proposed was ultimately not feasible, the effort represents the kind of cooperation that will be required in the search for sustainable water supply options on Long Island. Because the search has been abandoned in the wake of the $22 million recharge project failure is cause for alarm. A number of alternate avenues that must be pursued by a coalition of government and scientific agencies if water crises such as this one are to be defused. Aeration of treated wastewater prior to recharge, for example, may eliminate enough of the residual disinfectant byproducts to minimize THM development in groundwater storage. Sites for recharge may be chosen with more thought to the natural sedimentation of the area: instead of an impacted, urbanized substrate, a site chosen for looser, more permeable sediments may improve recharge infiltration and reduce the mounding that slows the recharge process. Clearly, the work of the Nassau County Department of Public Works was not finished when the East Meadow project failed: the experience, data, and technological infrastructure borne of that failure should support further research into sustainable water policy on Long Island. If the failure of this project signifies the end of proactive research, then it also forebodes an inevitable water crisis.

REFERENCES


April 2003 marked the completion of the Human Genome Project. Remarkably, this celebratory event occurred 50 years to the month after the landmark publication of Watson and Crick's discovery and description of DNA (1). With this recent milestone achieved, scientists project a new beginning in biological sciences. Visionaries anticipate that advances medicine and in agriculture will accelerate, human health diagnostics will be revolutionized, and individualized therapeutic options designed for patients will become commonplace (2).

Biology has indeed moved into a new era. Dr. Eric S. Lander, professor of biology at MIT, member of the Whitehead Institute and Director of the Whitehead Center for Genome Research located in Cambridge, MA, has described this scientific progression as a movement from the era of biology of organisms to the era of biology of molecules to the new era of biology of information (3). How will we read the information provided by the mapping of the human genome? With approximately three billion letters, or bases, of the human genetic code and currently some ten million common single nucleotide polymorphisms (SNPs) (points in the genome at which
one base can differ between individuals), progress in this new era of informational biology will be complex (4). The anticipated goal of establishing readily discernible paths from genomic information to human health is an immense challenge (2). Possessing a map of the human genome is only just the beginning.

Potentially complicating scientific progress in informational biology will be the necessary collateral issues of increased public awareness and significant protections against misuses such as genetic discrimination. Laboratory scientists will need to become even more connected to other talented scholars in the disciplines of ethics, law, social science, clinical research, theology, and public policy as progress is being made. As scientists learn to better read the human genetic blueprint, rapid advances regarding the emerging ethical, legal, and social issues will commensurately be needed (2). Additionally, recognizing that these discoveries are truly expensive, partnerships between private sector and government entities will be necessary to make collective scientific advances. Who owns the intellectual property rights then becomes a pertinent issue as investors seek returns, health care providers attempt to maintain confidentiality, and insurance brokers establish insurability (5).

What does the future hold with regard to genomic technology and its application? In November, 2002, a National Advisory Council for Human Genome Research, convened by the US National Human Genome Research Institute, invited several hundred researchers to offer insight into future research needs and directions as the Human Genome Project was nearing completion (2,6). Their contributions, distilled into three thematic areas with six crosscutting elements, can be visualized as a building with three floors and six pillars all supported by the foundation of the Human Genome Project. The first floor covers genomics to biology, the second, genomics to health, and the third, genomics to society. The pillars, or crosscutting issues, which intersect all three floors include resources; technology development, computational biology; training; ethical, legal, and social implications; and education (2).

Although DNA is relatively simple and chemically well understood, the human genome remains extraordinarily complex, with its specific functions poorly understood. Sequence information alone cannot be used to predict protein-coding sequences. Only 1-2% of its bases encode proteins (7) and not all of the protein-coding sequences are known. With approximately 30,000 protein-coding genes, they perhaps contain the bulk of the regulatory information controlling the expression of protein coding genes. Even less is known about the function of the roughly half of the genome that consists of highly repetitive sequences or of the remaining non-coding, non-repetitive DNA (8).

Before a full atlas can be achieved outlining biological and medical explanations of cellular metabolism, an interactive map of the proteins in a cell and their cellular locations will be needed (9). This will be difficult as genes and gene products do not function independently, but rather participate in complex interconnected pathways, networks, and molecular systems that when taken together give rise to the workings of cells, tissues, organs, and organisms. In order to accomplish this level of understanding, computational biology will by necessity be integrated into experimental systems for future biomedical research. As the amount and complexity of data increases, computational methods will become even more intrinsic to modern biological research (2). Organizing and storing the enormous amount of data, including the myriad of potential biological combinations and possibilities, will require massive relational databases that can be queried effectively and efficiently.

Correlating variation in DNA sequence with phenotypic traits is the essence of genetics. Advances in human genetics have to date been most notable for traits associated with variation in a single gene. Most phenotypes involving common diseases and variable responses to pharmacological agents have a complex origin that involves the interplay between multiple genetic factors (genes and their products) and non-genetic factors (environmental influences). Discovering how these phenotypes become expressed is dependent upon our understanding of the human genome and the technology available to apply such knowledge. “Unraveling such complexity will require both a complete description of the genetic variation in the human genome and the development of analytical tools for using that...
information to understand the genetic basis of disease” (2).

Cataloging all common genetic variants in the human population, including single-nucleotide polymorphisms (SNPs), small deletions and insertions, and other structural differences began several years ago. Many SNPs have been identified and are available for reference (10, 11).

Studying SNPs helps to identify points in the genome at which one base can differ between individuals. In this way, if a particular SNP is inherited with a disease, it is strong indication that a gene that confers susceptibility lies somewhere nearby (4).

To further refine the search, scientists in 2002 began a three-year, $100 million-dollar endeavor called the HapMap Project (12). Since genetic shuffling occurs during the production of sex cells, focusing on haplotypes, which are the specific DNA sequences of a block, has become the basis for a new approach (4). Pairs of chromosomes line up and exchange portions of genetic material in the cell divisions that give rise to eggs or sperm. The breaking, exchange, and resealing tends to occur at particular points and is not entirely random. Blocks of sequence, therefore, can be and have been inherited down through generations without being broken up. These blocks of sequence vary widely in size, but are thought to be 10,000 bases or more in length.

Common haplotypes can be identified by sampling only a handful of key SNPs. Studies have indicated that for each block there are only a few common haplotypes in the population (13, 14, 15). With the genome sequence already in hand, and the HapMap as an index, geneticists will have the means to scan the entire genome rapidly for disease genes, perhaps by analyzing as few as 300,000 SNPs (13). Determining how people respond differently to prescription drugs according to their particular genetic make-up could also be facilitated by the HapMap (4).

Moreover, the genome is a dynamic structure. Variation exists among individuals and, importantly, between species. Comparing various species genomic sequences is important for identifying functional elements; defining the genetic basis for speciation; and facilitating the characterization of mutational processes. Mutation drives long-term genetic change and is the underlying cause of inherited disease. Unfortunately, at present, our understanding of DNA mutation and repair, including the important role of environmental factors, is limited (2).

Regardless of advancements in genomic science, benefiting from such advances will depend upon effective access to the information. Effective access, however, will require negotiating around complex issues of intellectual property (such as patenting and licensing) and commercialization. Without commercialization, the diagnostic and therapeutic potential of genomic information will likely not be accessible in a clinical setting. Adding to this issue is the fact that genomic research is global in scope and international treaties, laws, regulations, practices, beliefs, and cultures also come into play. Maximizing public benefit should be the overarching goal (2).

Sequencing the human genome provides unparalleled opportunity to advance the understanding of the role of genetic factors in human health and disease, to provide more precise definition of the non-genetic factors involved, and to apply this insight rapidly to the prevention, diagnosis, and treatment of disease. Three strategies have been identified to achieve such progress: first, identify genes and pathways with a role in health and disease and determine how they interact with environmental factors; second, develop, evaluate, and apply genome-based diagnostic methods for the prediction of susceptibility to disease, the prediction of drug response, the early detection of illness, and the accurate molecular classification of disease; and, third, develop and deploy methods that catalyze the translation of genomic information into therapeutic advances (2).

Common diseases are often the result of interplay of multiple genes and multiple non-genetic factors rather than a single allele dictating disease susceptibility and response to treatments. As a result, deciphering the role of genes in human health and disease becomes difficult. Obstacles that scientists will have to overcome include defining biologically what is normal, identifying and quantifying environmental exposures, and generating not only sufficient, but also applicable genotypic information. For those common diseases in which rare alleles are involved, more efficient strategies will be needed (16).

Traditionally, genetic research has focused on identifying genes that predispose an individual to illness. An important alternative, and relatively unexplored area of research, is to focus on the role of genetic factors in maintaining good health. Identifying gene variants that are important for the maintenance of health, particularly in the presence of known environmental risk factors, will be needed. Genetically describing those individuals who do not exhibit symptoms of diabetes, cancer, heart disease and Alzheimer’s disease, among others, is essential. Additionally, rigorous examination of those individuals at high risk for specific diseases who do not develop them,
such as sedentary, obese smokers without heart disease or those with mutation risks for colon cancer, will also be scientifically profitable (2).

If illness can be more specifically diagnosed earlier in the course of disease and treatment designed for the individual patient with genomic information, does it not seem reasonable that illness classifications should be organized to facilitate therapeutic and preventative options? Some scientists advocate a new molecular taxonomy of diseases to replace the present, largely empirical, classification system. Genomic information rather than pathological information would form the basis of disease classification. Current examples are the reclassification of neuromuscular diseases (17) and certain types of cancer (18). This would truly be an aggressive overhaul of the medical sciences and a major shift in the ideological approach to disease diagnosis and therapy (2).

Understanding biological pathways provided by genomics should add fundamental knowledge to therapeutic design. Fewer than 500 human gene products are targeted by available pharmaceuticals (19). With 30,000 or so human protein-coding genes having products targetable for drug development, an enormous resource for designing therapeutic inventions remains untapped (2).

Beyond health and disease, genes influence human traits and behaviors. Attributes such as handedness and various behavioral characteristics are just now beginning to be unraveled. This type of information can lead to further ethical questions such as whether school officials should be alerted to the student with a predisposition to hyperactivity or whether behavioral traits should be admissible in civil or criminal proceedings. Within the realms of biology, health, and life, some human applications of genomics are and will be controversial and the propriety of scientific investigation questioned. Scientific inquiry is not infinite and society will need to define the appropriate and inappropriate use of genomics (2).

Long-term projections focus on sequencing one human genome for $1,000. Currently, even higher prices make access to this information prohibitive for the majority of individuals. With a humanitarian goal of providing genomic research benefits to all, it will be critical to examine how genomic health care is accessed and used. How can and how soon will barriers to equitable access be removed? This issue is not restricted to resource-poor nations, but also in wealthier countries where segments of society, such as indigenous populations, the uninsured, or rural and inner city communities, have traditionally not received adequate health care (2).

Although the benefits from genomic research may appear limited at present, they will continue to expand, bounded only by human imagination and the technology created to achieve the desired results. Genomics will clearly impact all members of society. Completion of the Human Genome Project is just the beginning. With regard to the ethical considerations and standards established and yet to be established along the way, Dr. Sydney Brenner, Distinguished Professor at The Salk Institute in La Jolla, CA states with foresight, “The first, common to all scientists, is to tell the truth. The second is to stand up for all humanity” (20).

REFERENCES
3. E. S. Lander, presented at the Scientific Symposium of the National Human Genome Research Institute, Natcher Auditorium, National Institutes of Health, Bethesda, MD, 14 April 2003.