in the graph above).

People want to know their ancestry. Comics are a very successful medium for communicating to community members, especially young minds. The SAMRC/University of Witwatersrand *"Routes*

to Roots: A Genomic Walk Into the Past" is a series which explains how DNA samples taken from people living all over the world can help us understand how we evolved as a species, and how this shows that as people we have much more in common with each other than differences. The drawings carried the storyline and set the tone, and were supported by the details provided in the boxes. And a representation of mtDNA tree was used to convey the same information as in the graph: the base of root is the same for all humans, which highlights issues related to race, racism and social cohesion.



mtDNA tree

Recognition of the importance of science communication led the South Africa Agency for Science and Technology Advancement (SAASTA) to develop a Science Engagement Framework. The Framework is tasked with facilitating the communication and advancement of science, with the following aims:

- Systematise collective effort of multiple role players
- Improve co-ordination
- Encourage science promotion and communication
- Foster better, more valuable science engagement
- Improve balance in portfolio of activities
- Enhance collective impact

The Framework's scope covers a number of institutions (including universities, museums, science centres and science councils) other government departments and the private sector. It is also open to international opportunities. The Framework calls for increased consideration of impacts and outcomes of research. All the entities need towards the framework contribute and to the formulation of science policies. The budget to support the framework is R67 million, with the aim of increasing the budget for science communication.

The Framework has four strategic aims:

- To popularise science, engineering, technology and innovation as attractive, relevant and accessible in order to enhance scientific literacy and awaken interest in relevant careers
- To develop a critical public that actively engages and participates in national

discourse of science and technology to the benefit of society

- To promote science communication that will enhance science engagement in South Africa
- To profile South African science and science achievements domestically and internationally, demonstrating their contribution to national development and global science, thereby enhancing its public understanding

A key question is how to change the conversation to align to the strategic aims of this framework. This requires facing intellectual, structural and emotional barriers.

In the discussion session it was noted that one measure of success in communicating science is when different stakeholders start contacting the scientist for information (to begin with it is usually the other way around).

The launch of the National Geographic Genographic project drew attention to the fact that genetics can help inform the public of their personal genetic histories, and that of their communities, and raised the awareness and interest in the general population.

Also discussed was the need to strengthen national science academies in their role of providing science-based policy advice. It is important to learn how to "put under the nose" of the relevant policymakers advice to inform policy. The Science Academy in South Africa presented a policy document on genetic birth defects, but none of the recommendations were implemented. Another challenge is to implement at a local level advice that was conceived for national implementation.

Working with artists presents its own problems, manly related to the management of needs and expectations, and the requirement to manage the level of detail required for science communication with providing an artistic impression. The overall aim must be to start a dialog, rather than convey detailed and nuanced information. A further complication is to satisfy the requirement of funding organisations. An area that needs much more attention is that of monitoring and evaluation, which requires the measurement of quantifiable components.

Developing genomic research in Tanzania

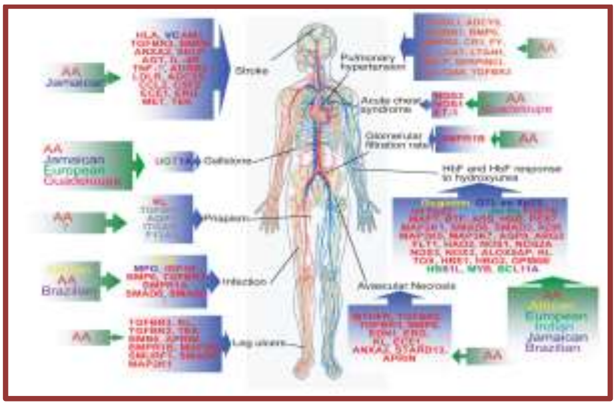
Dr Siana Nkya, Muhimbili Wellcome Programme Tanzania

Sickle cell disease (SCD) is recognized as a 'perfect model' to test the paradigm of translating genome-based knowledge to improvements in health. It is a single-gene disorder with considerable phenotypic variation, and is responsible for a significant burden of disease. With prospective surveillance of over 2,500 SCD patients, this Tanzanian study represents one of the largest, single-centre cohorts in the world. It integrates clinical, epidemiological, patho-physiological and genetic research in SCD. The study uses SCD as a model to establish scientific and technological solutions that are locally relevant but have global significance. Achieving success in SCD illustrates that with effective global partnerships, significant advances in health and advancement in biomedical science can be achieved. A large-

scale GWAS for SCD investigating modifying loci has been conducted.

Rare coding mutations with large effect with high heritability are especially informative in genetics studies because physiological studies of mutation carriers can help illuminate the biological basis of the disease, and because of the relatively easy with which they can be transferred to animal models for further investigation. Re-sequencing known disease loci in new populations can represent the 'low hanging fruits' of new genetic studies. These are most valuable in cases where there are high burdens of disease and insufficient medical care. In Tanzania, up to 11,000 babies are born with SCD annually and 50% may die before their 5th birthday.

The genetic basis of SCD is very complex, with a large number of loci implicated in disease. Fetal haemoglobin (HbF) is the strongest disease-modifier in SCD.



Schematics of genes where SNPs were reported to be significantly implicated on different phenotypes of SCD and on which population it was described.

In terms of intervention, newborn screening allows for early initiation of comprehensive care. And a new possibility of treatment, first demonstrated in mice and more recently in humans, is the interference with fetal haemoglobin silencing. However, most of the studies conducted on effect of fetal haemoglobin on disease conducted outside of Africa, and only three of a large number of genetic loci associated with fetal haemoglobin have been identified, and some of these are known to be specific to given populations. This programme aims to confirm the role of existing modifiers, and uncover new loci specific in Tanzanian populations. Sequencing is carried out in Kings' College London, United Kingdom. 5000 individuals have been enrolled on the SCD cohort.

Basic science studies will provide information on disease mechanisms and look at genetic and environmental factors that modify disease. This gives Tanzania a unique opportunity to understand the significance and biological importance of the genotype-phenotype relationships, and will allow the development of generic tools and models of engagement for other conditions.

The programme is run from Muhumbili University in close collaboration with the hospital. It proposes an integrated approach to SCD, comprising, research, training, advocacy and capacity building. The initiative also aims to engage traditional healers, an acknowledgement of the fact that the cultural background is very different in African countries with respect to other parts of the world. The experience of communicating with a wider public has also highlighted the importance of working with media professionals.

Future work include further genetic studies on fetal haemoglobin, population genetic studies, the establishment of national genetic databases; gene-gene interaction studies; epigenetics studies; and public engagement activities.

During the Q&A participants discussed the problem that heterozygous individuals (those with one copy of the disease allele, who are genetic carriers of the disease but do not develop it) receive no medical attention, mainly due to the lack of funds, even if they may be the parents of future SCD babies.

Also mentioned were the programmes carried out by Nigeria and Uganda on newborn screening for SCD, and the importance of cross referencing to learn from experience and not repeating common mistakes. There is not enough networking among countries in the region, and sharing of research results and intervention outcomes to influence policy.

The fact that a significant number of people in Africa live in very poor conditions the effect on individual priorities was also discussed. Genetic diseases are not among the highest or most pressing preoccupations when daily survival is struggle (for example, many families may lack a clean drinking water source). Researchers sometimes have a tendency to project priorities and values without fully appreciating the day-to-day realities of life for their patients and research subjects.

Session 5: Ethics and regulation

Ethics in Science and New Technologies

Prof Julian Kinderlerer, European Group on Ethics

Historically ethics was not considered part of science and technology. However, the realisation of the abuses committed during the Second World War in the name of science and subsequent exploitations – such as the deliberate infection of prisoners with syphilis, the forced sterilisation of women considered to be 'not very bright' by a family doctor, or the former possibility of carrying tests for medicines with no evidence that the new drugs were better than existing ones- brought to attention the responsibility of scientists to respect everybody, including minorities.

The start of the European Union Ethics Committee can be traced back to 1991, and this institution has evolved into a quite a sophisticated system since them. It aims to identify ethical priorities at the point of defining policy and ensure that research meets ethical guidelines, policies, and legislation.

Science advice to the European Commission is situated within the Directorate-General for Research and Innovation (DG RTD). Advice must be independent, and must have the responsibility to criticise any DG. It has two arms: the Science Advice Mechanism (SAM) and the European Group on Ethics (EGE) in Science and New Technologies.

The SAM has the overall objective of providing scientific advice to the Commission. This advice must:

- be of high quality, timely, transparent and independent of institutional or political interests
- bring together evidence and insights from different disciplines and approaches
- take into consideration the specificities of EU policy making (such as different national perspectives)

The EGE is an independent, pluralist and multidisciplinary body advising the European

Commission on ethics in science and new technologies in connection with Community legislation or policies. The EGE members serve in a personal capacity and are asked to offer independent advice to the Commission, Council and Parliament. It consists of 15 members (5 scientists, 5 lawyers and 5 ethicists) and 7 advisors to the EU president. It provides advice on issues referred to it by the Commission or on topics on the EGE members' own initiative. The EGE has also the powers to request evidence from scientists who receive EU funding. The EGE also drafts *Opinions*, high quality and independent advice documents on ethical aspects of science and new technologies in connection with EU legislation or policies.

The Opinion on the Ethical Implications of New Health Technologies and Citizen Participation is driven by the transformation of the health sector in recent years, as a result of a wave of innovation in health technologies, new medical breakthroughs, novel scientific approaches and the rise of digital health technologies. Pioneering methods of drug development and disease diagnosis, the rise of 'big health data', and new means of providing networked care have led to predictions that European health systems are on the cusp of transformation. While much of the promise held in these technological innovations remains to be fully realised, the rise of new health technologies are accompanied by a profound set of shifts in the way individuals – whether as patients, citizens or consumers – engage with matters of health.

Additional Opinions drafted recently include the Ethics on Information and Communication Technologies; an ethical framework for assessing research, production and use of energy; and issues related to New Genetic Technologies – in particular those relating to increased precision in modification of DNA sequences made possible by advances in the technology. These include:

- Modifications in and to animal cells
- Modifications to human somatic cells and their use in therapy
- Modifications to human germline cells: human stem cells and embryos (in the EU all parts of the embryo are protected)
- Enhancement/therapeutic use of genetic technologies
- "Three parent" babies
- Data Protection and Privacy

These advances have rendered the regulation of genetic technologies out-dated and in need of revision. The three R's legislation for the protection of animals in research (replace, reduce and refine) is more than 20 years old, for example.

But politics can be challenging in terms of technology adoption. Elections can have both positive and negative effects. Lack of continuity of policy and backsliding because of changes in ministerial appointments results in the unsustainability of political will, which affects the ability of decision-makers to deal sensibly with particularly controversial research issues.

Ethical implications for genomics research in African populations

Dr Nicki Tiffin, University of Cape Town

There are a number of reasons why human genomic research is a discipline that raises

many ethical considerations. The first pertains to the nature of human genomic data, which is of a highly sensitive nature. While clinical data cannot be associated with participant once it is uncoupled from their ID, it is impossible to truly anonymised genomic data (it would be like anonymising a fingerprint), and therefore it will be always linked to a specific individual and their descendants. And since the science of interpreting genomic data is its infancy, it is impossible to predict the consequences or potential harms that might come from sequencing human genomes for the participants of genomic studies. While the sequence of an individual will not change over time, our ability to mine data will improve. For example, a DNA sequence labelled as "junk DNA" originally, was then re-labelled as a non-coding region a few years later, and finally implicated in 2015 in autoimmune disease! Once genomic data are in the public domain, they cannot be completely recalled or destroyed, and as there are is no finite number for copies of data, there is also no way of ascertaining all the copies have been destroyed.

If we do not know the potential harms, how can we guarantee the full protection of participants? What types of informed consent should we request? How do we communicate risks for different levels of informed consent?

The challenges in Africa are particularly severe. There is an enormous diversity in African genomes (the 'Out of Africa' hypothesis of human evolution) and African genomes are under-researched. Genomic databases (and cloud storage) are mostly not hosted in Africa, which also implies that the data leaves African countries and moves into jurisdiction of host country.

Informed consent for genomic studies can be for primary and for secondary uses. In the first instances consent is provided for a single study or several specific studies, and data cannot be used for further research. Normally the raw data and the samples should be destroyed or securely archived when study complete. Secondary use informed consent allows the use of samples and/or data for other studies, beyond the primary study being undertaken. One of the ethical issues with respect to secondary use consents is the return of secondary or incidental findings, for example, the discovery of genetic factors that increase risk of illness for the participant.

Is the information actionable for participants in the context of very limited affordable health care in the African context? Should this information be communicated to the participant and if so, how and by whom? There are very few trained genetic counsellors in the continent. For these reasons informed consent needs to be tiered, with appropriate processes for requesting independently both primary and secondary informed consent.

African researchers should take the role of honest brokers for African people, requiring the need to take a bigger role and greater responsibilities. The fact that the implications of genomics research are not fully understood mean that participants have to consent to unknown risks.

The information that should be provided to participants in lay language includes:

- Subject and nature of study

- Expected outputs
- Impact on participants, society
- Potential risks and benefits
- Contact information for queries

Informed consent forms should clearly communicate that participation is voluntary and that consent can be withdrawn at any time (both for primary and secondary uses); respect of local cultural and ethnic values, and ensure that participation will not lead to the stigmatization of participants.

Informed consent forms present a number of challenges specific to Africa. Different countries have differing legislations which were not designed for the context of genomics studies. Ethical Institutional Review Boards (IRBs) are not sufficient in number; are often under-resourced; and tend to have limited familiarity with genomics principles. And while consent forms should state that non-participation does not compromise medical care, the reality of poor access to healthcare in the continent mean that non-participation often does result in less access to health care, or indeed no access at all. Participants are sometimes pressured into taking part in research activities by their community leaders, making participation less voluntary. In addition, language and cultural differences may lead to misunderstanding.

Recommendations going forward:

- Ethics planning and preparation with local stakeholders before project begins.
- Employ local personnel wherever possible.
- Increased training and resources for IRB's and genetic counseling
- Informed consent not conducted by study researchers
- Advocacy for national policies and legislation for participant protection in genomics research.
- Within-Africa genomic data storage solutions.

In the Q&A session ethical issues related to open source data versus privacy of personal information were discussed.

It was also noted that currently the currently informed consent is carried out by the researchers of the study to be undertaken, which represents an inherent conflict of interest that should be addressed by establishing an independent professional body to overtake the process. Communication of how genomics data are actually being used in the country is complicated by the fact that up to the sequencing of newborn for sickle cell disease there were no specific examples.

For the population to benefit from genomics there is a need to train a much large number of genetic counsellors and medical geneticists (currently in South Africa there is 1 medical geneticist per 4 million people, a much higher number than in the rest of the continent). Also required is the funding of translational research, and the establishment of feedback mechanisms for communicating back to participants study findings.

Public benefit in African health genomics science

Nchangwi Munung, University of Cape Town

The past decade has seen an increasing number of large-scale genomics research studies in African countries. Reasons why Africa must come on board the genomics bandwagon include:

- Rich genetic diversity in African populations could provide clues to human heredity and health
- An entire continent could be left out of the promise of genomic medicine, if they are not included in future genomics studies
- African countries may have to import the products of advances in genomics if it fails to invest in the technology

A number of continent-wide initiatives are taking place. The African Genome Variation Project (AVGP) aims to increase our understanding of the African genome variation and collect essential information about the structure of African genomes to provide a basic framework for genetic disease studies in Africa. AVGP is a collaborative network of scientists, primarily from the African Partnership for Chronic Disease Research, and one of its objectives the genotyping of 2.5 million genetic variants in over 1400 individuals from 18 ethno-linguistic groups across 7 countries (Kenya, Nigeria, Uganda, Ethiopia, Ghana, the Gambia, and South Africa). It is funded by the Wellcome Trust, United Kingdom.

B3Africa (Bridging Biobanking and Biomedical Research Across Europe and Africa) is formed by more than 40 biobank and ethics experts from 5 institutions in 4 African countries. It receives funding from the EU Horizon 2020 work programme. It has two main strategic aims

- Create a harmonised ethical and legal framework between European and African partner institutions that will allow for sharing bio-resources and data and also consolidate the Africa-EU biobank cooperation.
- Provide an “out-of-the-box” informatics solution that facilitates data management, processing and sharing and can also be used under challenging networking conditions in Africa and Europe.

In Africa, genomics research often involves the cross-border movement of human biological samples for the purpose of analysis due to a lack of required technology, limited human capacity for genomics analysis and the near absence of biobanks in many countries.

With respect to ethics, benefits in health research are usually based on justice and the equitable distribution of both the burdens and benefits of research. Positive aspects of international collaborations, in particular those involving North-South collaboration include the advancement of science; increase funding opportunities and knowledge and technology transfer and sharing. They can represent win-win partnership for all the parties involved. However, and partly due to historical events, a fear remains about the potential exploitation of African scientists and research resources (‘helicopter research’), especially while there is still limited capacity to conduct genomics research in the continent. Fears of exploitation can be addressed by increasing transparency; setting the rules of engagement; promoting fairness and equity and African leadership; and by increasing local research capacity. Challenges include improving the sustainability of capacity building by ensuring the commitment of national government; securing long-term funding; retaining trained African genomics scientists in Africa; promoting translational research; and maintaining and managing biobanks.

Regulatory implications of New Genetic Engineering Technologies

Prof Jasper Rees, Agricultural Research Council

The ASSAf Panel on NPBTs was convened in 2015 to ensure an independent process for advising on the regulatory status of NPBTs, inspired in part by the report on NPBTs published by the JRC in 2011. A Consensus Study Panel will be active 2015-2016 to determine the regulatory implications of the New Genetic Engineering Technologies, with the aim to provide credible, independent and unbiased evidence-based policy recommendations.

Why address new GM technologies in African countries now? While at the moment there are only three 3 GM crops in commercial production in the continent, 7 countries are carrying confined field trials; 14 countries are engaged in contained research and development; and 27 countries are building up their capacity for biotechnology R&D.

The panel group, chosen to comprise a comprehensive and balanced set of experts) has the following mandate:

- Evaluate the risk/benefit implications and ethics of all relevant new technologies (generally, but also with specific reference to their ability to sustain the diversity of agricultural crops, their ability to improve the agronomy, production and/or value of the crops).
- Determine – with justification - which new technologies should fall under the GMO Act and which should not.
- Outline a framework that can be used to assess the applicability of future technologies to the existing GMO Act & regulations.
- Assess the appropriateness of the South African biosafety regulatory framework for biosafety risk evaluation and management of all relevant new technologies.
- Where appropriate, recommend modifications/revisions and/or additions to the existing regulations, individually or collectively, for the new technologies.

Consensus in the Panel will be reached through study panel deliberations, in a process that is intended to be free from the influence of sponsors or organisations with vested interests in the outcome of the study findings. Interests groups may however be invited to present to the panel in order to discuss their expectations and to provide relevant information to the study.

Possible policy recommendations include: to leave the GM Act and Regulations unchanged; recommend minor changes to the regulations; recommend changes to exclude some or all of these technologies from regulation; or recommend a major review of GMO Act to address the review and regulation of novel traits.

The Agricultural Research Council Biotechnology Platform (ARC-BTP) of South Africa has a number of projects focusing on livestock genomics. The mapping of the *No Horns* gene in cattle has marked the start of a genetic engineering project. And genetic analysis of the Senepol cattle (a heat resistant temperate zone breed) identified a mutation truncating the PRLR (prolactin receptor) protein, which results in resistance to heat stress and which may be engineered in other breeds to improve heat tolerance.

In a more recent application of the sterile insect technique, which was originally developed in the 1950s and awarded the 1992 World Food Prize, GM is used to introduce a Self-Limiting Gene in transgenic insects. GM mosquitoes develop normally only if supplemented with tetracycline (an antibiotic), so once they are released in the wild to mate with wild populations for the control of malaria their offspring are unable to survive.

What about human genetics?

The ARC-BTP has high-throughput DNA and RNA sequencing and genotyping technologies within the platform, with the capacity to genotype thousands of samples or to generate large volumes of data from individual samples. It operates three next generation Illumina sequencers, a HiSeq2500 and two MiSeq systems, and also offers single nucleotide polymorphism (SNP) genotyping services.

Although the platform is open to providing sequencing and genotyping services to the human genetics research community, there is currently no demand. Although the price per sample sequenced by ARC-BTP is more expensive than those provided by sequencing facilities in the United Kingdom, United States or China, using a national, public service presents a number of advantages. Especially important with respect to human samples for which data sharing and secondary use are linked to many ethical issues, is that the information would never leave the country. ARC-BTP does not keep the original data files and provides users also with the raw data files (which contain additional important information), while foreign companies may either charge a higher rate for not keeping a copy of the data generated, or simply may just keep it, while they generally do not hand over raw data files.

The sequencing platform represents a very significant investment by the government of South Africa, and a commitment to develop the infrastructure and capacity to carry out genomics research in the country. Therefore the government should also implement policy measures to encourage wider use of the facilities. This may entail providing more funds for sequencing in government research grants on the condition that national, public platforms are used.

Conclusions and Recommendations

In the discussion session participants agreed on the need to improve communication among researchers and to develop a professional network to increase synergy and to avoid the duplication of efforts (of which there is too much at the moment). This would both save costs, since sequencing projects are expensive, and increase the impact of research activities.

When continent-wide initiatives are considered, Africa has few networks of science communicators, and while these professionals are active at the personal, individual level, follow-up activities are rare. Who is engaged in outreach and what exactly do they do? Where is the expertise in the continent, and who could you contact for information or to start a collaboration? Who is involved in coordinating activities, and how could these efforts be supported and sustained? To begin to answer these questions H3Africa has employed short-term staff to create a ‘genomics catalogue’.

The main problem with genetics research and outreach activities is the difficulty of securing the funding needed for continuity. Continent-wide research initiatives are also hampered by the very different Material Transfer Agreements systems operating in different countries, which makes the movement of samples between African nations very difficult (in cases it is actually easier to send samples outside of the continent). The creation of a specific body to improve the movement of samples would be very beneficial. A widely accepted protocol, from how to prepare and package materials to how they are transported and handled at the receiving institute would also greatly improve the situation.

A participant remarked that South Africa has accepted recommendations and operational guidelines from professionals working in the field. What is however lacking in the human genetics field are appropriate policies and governance. For example, the policies recommended by a previous Consensus Working Group of the Academy of Science of South Africa (ASSAf) on human genomics were largely ignored. Who should take the leadership of the process?

Providing feedback to the programme of the G4ASO human genetics workshop, Prof Soodyall indicated that the first part of the programme might be too broad. In order to improve public understanding of science it is important to identify very early on who should be targeted. A clear objective will make it easier to provide clear recommendations. One of the key communication messages should be science and research carried out for public benefit. The research topics need to 'translated' to improve the message, and convey clearly "*what are we doing and why"*.

Also discussed was the fact that the allocation of resources for research tends to follow "trends" instead of originating from a strategic approach to research aimed at improving development targets. One example is arguably precision medicine, which will mainly cater to relatively well-off individuals whereas large parts of the population in African countries still lack access to basic health care. It is important that investments aim to improve the wellbeing of the population at large. The fact that many people lack basic health services also raises the question of whether informed consent forms are really being used to protect participants, rather than mainly benefiting the scientific community. Promoting a genuine dialogue with research participants and involving them in the co-creation of research should be encouraged.

Appendix 1: Workshop programme

Genetics for Africa – Strategies & Opportunities

Workshop on human genetic research for Africa: improving outreach and public understanding

February 25th – 26th 2016; ICGEB, Cape Town

Day 1 – Thursday 25th February

Chair: *Prof Sir Brian Heap*

Session 1: Introduction

09.00 Genetics for Africa – Strategies & Opportunities: *Dr Bernie Jones, Co-leader G4ASO*

09.30 The B4FA experience: Dr Claudia Canales, *Co-leader G4ASO*

10.00 Human genetic research and why it matters to Africa: *Prof Iqbal Parker, ICGEB*

10.30 H3Africa: *Dr Michelle Skelton, H3Africa Coordinator, UCT*

11.00 Funders perspective: *Dr Rizwana Mia, South African Medical Research Council*

11.30 Coffee Break

Session 2: Human genetic research – health

12.00 Genetic basis of disease: *Dr Zane Lombard, University of Witwatersrand*

12.30 Medical Genetics in Africa and beyond: *Prof Ambroise Wonkam, UCT*

13.00 Lunch

Chair: *Prof Iqbal Parker*

Session 2 cont: Human genetic research – health

14.00 mGenAfrica: *Dr Vicky Nembaware, UCT*

14.30 Sequencing Ebola: *Dr Luke Meredith, Cambridge University*

15.00 Coffee break

Session 3: Human genetic research – other approaches

15.30 Indigene Project: *Dr Elonna Obiefuna, Institute of Human Virology, Abuja*

16.00 Enhancing youth genetic literacy: *Dr Getnet Tadele, University of Addis Ababa*

16.30 Continental Policy Formulation Processes and Sustainability of Political Will:*Prof Diran Makinde, ABNE*

19.00 Dinner

Day 2 – Friday 26th February

Chair: Prof Jasper Rees

Session 4. Human genetic research – outreach

09.00 Cafgen Botswana and public engagement: *Dr Matshaba, Baylor Botswana Centre*

09.30 Genome Adventures: Exploring Creative Engagement: A Case of Genome Adventures: *Abraham Mamela, Science communicator and writer*

10.00 Biobanking and public engagement: *Dr Ciara Staunton, University of Stellenbosch*

10.30 Coffee Break

11.00 Human genetic research for Africa – outreach and understanding: *Prof Himla Soodyall, University of Witwatersrand*

12.00 SCD research programme in Tanzania: *Dr Siana Nkya*, *Muhimbili Wellcome Programme*

12:45 Lunch

Chair: Dr Bernie Jones

Session 5. Ethics, Regulation and other considerations

14.00 Ethics in Science and new technologies: *Prof Julian Kinderlerer, European Group on Ethics*

14.30 Ethical considerations for genomics research in Africa: *Dr Nicki Tiffin, UCT*

15.00 Public benefit and ethics in African health genomics science: *Syntia Munung, UCT*

15.30 Coffee break

16:00 Regulation and new genetic technologies: *Dr Jasper Rees, Agricultural Research Council*

16.30 Plenary discussion on workshop recommendations

17.30 Close

Appendix 2: Workshop participants

1. Dr Kevin Arnold, Program Officer, Genetics and Life Science, John Templeton Foundation, Pennsylvania, USA. Email: karnold@templeton.org
2. Prof Sir Brian Heap, B4FA Project Leader Email: brianheap1@gmail.com
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7. Dr Michelle Skelton, H3Africa Coordinator. Email: michelle.skelton@uct.ac.za
8. Dr Zane Lombard, Southern African Society for Human Genetics (SASHG). National Health Laboratory Service & University of the Witwatersrand. Email: zane.lombard@wits.ac.za
9. Abraham Mamela, Lead Science Communications Advisor for Genome Adventures. Science Communication and writer. Email: abraham.mamela@gmail.com
10. Prof Diran Makinde, Director, African Biosafety Network of Expertise (ABNE), New Partnership for Africa's Development (NEPAD). Email: diran.makinde@gmail.com
11. Dr Luke Meredith, Department of Pathology, Cambridge University. Email: lm695@cam.ac.uk
12. Syntia Munung, University of Cape Town. Email: mnnnch001@myuct.ac.za
13. Victoria Nembaware, Training coordinator and a bioinformatician for the H3Africa and H3ABioNet consortiums, University of Cape Town. Email: vnembaware@gmail.com
14. Dr Siana Nkya. Assistant lecturer at DUCE; SCD PROGRAM, Muhimbili Wellcome Programme. Email: siana.nkya@muhimbili-wellcome.org
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16. Prof Iqbal Parker, Director, ICGEB Cape Town Component, International Centre for Genetic Engineering and Biotechnology. Email: iqbal.parker@icgeb.org
17. Prof Jasper Rees, Head, Biotechnology Platform of the Agricultural Research Council (ARC) ARC South Africa. Email: reesj@arc.agric.za
18. Prof Himla Soodyall, Human Genomic Diversity & Disease Research Unit, University of the Witwatersrand (Wits), Johannesburg. Email: hxsood@icloud.com
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