Genomic Medicine III: Setting the Context

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Director, NHGRI

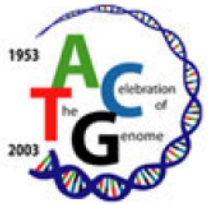
April, 2003

Human Genome Project Ends

April 14, 2003

National Human Genome Research Institute

National Institutes of Health
U.S. Department of Health and Human Services



National Human Genome Research Institute
National Institutes of Health
Department of Health and Human Services
and
Office of Science
U.S. Department of Energy

International Consortium Completes Human Genome Project

All Goals Achieved; New Vision for Genome Research Unveiled

BETHESDA, Md., April 14, 2003 - The International Human Genome Sequencing Consortium, led in the United States by the National Human Genome Research Institute (NHGRI) and the Department of Energy (DOE), today announced the successful completion of the Human Genome Project more than two years ahead of schedule.

Since the completion of the Human Genome Project:

3,307 days
~79,000 hours
~4,590,000 minutes
~285,000,000 seconds

Has this time been 'well spent'?

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 determination of a legion of talented scientists who decided to make this project their overarching focus, all of the initial objectives of the HGP have now been achieved at least two years ahead of expectation, and a revolution in biological research has begun.

The project's new research
experimental technologies ha
steady stream of ever-larger a
plex genomic data sets that ha
public databases and have tr
study of virtually all life p
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important new dimension into
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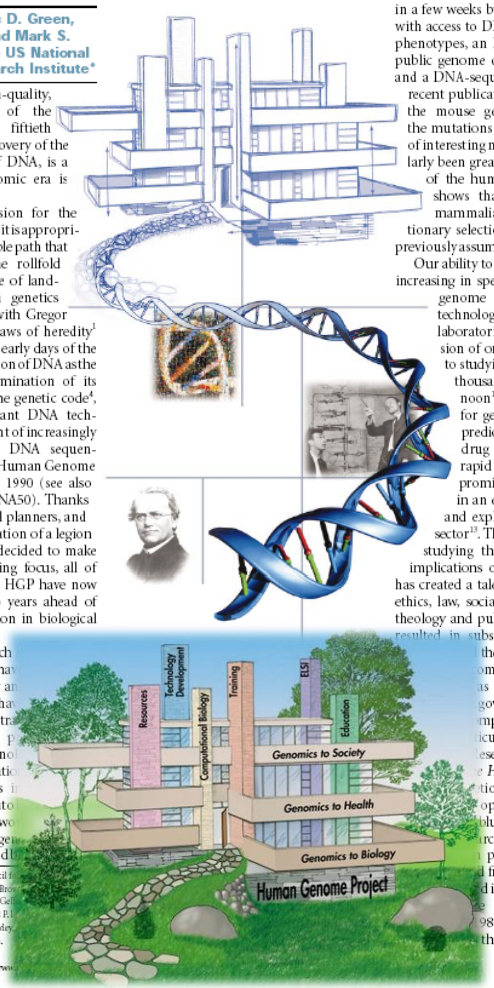
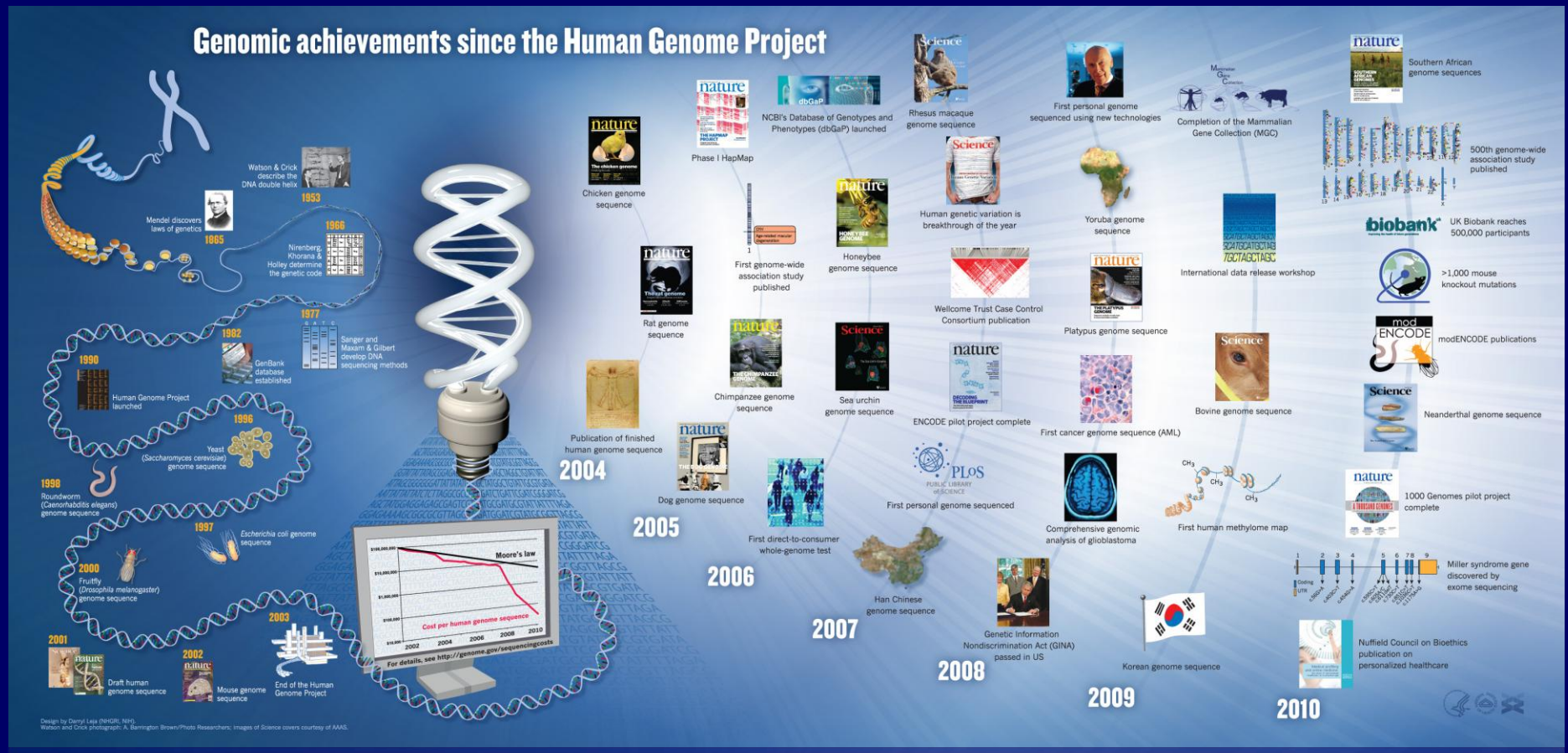


in a few weeks by a single graduate student with access to DNA samples and associated phenotypes, an Internet connection to the public genome databases, a thermal cycler and a DNA-sequencing machine. With the recent publication of a draft sequence of the mouse genome[11], identification of the mutations 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.

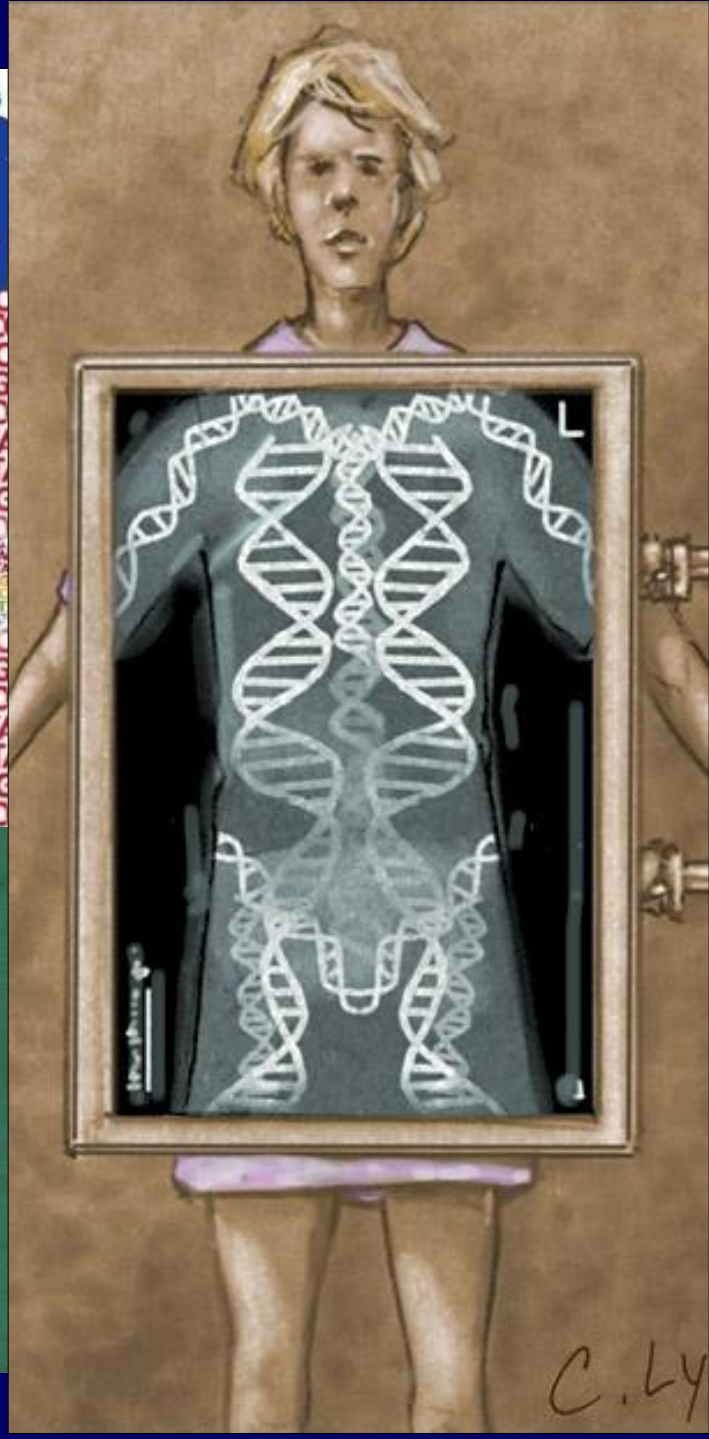
Our ability to explore genome function is increasing in specificity as each subsequent genome is sequenced. Microarray technologies have catapulted many laboratories from studying the expression of one or two genes in a month to studying the expression of tens of thousands of genes in a single afternoon[12]. 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 sector[13]. The investment of the HGP in studying the ethical, legal and social implications of these scientific advances has created a talented cohort of scholars in ethics, law, social science, clinical research, theology and public policy, and has already resulted in substantial increases in public
the introduction of significant
omplete) protections against
s genetic discrimination (see
gov/PolicyEthics).
mplishments fulfil the expan-
iculated in the 1988 report of
esearch Council, *Mapping and*
Human Genome[14]. The suc-
tion of the HGP this year thus
opportunity to look forward
blueprint for the future of
rch over the next several years.
presented here addresses a
from that reflected in earlier
d in 1990, 1993 and 1998 (refs
documents addressed the
988 report, defining detailed
the development of genome-

*Endorsed by the National Advisory Council
Research, whose members are Vickie Yates Br
Wylie Burke, Ronald W. Davis, William M. Ge
Bronya J. Keats, Rajto Kitcherlapati, Richard P.
Nickerson, Maynard V. Olson, Janet D. Rowley
Robert H. Waterston and Tadataka Yamada.

***Nature*, April 2003**



Green et al., *Nature* (2011)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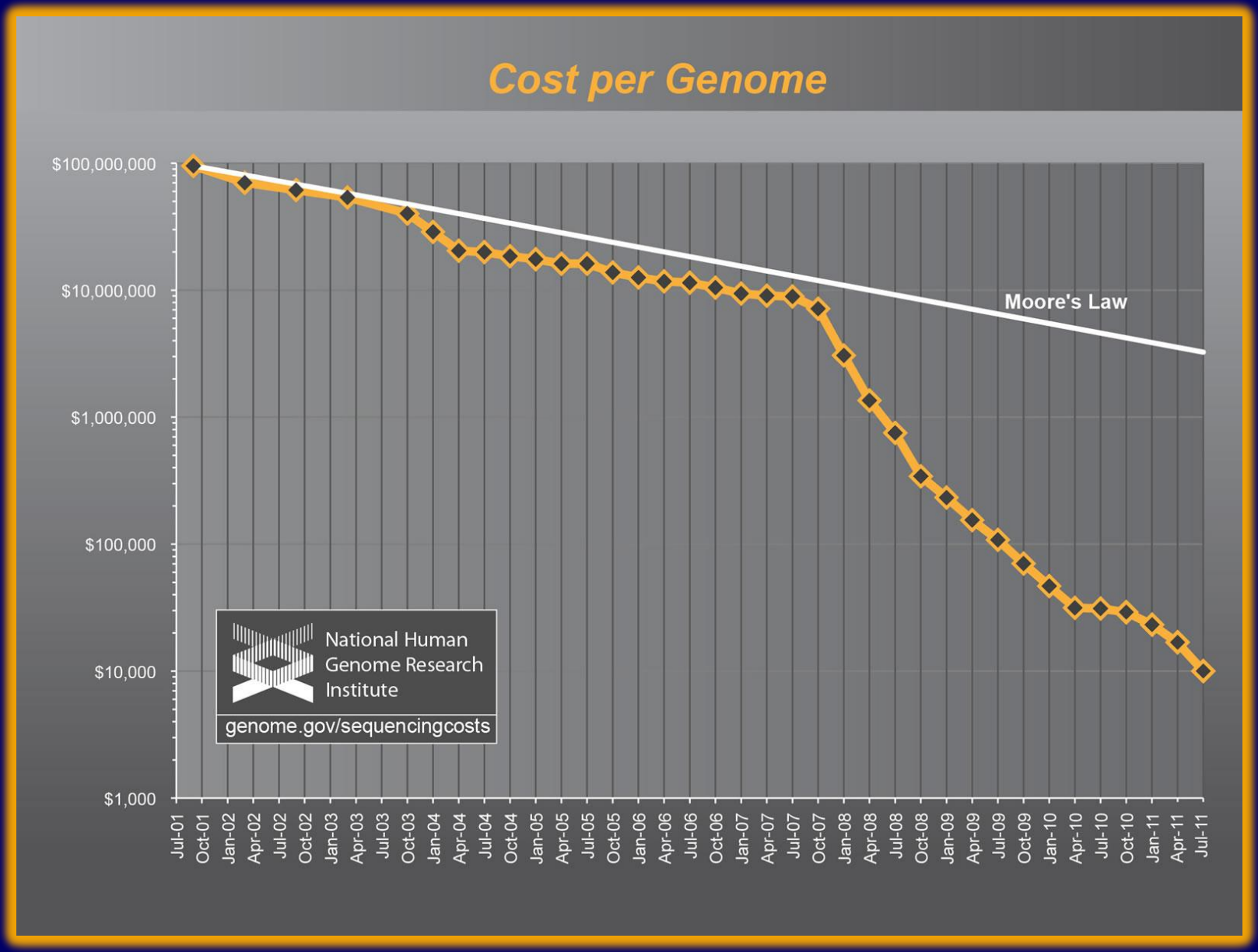
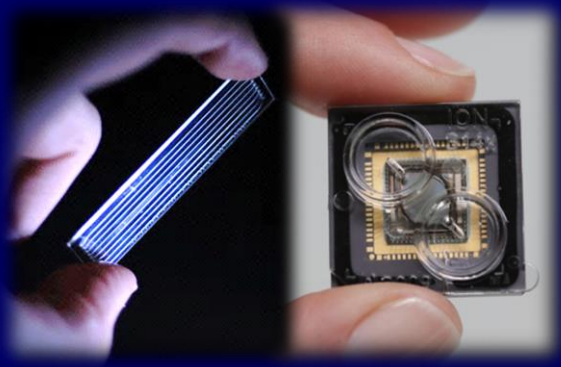
Cost per Sequenced Human Genome



Sequencing a Human Genome

HGP (1st Sequence)	*Immediate Post-HGP*	*Today*
		
~6-8 years	**~3-4 months**	**~2-3 days**
~$1B	**~$10-50M**	**~$4-8K**

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 division 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). ▶

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*Lists of participants and their affiliations appear at the end of the paper.

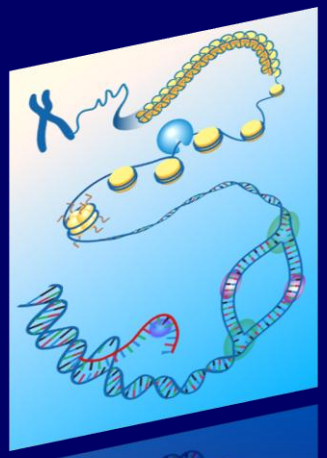
genome.gov/sp2011

New NHGRI Vision for Genomics Published

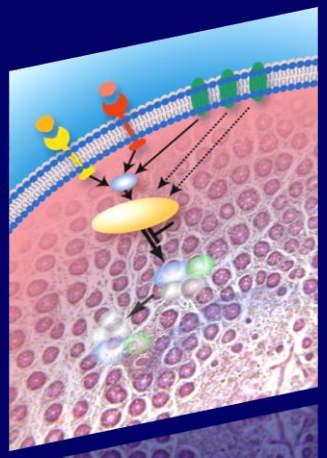
Five Domains of Genomics Research

Understanding the Structure of Genomes

Understanding the Biology of Genomes

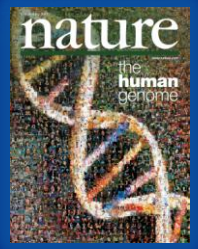


Understanding the Biology of Disease



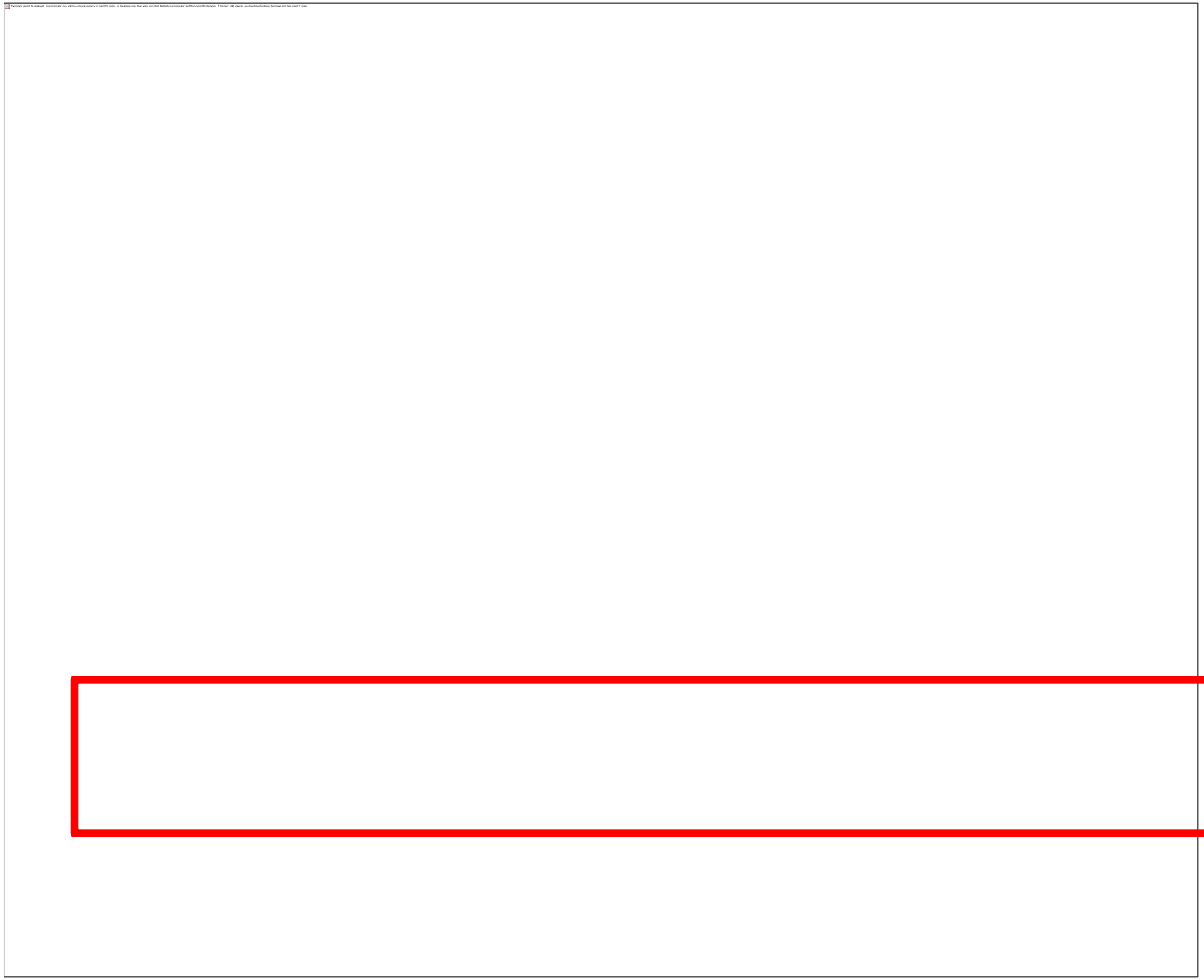
Advancing the Science of Medicine

Improving the Effectiveness of Healthcare



Base Pairs to Bedside

Helix to Health



Green et al. 2011


The Future
NEXT EXIT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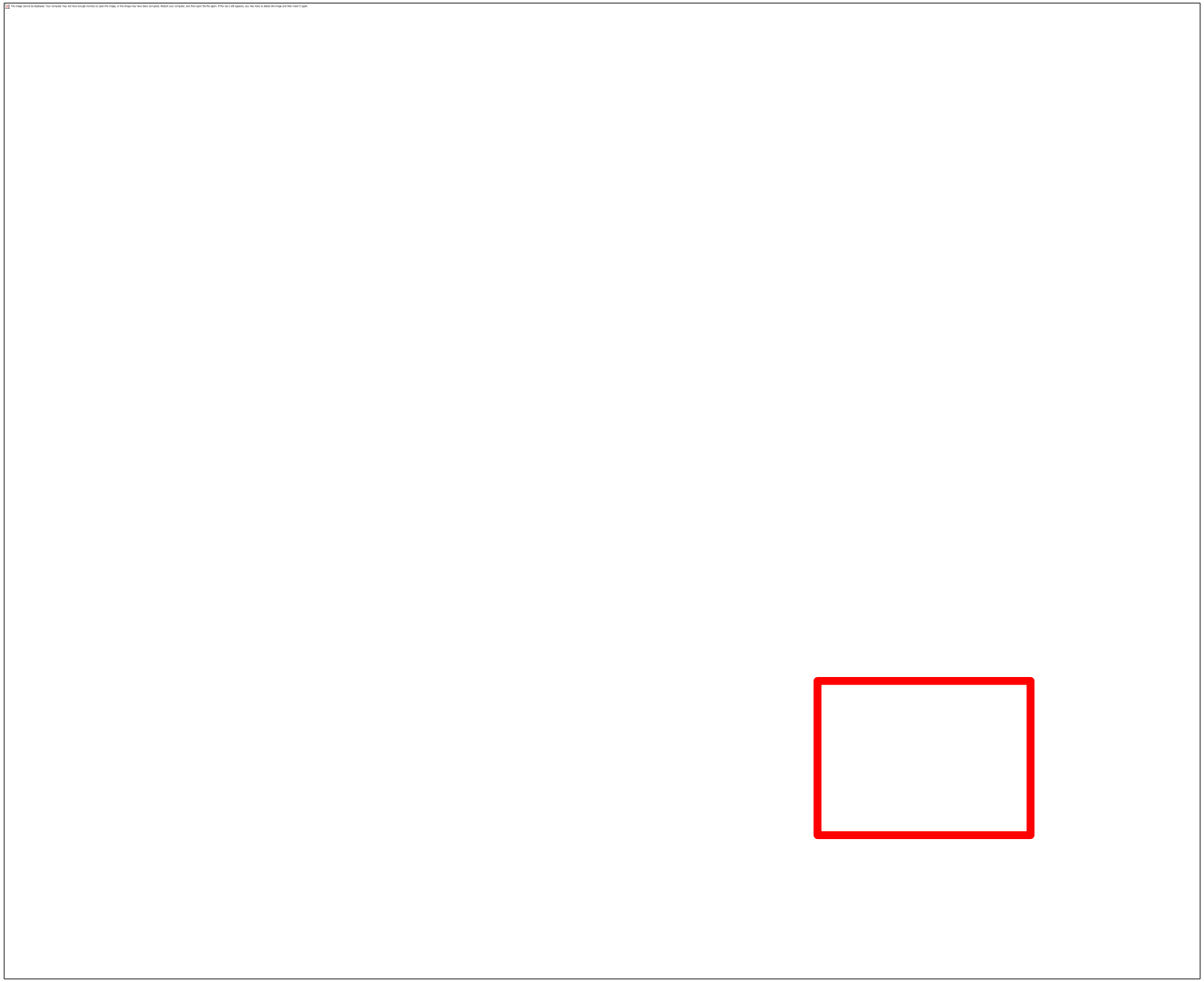

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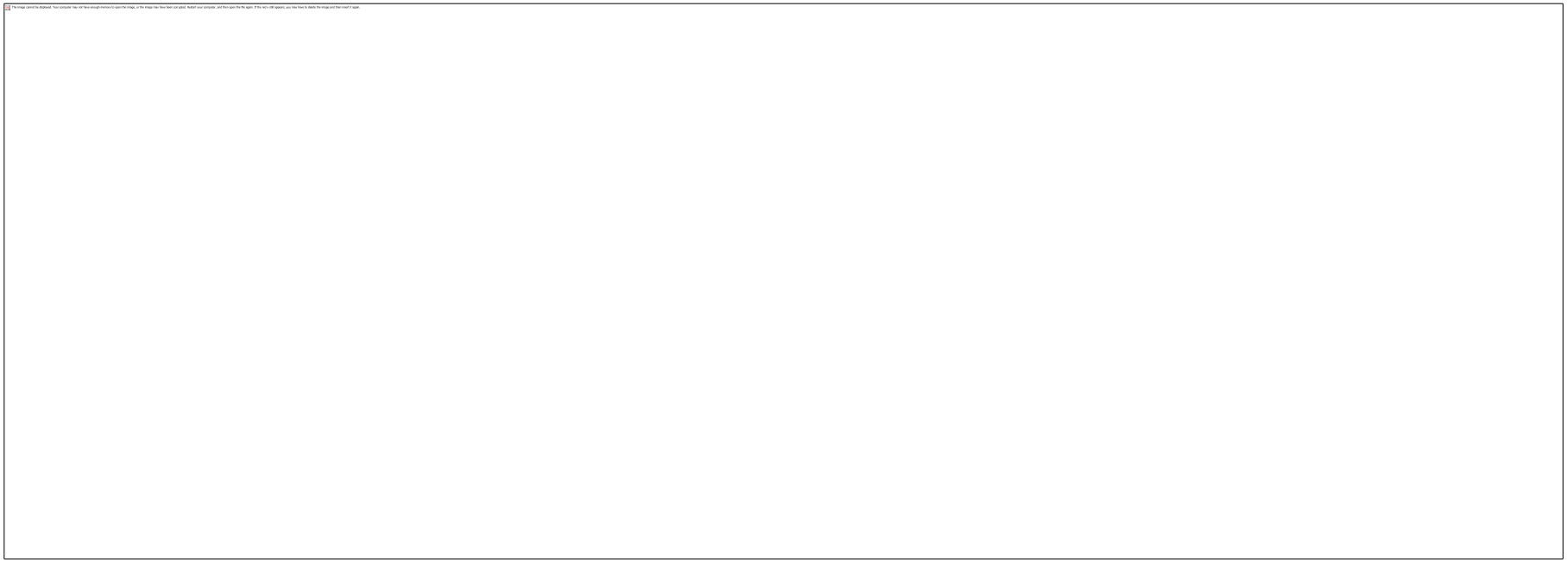
NHGRI Aims to Learn



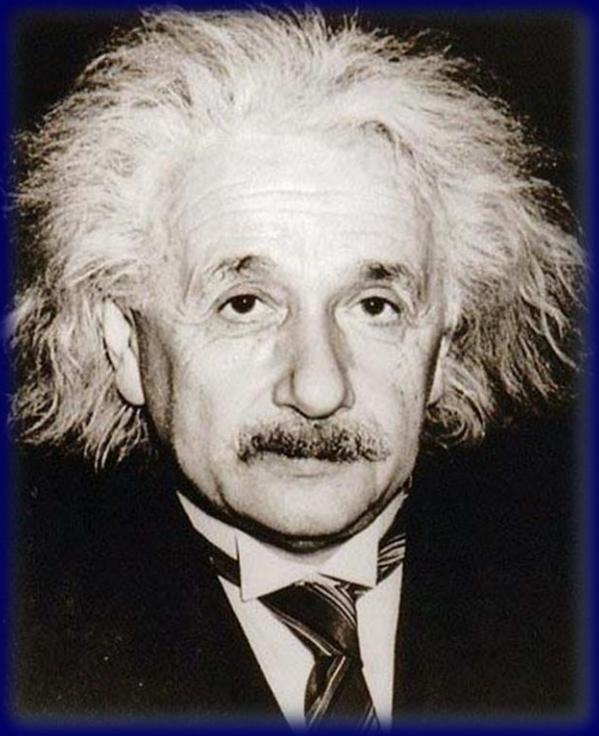
Basic Science

Translational Science

Implementation Science

If we knew what we were doing, it wouldn't be called Research.

–A. Einstein

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