H3Africa:
The NIH Perspective and Context

Eric Green
Director, NHGRI

Inaugural H3Africa Meeting
October 2012

I. The National Institutes of Health (NIH)

II. The NIH Common Fund

III. NHGRI and the Genomics Landscape

IV. H3Africa @ NIH

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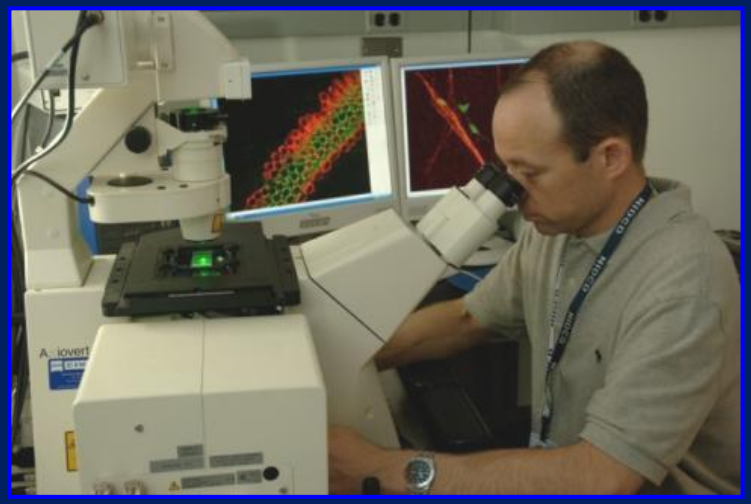
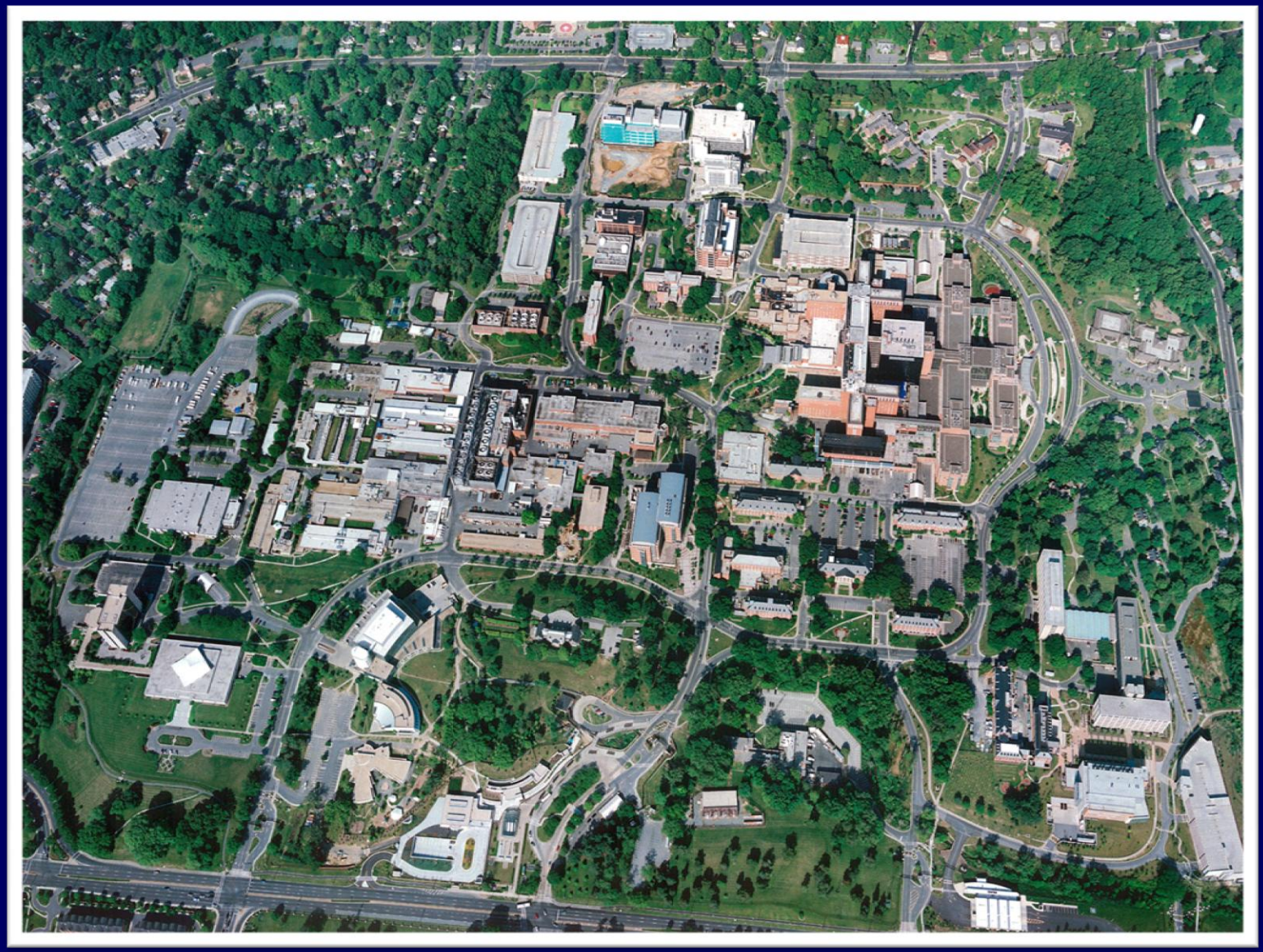
The NIH: Steward of Medical and Behavioral Research in the United States

"Science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability"

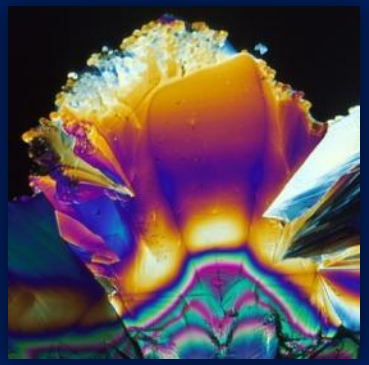


The Main NIH (Bethesda) Campus

75 Buildings on 322 acres

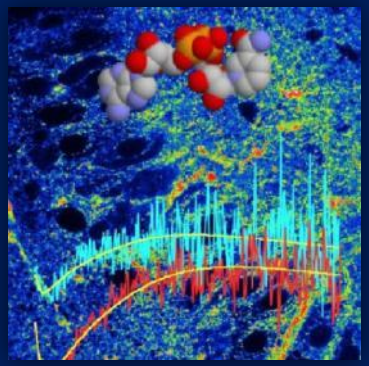
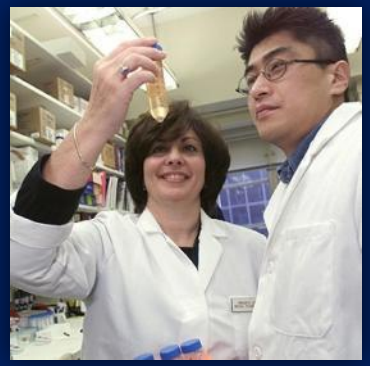




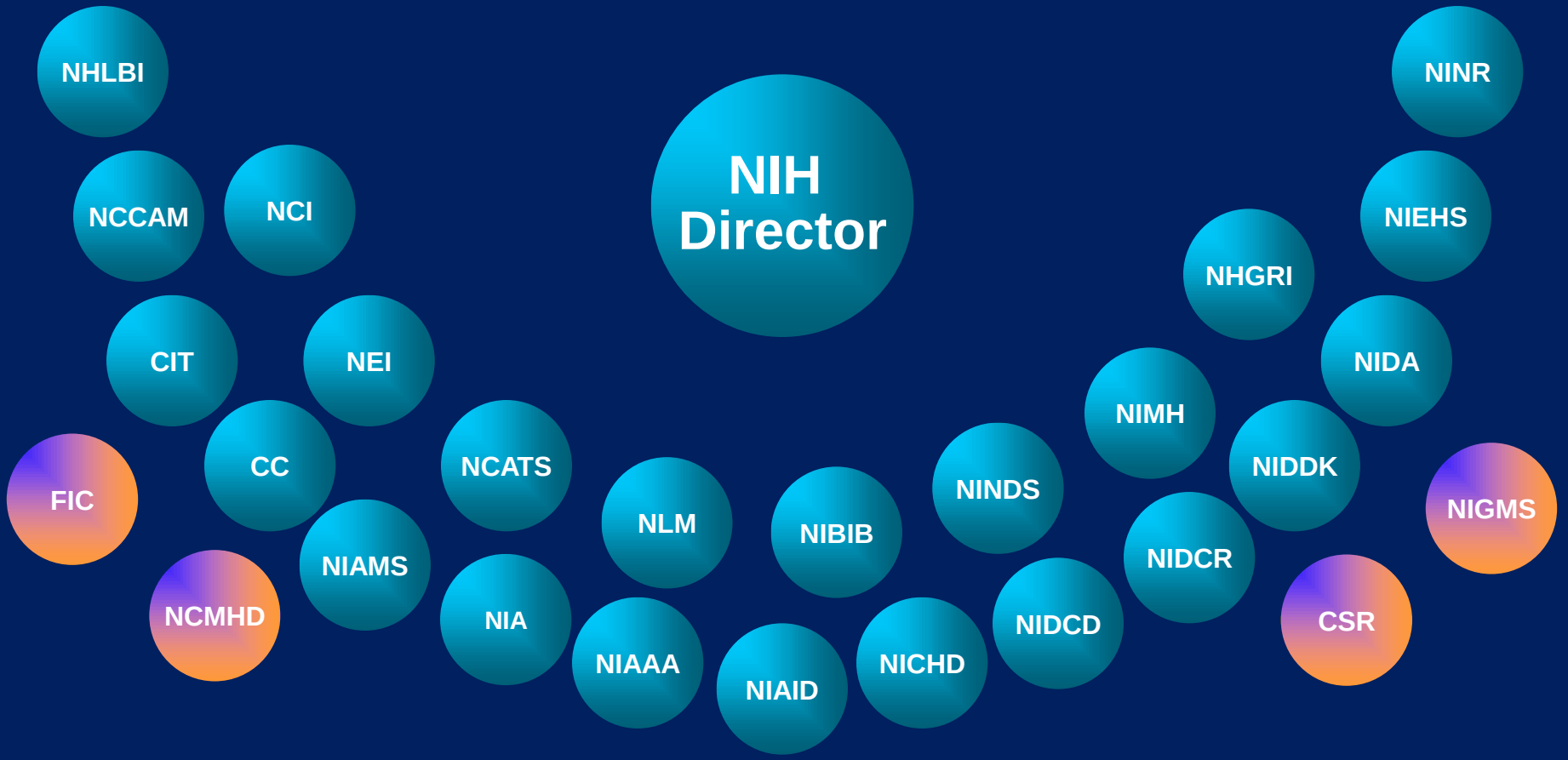



NIH

Turning discovery into health


NIH Consists of 27 Institutes and Centers



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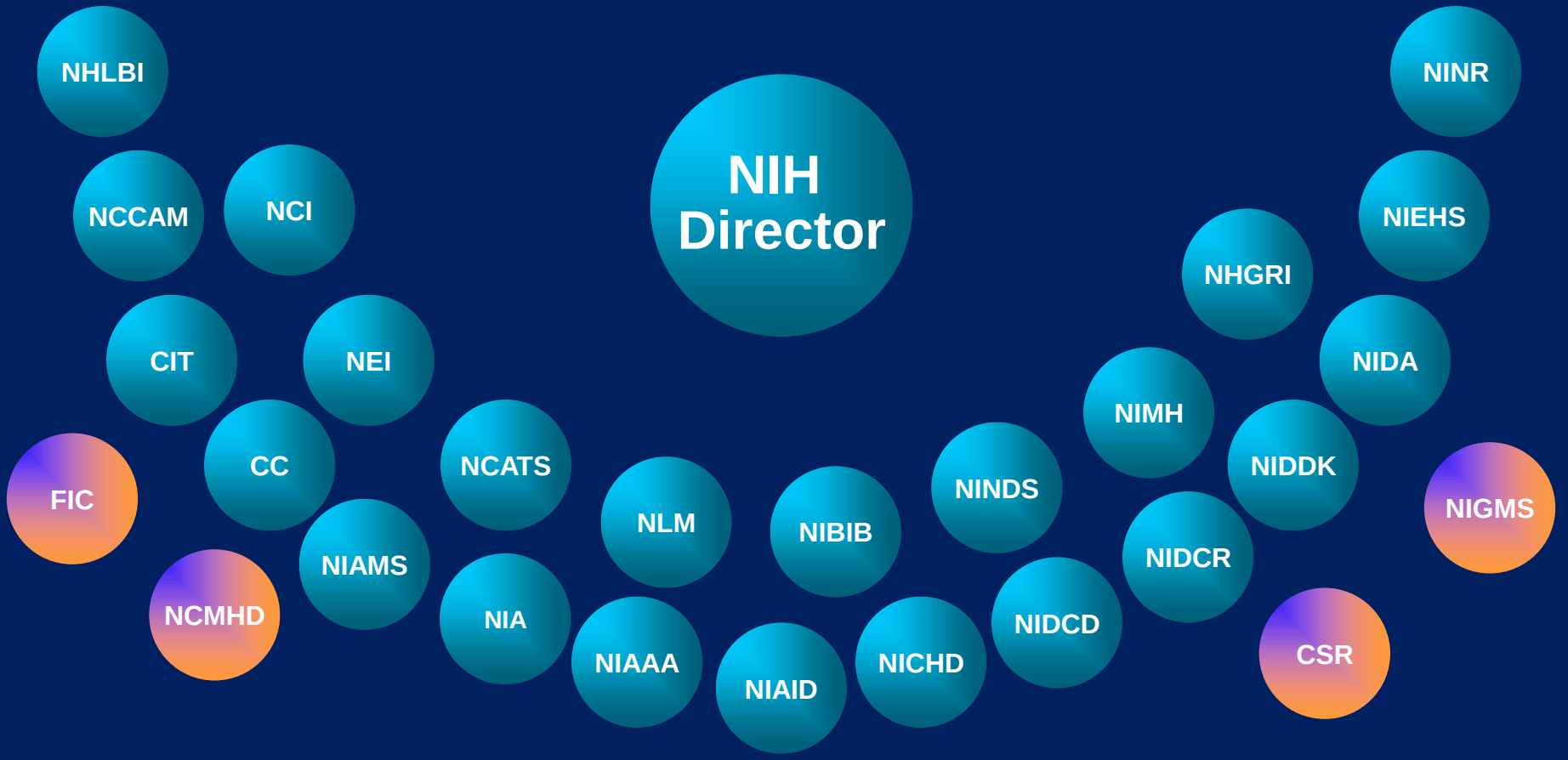

NIH Common Fund

We accelerate discovery

I. The National Institutes of Health (NIH)

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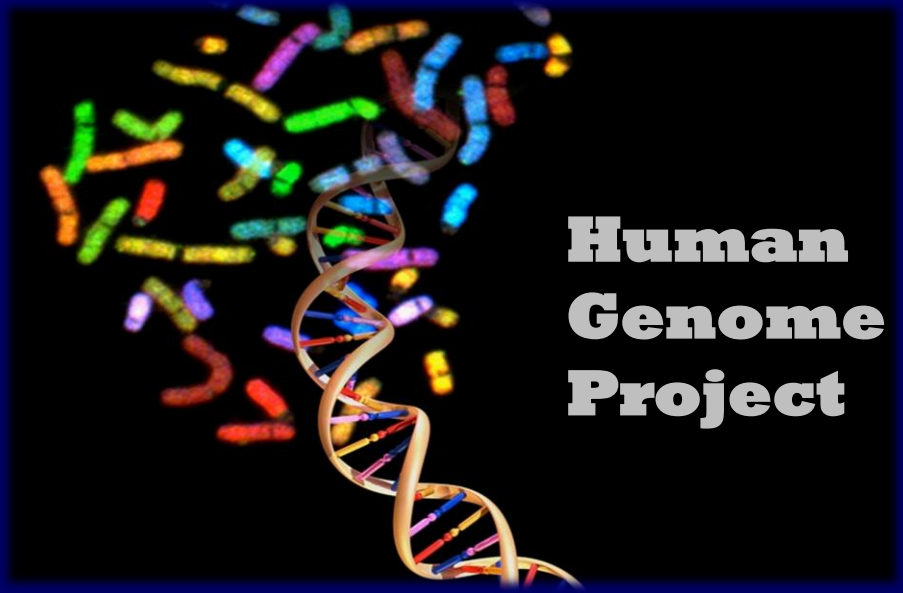
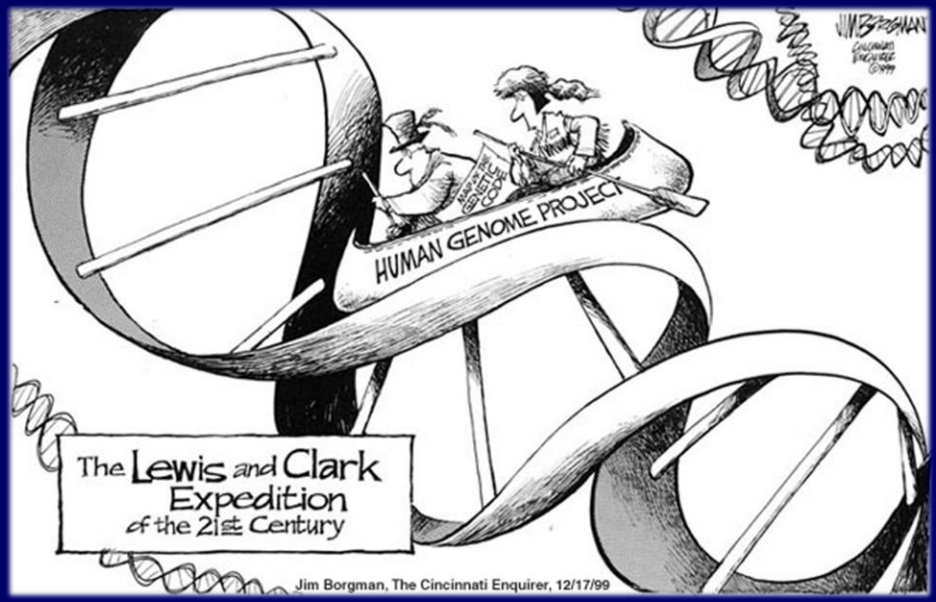
National Human Genome Research Institute

Advancing human health through genomics research

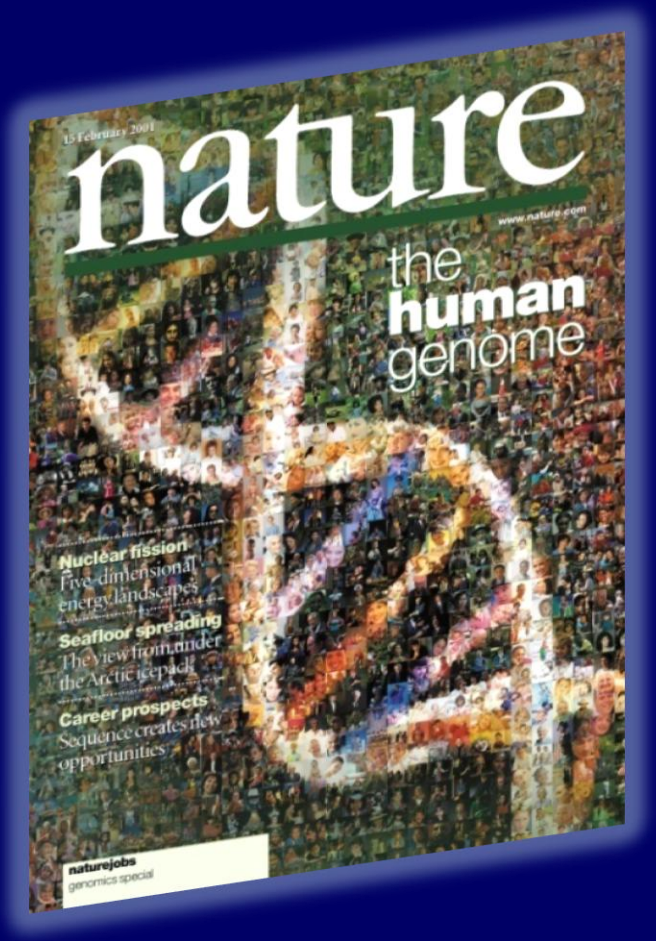
October, 1990





Human Genome Project Begins

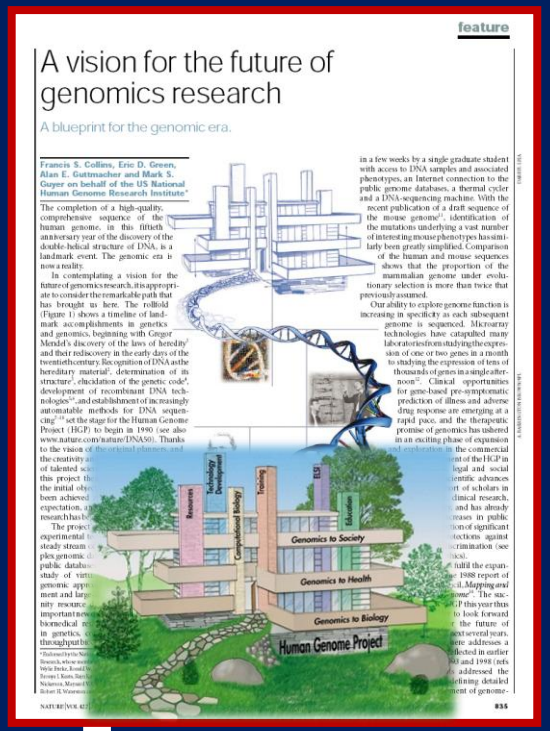
February, 2001



Draft Human Genome Sequence Published

April, 2003

Human Genome Project Ends



feature

A vision for the future of genomics research

A blueprint for the genomic era.

Francis S. Collins, Eric D. Green, Alan E. Guttmacher and Mark S. Guyer on behalf of the US National Human Genome Research Institute*

The completion of a high-quality, comprehensive sequence of the human genome, in this fiftieth anniversary year of the discovery of the double-helical structure of DNA, is a landmark event. The genomic era is now a reality.

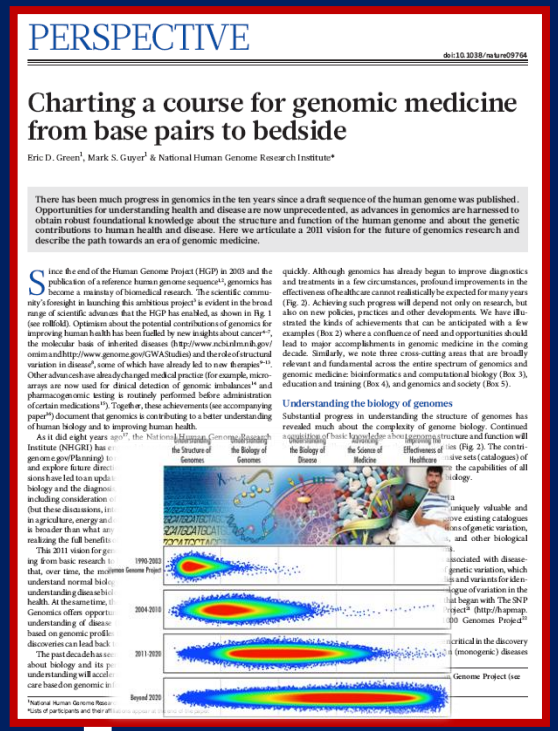
In contemplating a vision for the future of genomics research, it is appropriate to consider the remarkable path that has brought us here. The rollfold (Figure 1) shows a timeline of landmark accomplishments in genetics and genomics, beginning with Gregor Mendel's discovery of the laws of heredity[1] and their rediscovery in the early days of the twentieth century. Recognition of DNA as the hereditary material[2], determination of its structure[3], elucidation of the genetic code[4], development of recombinant DNA technologies[5,6], and establishment of increasingly automatable methods for DNA sequencing[7–10] set the stage for the Human Genome Project (HGP) to begin in 1990 (see also www.nature.com/nature/DNA50). Thanks to the vision of the original planners and the creativity and of talented sci this project th the initial obj been achieved expectation, a research has

The project experimental steady stream pkn genomic d public databas study of virtu genomic appr ment and larg nity resource important new biomedical re in genetics, c throughput te

in a few weeks by a single graduate student with access to DNA samples and associated phenotypes, an Internet connection to the public genome databases, a thermal cycler and a DNA-sequencing machine. With the recent publication of a draft sequence of the mouse genome[11], identification of the mutations underlying a vast number of interesting mouse phenotypes has similarly been greatly simplified. Comparison of the human and mouse sequences shows that the proportion of the mammalian genome under evolutionary selection is more than twice that previously assumed.

Our ability to explore genome function is increasing in specificity as each subsequent genome is sequenced. Microarray technologies have catapulted many laboratories from studying the expression of one or two genes in a month to studying the expression of tens of thousands of genes in a single afternoon[12]. Clinical opportunities for gene-based pre-symptomatic prediction of illness and adverse drug response are emerging at a rapid pace, and the therapeutic promise of genomics has ushered in an exciting phase of expansion and exploration in the commercial ent of the HGP in legal and social ientific advances ort of scholars in clinical research, and has already reases in public ion of significant tections against crimination (see ocial fulfil the expan- he 1988 report of ...l, *Mapping and* ...nome*[13]. The suc- GP this year thus to look forward r the future of ext several years. ere addresses a llected in earlier 03 and 1998 (refs o addressed the efining detailed ment of genome-

Nature



PERSPECTIVE

doi:10.1038/nature09764

Charting a course for genomic medicine from base pairs to bedside

Eric D. Green[1], Mark S. Guyer[1] & National Human Genome Research Institute*

There has been much progress in genomics in the ten years since a draft sequence of the human genome was published. Opportunities for understanding health and disease are now unprecedented, as advances in genomics are harnessed to obtain robust foundational knowledge about the structure and function of the human genome and about the genetic contributions to human health and disease. Here we articulate a 2011 vision for the future of genomics research and describe the path towards an era of genomic medicine.

Since the end of the Human Genome Project (HGP) in 2003 and the publication of a reference human genome sequence[1,2], genomics has become a mainstay of biomedical research. The scientific community's foresight in launching this ambitious project[3] is evident in the broad range of scientific advances that the HGP has enabled, as shown in Fig. 1 (see rollfold). Optimism about the potential contributions of genomics for improving human health has been fuelled by new insights about cancer[4–7], the molecular basis of inherited diseases (http://www.ncbi.nlm.nih.gov/omim and http://www.genome.gov/GWAStudies) and the role of structural variation in disease[8], some of which have already led to new therapies[9–12]. Other advances have already changed medical practice (for example, microarrays are now used for clinical detection of genomic imbalances[14] and pharmacogenomic testing is routinely performed before administration of certain medications[15]). Together, these achievements (see accompanying paper[16]) document that genomics is contributing to a better understanding of human biology and to improving human health.

As it did eight years ago[17], the National Human Genome Research Institute (NHGRI) has e genome.gov/Planning) to and explore future direct sions have led to an upda biology and the diagnos including consideration (but these discussions, in in agriculture, energy and is broader than what an realizing the full benefits

This 2011 vision for ge ing from basic research t that, over time, the m understand normal biolo understanding disease bi health. At the same time, t Genomics offers opportu understanding of disease based on genomic profiles discoveries can lead back t

The past decade has se about biology and its po understanding will accele care based on genomic in

quickly. Although genomics has already begun to improve diagnostics and treatments in a few circumstances, profound improvements in the effectiveness of the healthcare cannot realistically be expected for many years (Fig. 2). Achieving such progress will depend not only on research, but also on new policies, practices and other developments. We have illustrated the kinds of achievements that can be anticipated with a few examples (Box 2) where a confluence of need and opportunities should lead to major accomplishments in genomic medicine in the coming decade. Similarly, we note three cross-cutting areas that are broadly relevant and fundamental across the entire spectrum of genomics and genomic medicine: bioinformatics and computational biology (Box 3), education and training (Box 4), and genomics and society (Box 5).

Understanding the biology of genomes

Substantial progress in understanding the structure of genomes has revealed much about the complexity of genome biology. Continued acquisition of basic knowledge about genome structure and function will

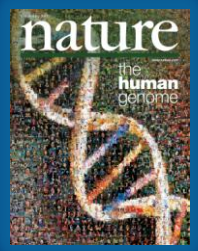
uniquely valuable and ove existing catalogues ons of genetic variation, , and other biological

ssociated with disease- genetic variation, which ns and variants for iden- gue of variation in the at began with The SNP roject[18] (http://hapmap. 00 Genomes Project[19]

critical in the discovery n (monogenic) diseases

Genome Project (see

Nature



Base Pairs to Bedside

2003

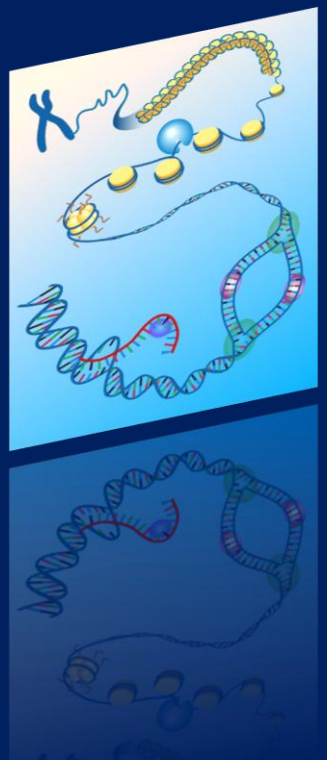
2011

Helix 2014 Health

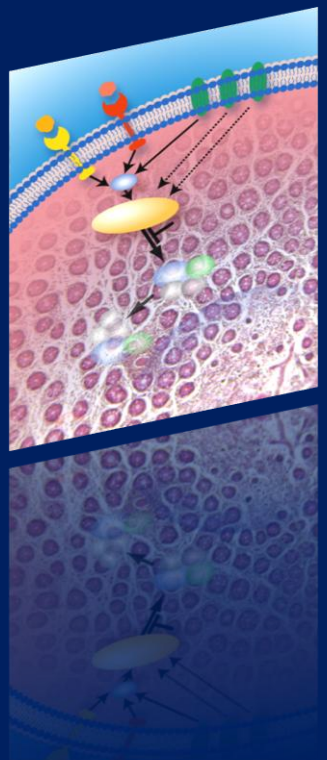
Five Domains of Genomics Research

Understanding the Structure of Genomes

Understanding the Biology of Genomes

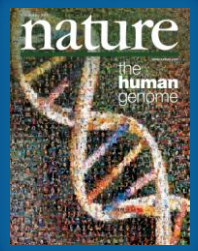


Understanding the Biology of Disease

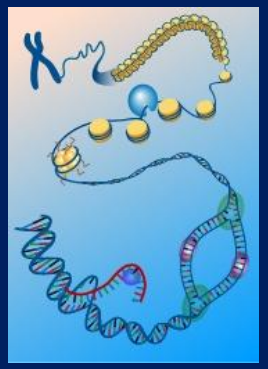
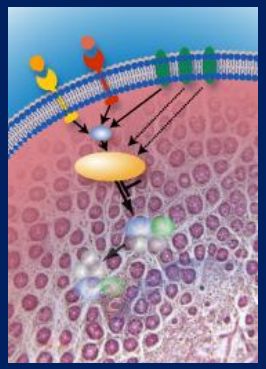
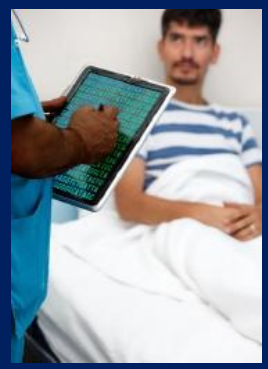


Advancing the Science of Medicine

Improving the Effectiveness of Healthcare



Genomic Accomplishments Across Domains

	Understanding the Structure of Genomes	Understanding the Biology of Genomes	Understanding the Biology of Disease	Advancing the Science of Medicine	Improving the Effectiveness of Healthcare
1990-2003 *Human Genome Project*					
2004-2010					
2011-2020					
Beyond 2020					

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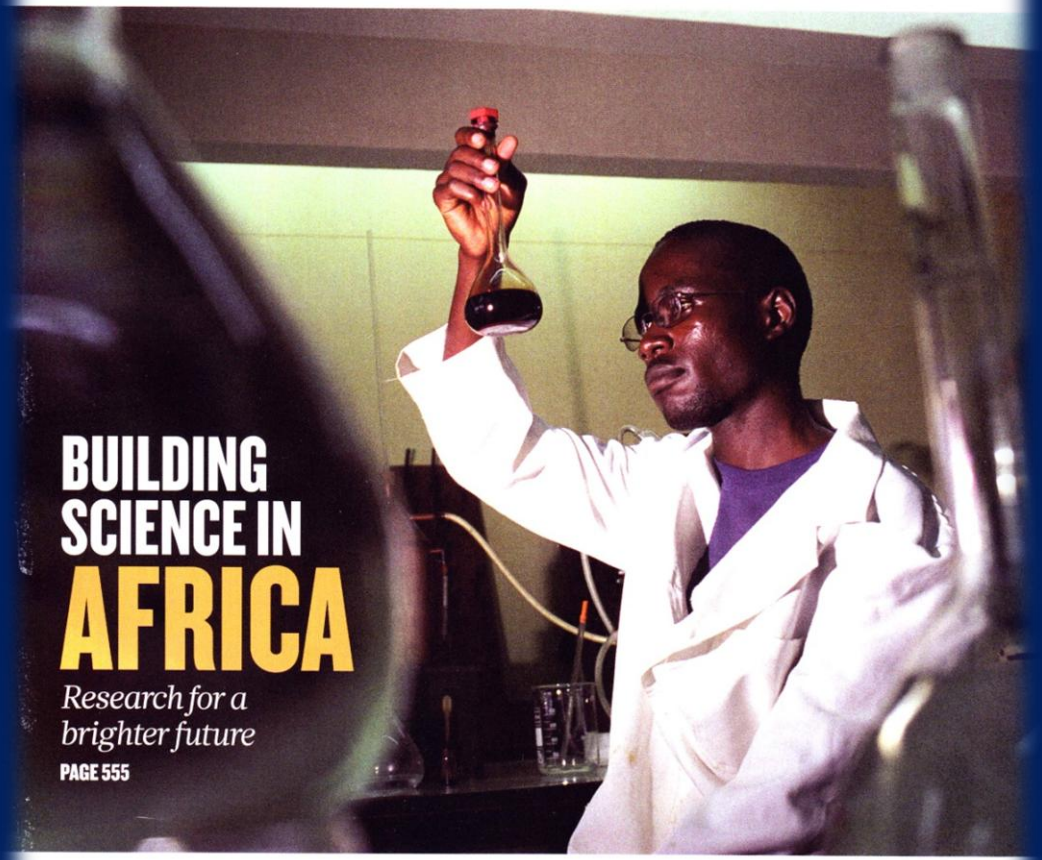
THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE



BUILDING SCIENCE IN AFRICA

Research for a brighter future

PAGE 555

COSMOLOGY

GOING THE DISTANCE

High-redshift quasar beats the record

PAGES 583 & 616

EVOLUTIONARY THEORY

WON IN THE EYE

Fossils confirm early arrival of complex vision

PAGE 631

ECOLOGY

A NEW WORLD VIEW

The lasting legacy of the Whole Earth Catalog

PAGE 578

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NIH Common Fund Global Health Program

Medical Education Partnership Initiative (MEPI)

Human Heredity and Health in Africa (H3Africa)

H3Africa

Human Heredity and Health in Africa

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Welcome

The **Human Heredity and Health in Africa (H3Africa) Initiative** aims to facilitate a contemporary research approach to the study of genomics and environmental determinants of common diseases with the goal of improving the health of African populations. To accomplish this, the H3Africa Initiative aims to create and support the development of the necessary expertise among African scientists, and to establish networks of African investigators. It is envisaged that studies performed in the H3Africa Initiative will inform subsequent strategies to address more broadly health inequities in both communicable and non-communicable diseases eventually leading to health benefits in Africa.

Note from the NIH and Wellcome Trust (April 13, 2011)
About upcoming funding and calls for proposals

H3Africa Conference: Photos

H3Africa Conference: Submit Your Feedback

H3Africa Working Group White Paper

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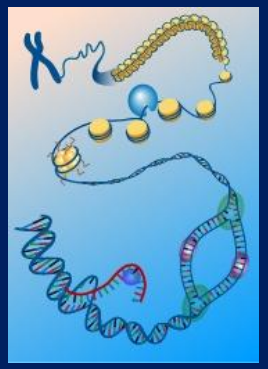
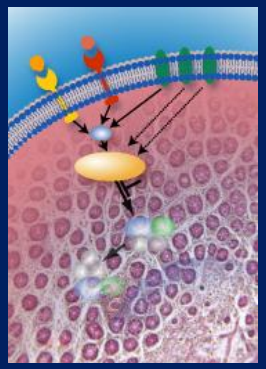
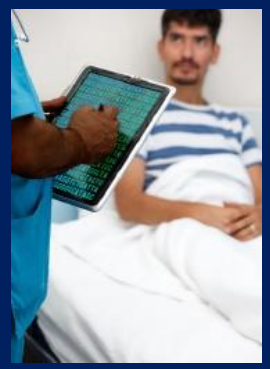
NATIONAL INSTITUTES OF HEALTH | wellcome trust

h3africa.org

Genomic Accomplishments Across Domains

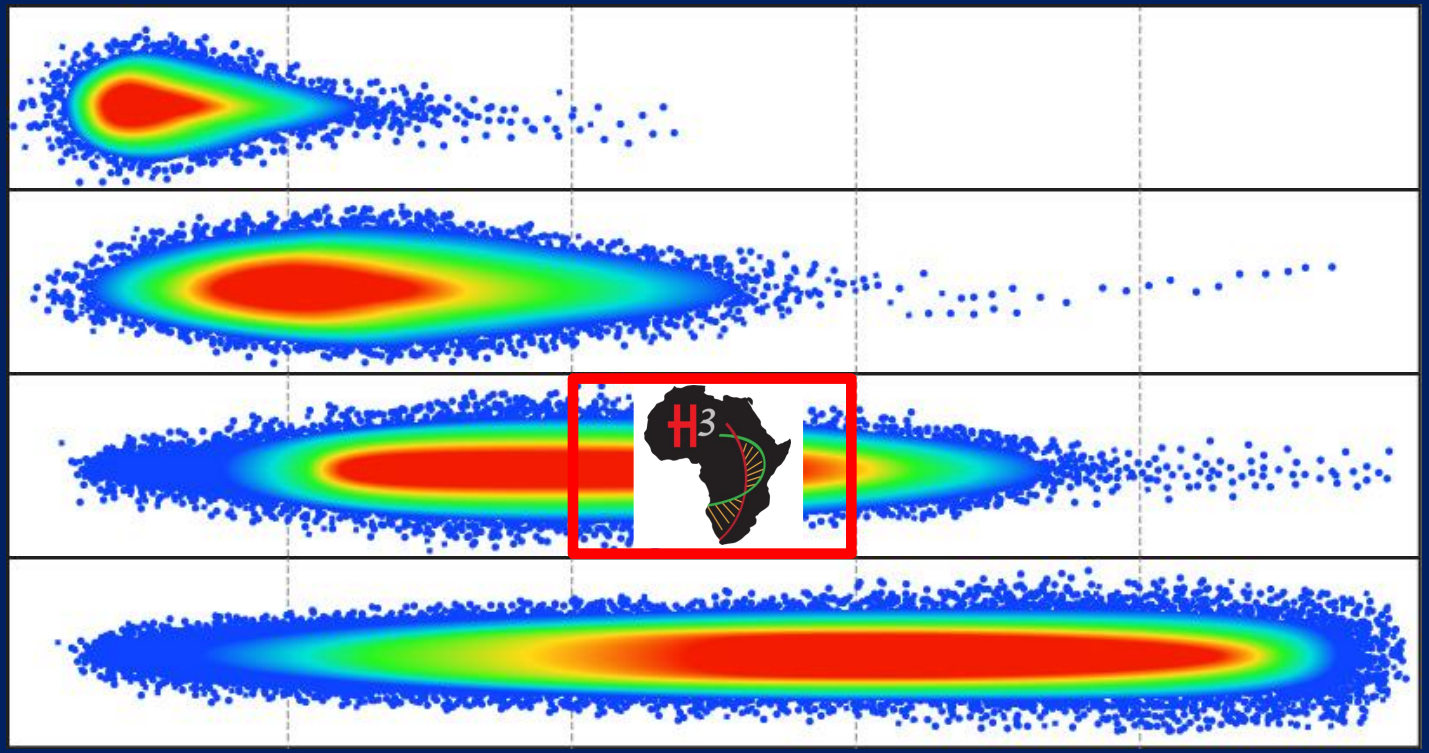
Understanding the Structure of Genomes	Understanding the Biology of Genomes	Understanding the Biology of Disease	Advancing the Science of Medicine	Improving the Effectiveness of Healthcare
				

1990-2003
Human Genome Project

2004-2010

2011-2020

Beyond 2020



National Institutes of Health - H3Africa Research Network

Alash'le Abimiku
Institute of Human Virology Nigeria, Nigeria
IHVN H3Africa Biorepository (I-HAB)

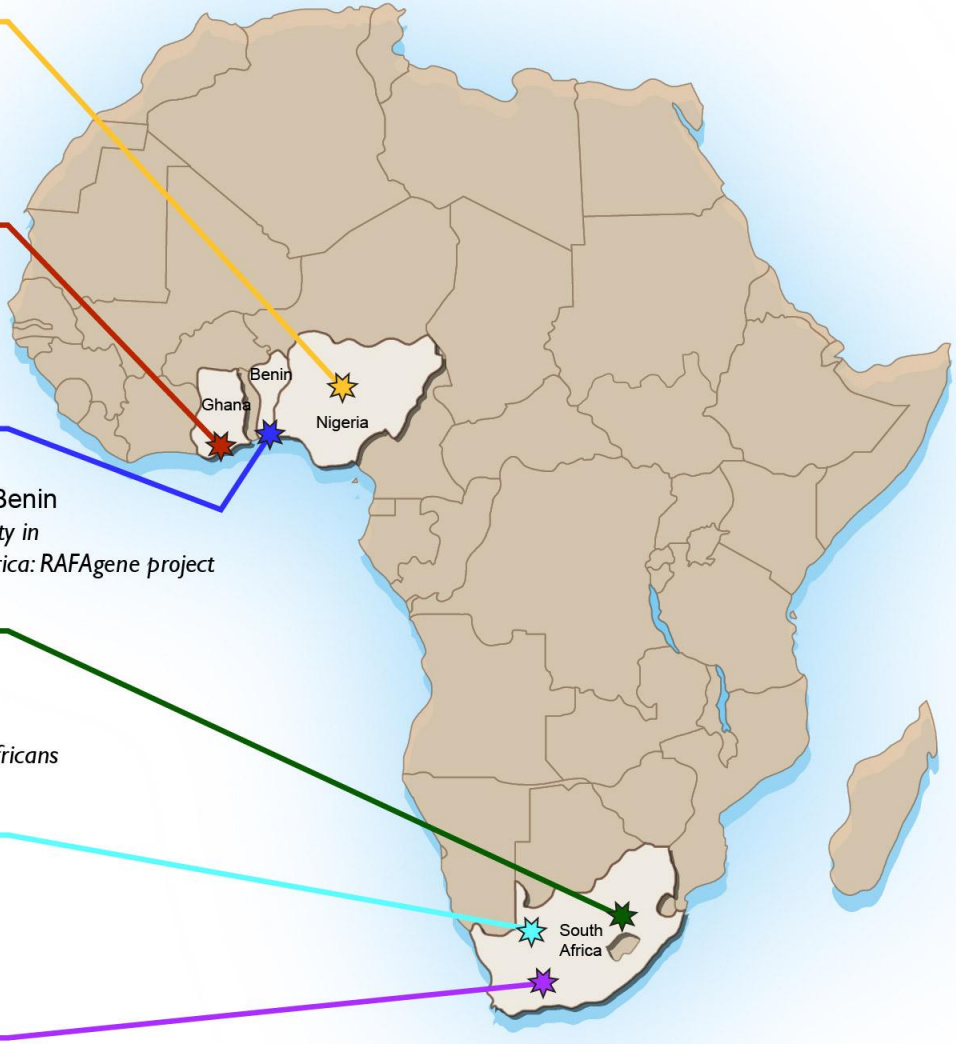
Dwomoa Adu and Akinlolu Ojo
University of Ghana Medical School &
University of Michigan, Ghana & USA
H3Africa Kidney Disease Research Network

Dissou Affolabi
National Hospital for Tuberculosis and Pulmonary Diseases, Benin
Contribution of genetic variation to pharmacokinetic variability and toxicity in patients undergoing multi-drug tuberculosis treatment in Sub-Saharan Africa: RAFAgene project

Michele Ramsay
University of the Witwatersrand & NHLS, South Africa
Genomic and environmental risk factors for cardiometabolic disease in Africans

Akin Abayomi
Stellenbosch University, South Africa
Development of stem cell, blood & DNA bio repositories to facilitate studies on Health, Disease & Pharmacogenomics of African Populations

Nicola Mulder
University of Cape Town, South Africa
H3ABioNet: a sustainable African Bioinformatics Network for H3Africa



NIH Staff @ This Meeting: NHGRI

Eric Green, NIH Common Fund Global Health Program, Co-Chair

Jane Peterson, H3Africa Project Coordinator

Mark Guyer, H3Africa Co-Project Coordinator

Ebony Bookman, H3Africa Program Director

Margret Penno, H3Africa Biorepository Consultant

Karen Hofman, H3Africa Human Subjects Consultant

Chengetai Mahomva, H3Africa Program Analyst

NIH Staff @ This Meeting: Others

Common Fund

Leslie Derr, H3Africa and MEPI Program Director

National Institute on Drug Abuse

Louise Wideroff, H3Africa Biorepository Program Director

National Institute of Child Health & Human Development

Jean Flagg-Newton, H3Africa IEARD Program Director

National Institute of Diabetes and Digestive and Kidney Diseases

Marva Moxy-Mims, H3Africa Program Director

Wellcome Trust

NIH

Genomics/Genetics

February, 2011

PERSPECTIVE

doi:10.1038/nature09764

Charting a course for genomic medicine from base pairs to bedside

omim and http://www.genome.gov/GWAStudies) and the role of structural variation in disease[8], some of which have already led to new therapies[9–13]. Other advances have already changed medical practice (for example, microarrays are now used for clinical detection of genomic imbalances[14] and pharmacogenomic testing is routinely performed before administration of certain medications[15]). Together, these achievements (see accompanying paper[16]) document that genomics is contributing to a better understanding of human biology and to improving human health.

As it did eight years ago[17], the National Human Genome Research Institute (NHGRI) has engaged the scientific community (http://www.genome.gov/Planning) to reflect on the key attributes of genomics (Box 1) and explore future directions and challenges for the field. These discussions have led to an update dvision that focuses on understanding human biology and the diagnosis, prevention and treatment of human disease, including consideration of the implications of those advances for society (but these discussions, intentionally did not address the role of genomics in agriculture, energy and other areas). Like the HGP, achieving this vision is broader than what any single organization or country can achieve—realizing the full benefits of genomics will be a global effort.

This 2011 vision for genomics is organized around five domains extending from basic research to health applications (Fig. 2). It reflects the view that, over time, the most effective way to improve human health is to understand normal biology (in this case, genome biology) as a basis for understanding disease biology, which then becomes the basis for improving health. At the same time, there are other connections among these domains. Genomics offers opportunities for improving health without a thorough understanding of disease (for example, cancer therapies can be selected based on genomic profiles that identify tumour subtypes[18,19]), and clinical discoveries can lead back to understanding disease or even basic biology.

The past decade has seen genomics contribute fundamental knowledge about biology and its perturbation in disease. Further deepening this understanding will accelerate the transition to genomic medicine (clinical care based on genomic information). But significant change rarely comes

decade. Similarly, we note three cross-cutting areas that are broadly relevant and fundamental across the entire spectrum of genomics and genomic medicine: bioinformatics and computational biology (Box 3), education and training (Box 4), and genomics and society (Box 5).

Understanding the biology of genomes

Substantial progress in understanding the structure of genomes has revealed much about the complexity of genome biology. Continued acquisition of basic knowledge about genome structure and function will be needed to illuminate further those complexities (Fig. 2). The contribution of genomics will include more comprehensive sets (catalogues) of data and new research tools, which will enhance the capabilities of all researchers to reveal fundamental principles of biology.

Comprehensive catalogues of genomic data

Comprehensive genomic catalogues have been uniquely valuable and widely used. There is a compelling need to improve existing catalogues and to generate new ones, such as complete collections of genetic variation, functional genomic elements, RNAs, proteins, and other biological molecules, for both human and model organisms.

Genomic studies of the genes and pathways associated with disease-related traits require comprehensive catalogues of genetic variation, which provide both genetic markers for association studies and variants for identifying candidate genes. Developing a detailed catalogue of variation in the human genome has been an international effort that began with The SNP Consortium[20] and the International HapMap Project[3] (http://hapmap.ncbi.nlm.nih.gov), and is ongoing with the 1000 Genomes Project[22] (http://www.1000genomes.org).

Over the past decade, these catalogues have been critical in the discovery of the specific genes for roughly 3,000 Mendelian (monogenic) diseases

Figure 1 | Genomic achievements since the Human Genome Project (see accompanying rollfold). ▶

[1]National Human Genome Research Institute, National Institutes of Health, 31 Center Dr., Bethesda, Maryland 20892-2152, USA.
*Lists of participants and their affiliations appear at the end of the paper.

genome.gov/sp2011

New NHGRI Vision for Genomics Published

And away we go!

Questions?