

MEETING REPORT

Exploring genomic studies in Africa

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Abstract

A report on the African Society of Human Genetics meeting, Cape Town, South Africa, 6-9 March 2011.

Introduction: building capacity and expanding genomics research in Africa

The 6th Meeting of the African Society of Human Genetics (AfSHG) and the 14th Southern African Society of Human Genetics (SASHG) Congress were held jointly in Cape Town. These meetings overlapped with the 2011 International Society for Computational Biology and African Society for Bioinformatics and Computational Biology Conferences, thereby appealing to a wide array of biomedical researchers. The AfSHG and SASHG meetings were held on the tail of a meeting discussing the new initiative jointly funded by NIH and The Wellcome Trust, 'Human Heredity and Health in Africa (H3Africa)', and the theme, 'Building Capacity for Genomic and Translational Research in Africa', complemented the other meetings.

The meeting emphasized the importance of genomics studies in Africa for increasing our understanding of human evolutionary history and the genetic bases of disease susceptibility and drug response. The introductory talks made by the presidents of the two organizing societies, Charles Rotimi (AfSHG) and Michele Ramsay (SASHG), discussed the crucial role that genomic studies in Africa should play in helping us to understand the relationship between human diversity and disease predisposition, and how it is imperative to build capacity on the continent to make such studies possible. The building of both human and physical capacities provided a common thread throughout many of the talks. Representatives of several genetics and genomics societies in

Africa presented overviews of how their organizations facilitate research collaborations both amongst African scientists and between African scientists and the international community, thereby increasing the capacity for genomics research in Africa. The speakers included Charles Rotimi (National Human Genome Research Institute, USA (NHGRI)), Michele Ramsay (University of Witwatersrand, SA), Amal M Mohamed (National Society of Human Genetics, National Research Centre, Egypt) and Ambrose Wonkam (Cameroon Society of Human Genetics, University of Yaounde, Cameroon, and University of Cape Town, SA). Sir Mark Walport (The Wellcome Trust, UK) discussed the role of The Wellcome Trust, providing both historical context and an overview of modern funding initiatives in Africa. Here, we cover the main themes of the meeting and describe how research in Africa can inform the biomedical community on the role of genetics and genomes in understanding many diseases.

Human genetic diversity and history

The opening talks of the meeting focused on how the information contained in our genomes provides key data that can be used to unravel our histories. This theme began with Sydney Brenner (Janelia Farms, Howard Hughes Medical Institute, USA) who discussed 'Reading the Human Genome' in an almost literal sense (that is, from one end of chromosome 1 to the opposite end of the X chromosome). Brenner argued that the human genome contains extensive information about the historical and biological properties of our species, and that even if we read the 'Cliffnote' version of the genome, the exons only, we can extract an enormous amount of information that could be translated into genomic medicine. Of particular note were his final comments; Brenner argued not for bench-to-bedside medicine, but rather for bedside-to-bench medicine, making use of the extensive genetic data currently available from the genetic text.

Several additional talks addressed the evolution of human populations (especially within Africa) and their cultures and languages from multiple perspectives. Sarah Tishkoff (University of Pennsylvania, USA), Daniel Shriner (NHGRI), Christopher Gagneaux (University of California, San Francisco, USA) and Brenna Henn

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(Stanford University, USA) took a genetic perspective, whereas John Parkinson (University of Cape Town, SA) and Shomarka Keita (Howard University, USA) approached these topics from archaeological and anthropological perspectives, respectively. These talks were of note in that it became obvious that differing approaches can lead to a variety of conclusions that will require integration and resolution.

Genomic research: translational limits and resource limitations in Africa

Eric Green (NHGRI) opened a session on public health genetics with an overview of his institutes' research portfolio, importantly cautioning that work being done today will require years to translate into clinical practice. This adjustment of expectations is arguably amongst the most important thing genomicists can do to ensure continued research. Edison Liu (Genome Institute of Singapore, Singapore) followed by presenting the reasons for prioritizing genomics research in resource-limited environments, arguing that such research can provide bases for health policy and human sustainability and that it can be of top quality. Extending the idea of how research can impact health policy requires the development of appropriate infrastructures, both intellectual and technological. The session on networks, infrastructure and training began with a talk by Dominic Kwiatkowski (Oxford University, UK), who laid out key issues relating to the use of the MalariaGen network as a model for understanding the evolution of malaria as a disease, from the perspective of both host and parasite. Doris Schroeder (University of Central Lancashire, UK) emphasized that the development of successful research and the anticipated successes that are eventually translated need to be shared with the local populations and researchers that made them possible, although the exact parameters are not presently defined, either ethically or legally in human genomics research. Arnold Christiansen (University of Witwatersrand, SA) gave a presentation that dealt with the problem of reduced funding for medical genetics and how it has adversely impacted aspects of medical care in South Africa, and Pasquale de Blasio (BioRep SRL, Italy) led a discussion on the steps and resources needed to develop crucial biobanking facilities on the African continent. Both of these talks raised the issue of limited resources in Africa for both research and medicine, and emphasized the need to increase the funding and thus capacity for genomics research on the continent.

Genomic medicine: current applications

In a session focusing on molecular pathology, Griffin Rodgers (National Institute of Diabetes and Digestive and Kidney Disease, USA) gave a presentation that focused

on treatments for sickle cell disease, including allogenic transplantation. This was followed by a talk on the genetics of type 2 diabetes mellitus by Mark McCarthy (Oxford University, UK), who reviewed the identification of more than 40 genes that are associated with the disease. Most previous studies have focused on populations of European ancestry and many of the identified genes are involved in reduced beta cell function and cell cycling. Expansion to African populations will be essential for fine-mapping and to identify disease risk variants that may be geographically restricted to Africa.

Several talks focused on the theme of translational research and pharmacogenetics. Howard McLeod (University of North Carolina at Chapel Hill, USA) discussed the importance of how drugs are prescribed: drug familiarity being a major factor in wealthier nations where a different drug is substituted if the first-prescribed drug is ineffective. This luxury does not exist in lower and middle income countries (LMICs) where much shorter drug lists exist. In LMICs, it is important to have an idea of what will work before choosing a drug, and this may be accomplished by identifying and characterizing the distribution of polymorphisms that affect drug metabolism. McLeod proposed that this can be achieved with extensive genetic characterization across LMICs and by applying pharmacogenetic principles in a way that, although less than perfect, is a substantial improvement over current practice in terms of both treatment outcome and cost.

Michael Hayden (University of British Columbia, Vancouver, Canada) followed with a discussion of analyses of patients with extreme drug-response phenotypes, which aim to identify factors that are associated with large effects. This approach contrasts with modern genome-wide association studies of common traits, which typically identify variants of small effect, and can lead quickly to clinical applications. Among other examples, Hayden discussed the adverse effects of cisplatin, describing how variants at two genes (*Catechol-O-methyltransferase (COMT)* and *Thiopurine S-methyltransferase (TPMT)*) are associated with most cases of cisplatin-related deafness in children. This study involved fewer than 200 children, arguing for the role of large-effect genes in pharmacogenetics. These studies demonstrate the utility of genetics in medical care, even in resource-limited environments.

John Burns (University of Newcastle, UK) spoke about targeted approaches used to study specific diseases, many of which are caused by single genes with large effects, and Olufunmilayo Olopade (University of Chicago, USA) discussed how genetic risk factors that are associated with breast and ovarian cancers in populations of European descent do not necessarily replicate in populations of African descent because of, for example, the different

distribution of estrogen receptor status in African populations.

Taken together, these talks demonstrated not only that genes of potential clinical importance can be found but also that, even at present, some of them may be translated into practice. Nevertheless, transferability among populations is still a substantial issue that requires intensive study.

Infrastructure and educational development in Africa

Abdallah Daar (University of Toronto, Canada) discussed the needs for and challenges in the development of African biorepositories. He argued that the main consumers of genomics in the future will be from LMICs, and therefore that these countries should be developing resources that are currently limited, including basic research capacity, basic financial and health-care systems, and regulatory infrastructures that can provide guidelines for appropriate access to samples that will ensure local benefit.

Patricia Marshall (Case Western University, USA) followed with a discussion of how education can affect the answer to the question 'What were you told about the purpose of this study?'. As might be expected, education was crucial to achieving an understanding of research goals, but its effect was modified by a variety of factors, including the medium used to educate and the perceived severity of the disease.

The final topic covered at the meeting was the development and use of new technologies and methodologies to understand biological and biomedical questions. Jason Moore (Dartmouth College, USA) introduced the concept of epistasis or gene-gene interaction and how it is important for studies of human phenotypes. He emphasized that our ability to understand the genetic basis of common disease is tied to the underlying complexity of the genetic models, and that we need to expand our capacity to develop models beyond those that are mired solely in single-gene association. He described a method that uses dimensionality reduction, called MDR, to address this issue. David Bentley (Illumina)

discussed the development of next generation sequencing technologies and how these have been used to identify previously unknown mutations. He presented several cases in which high-throughput sequence data generation allowed the identification of previously unknown mutations that cause disease, making the case that technology will provide a permissive environment for disease gene discovery.

Genomic research in Africa: opportunities and challenges

The focus of this meeting was on building capacity for genomics research in Africa to better understand, prevent and treat human disease, and to better understand human history and evolution. The speakers made key points about how researchers and clinicians have worked together to translate a few genomic discoveries into health-care practice, but reported that progress is mostly being made in the developed world. Nevertheless, the needs and opportunities in LMICs, and in Africa in particular because of its unique position in human evolution, are substantial. Speakers repeatedly emphasized the requirement to build research capacity within Africa for genomics, both by building physical research infrastructure and by training and retaining African scientists. New approaches, either under development or already in practice, that were presented at the meeting provided insight into how genomics research might begin to meet important goals on the African continent.

Abbreviations

AfSHG, African Society of Human Genetics; LMIC, low and middle income country; NHGRI, National Human Genome Research Institute, USA; SASHG, Southern African Society of Human Genetics.

Competing interests

The authors declare that they have no competing interests.

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