THE NEW ATLANTIS
A JOURNAL OF TECHNOLOGY & SOCIETY

HapMap: Revolution or Hype?

The Controversy Surrounding the Next Gene-Mapping Project

Although the mapping of the human genome is more or less complete, it is becoming clear that using the newly compiled data for medical research will not be as simple as some imagined. While in the past scientists have had some success in identifying the roots of diseases caused by single-gene abnormalities (like cystic fibrosis or Huntington's disease), the genetic sources of more common but more complicated multi-gene diseases remain elusive.

One promising approach to the problem would make use of a recent discovery about the limits of human genetic variability. Rather than being transmitted to new generations nearly at random, it appears that many genes are passed down in blocks—known as haplotypes—that remain largely unchanged through generations, and may not have changed much from the time of the earliest human ancestors. In each haplotype, researchers believe there may be only a handful of variations across the entire human population, and these small variations may play an important role in the development of many diseases.

Scientists hope that a map of these haplotype blocks could be a useful aid to researchers seeking the variant genes thought to be involved in common diseases like diabetes, asthma, and several cancers. A number of the major research institutions involved in the Human Genome Project have made this new mapping effort their next priority, and a consortium of researchers in Japan, China, Canada, Britain, and the United States recently launched the new $100 million "HapMap" project, to be undertaken over the next three years. The work will involve analysis of the genomes of individuals from four ethnic groups: Japanese, Han Chinese, the Yoruba people of Nigeria, and Americans of northern and western European descent. (This list may be expanded in the future.) The project will seek out haplotype variations within and between these groups, in the hope that such knowledge will offer clues to the genetic sources of disease.

The NIH will provide about one-third of the funding, with the rest coming from a biotech industry consortium, the Wellcome Trust in Britain, Genome Canada, and the governments of China and Japan. The immediate goal of the project is not to find disease-related genes, but to provide a tool that other researchers could use in tracking down such genes. All the data gathered by the HapMap project will be in the public domain, and will be made available on the Internet for public and private researchers to use.

But the project is not without controversy. For one thing, the study of a number of ethnically distinct populations opens the door to potential disputes over new discoveries (or hypotheses) about genetic differences between the races. This was a topic recently broached by Charles Murray, coauthor of *The Bell Curve*, the 1994 book that caused great controversy because of

the connections it drew between race and intelligence. In a recent message to an online mailing list, Murray wrote, "As the HapMap project gets underway, this would seem to be a good time to put bets on the table regarding how the results will affect the ongoing debate about whether race is a valid and/or useful construct." Murray believes that "the HapMap results will move the current consensus toward the traditional end. Race will regain credibility as a useful, albeit imprecise, way to categorize human beings."

Another possible source of contention relates to the development of patentable new treatments. A decade ago, the Human Genome Diversity Project ran into similar difficulties in its effort to map genetic variations across ethnic groups, and the project was scrapped before its completion, after coming under heavy fire from groups in the Third World concerned that Western pharmaceutical companies aimed to profit from the genomes of the underprivileged.

The HapMap project also faces more conventional scientific objections. A number of prominent geneticists have argued that the project is based on very recent and still uncertain discoveries, and that such a massive investment of time and money is unwise.

Some have also expressed suspicion that the importance of these massive biotech research projects—first the genome, now the HapMap—is disingenuously hyped just to keep the grant money flowing. These critics suggest that the HapMap project exists largely because the major genome research centers formerly involved in the Human Genome Project are now in need of work and must offer some justification for their massive budgets. Dr. Francis Collins, who heads the NIH's National Human Genome Research Institute, flatly disagrees: "I completely reject the idea that this is a make-work project for the genome centers."

Whatever the motivations or ambitions driving this new project, it will surely make work for Collins and the genome mappers. In the wake of the Human Genome Project, the HapMap offers a new hook on which to hang the high hopes of genetic research and medicine. It also demonstrates that one of the implicit suppositions of the Human Genome Project—that the genetic code could be "deciphered" by being broken down into its most basic components—is not quite right. It now appears that blocks of genes, and their arrangements, have as much to do with the expression of normal and abnormal traits as individual genes and their locations in the genome. Even genetic wholes are not entirely the sum of their parts.