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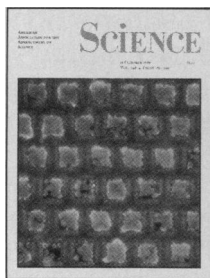
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COVER Living nonadherent P388D1 cells (from murine lymphoid neoplasm), stained here with a red fluorescent dye, are retained in wells (50 μm square and 50 μm deep) etched into the surface of a potentiometric silicon biosensor. The sensor measures metabolic rates, which are affected by a variety of biological and chemical agents. See page 243. [Photograph by J. C. Owicki and K. M. Kercso, Molecular Devices Corporation, Menlo Park, CA 94025]

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Sequences and Consequences of the Human Genome

The sequencing of the human genome involves big money, big consequences, and big controversies. Within the scientific community there is the question of money because of the "big science" image. The cost of the genome project (\$3 billion in 15 years) is much smaller than the cost of a supercollider or of a space station, and it is more of a mom-and-pop store enterprise than the mass production assembly line of real big science. The Cystic Fibrosis Foundation has spent \$120 million in the past 4 years on one illness, to say nothing of the other foundation and federal money spent on the same project. In that context a price of \$200 million per year, the figure for the human genome project, for work that applies to many diseases and untold discoveries in biology sounds cost-effective.

The benefits to science of the genome project are clear. Illnesses such as manic depression, Alzheimer's, schizophrenia, and heart disease are probably all multigenic and even more difficult to unravel than cystic fibrosis. Yet these diseases are at the root of many current societal problems. The costs of mental illness, the difficult civil liberties problems they cause, the pain to the individual, all cry out for an early solution that involves prevention, not caretaking. To continue the current warehousing or neglect of these people, many of whom are in the ranks of the homeless, is the equivalent of providing iron lungs to polio victims at the expense of working on a vaccine.

Other medical applications of a genome sequence include an early warning system that may help individuals predisposed to diseases such as alcoholism, colon cancer, and depression. The early warning may allow them to avoid the problems by behavior or diet modification or frequent medical checkups. Family planning also will be made more accurate. No individual should be forced to obtain genetic information but none should be denied information either.

The "sky is falling" group, who denounce the genome project, sound like they are paraphrasing a Woody Allen admonition by saying, "We stand at the crossroads. One road leads to hopelessness, the other to utter despair. We must have the courage to make the right decision." The potential risks from the new knowledge gained by sequencing the human genome appear, on close examination, to be old problems revisited. Genetic counseling already exists for Down syndrome, Tay Sachs, and sickle cell anemia. Personal insurance policies already ask for lung x-rays, heart condition tests, and information on such behaviors as smoking. Group insurance is available without test. Fingerprints are not required of the general population but are kept on file for those who commit a crime. The information in the genome adds accuracy and scope to many of these applications but no new or threatening principles. If the higher visibility of the genome project causes a qualitative change, then, of course, new procedures may be needed.

A genome sequence should not be a precondition of employment, and legislation might be needed if that problem were to arise. However, less accurate data of the same type would be available today from family histories, and that does not seem to be part of current employment forms. If more accurate information provides temptation for abuse, action will be needed.

The argument that dictators would alter genes to convert their enemies is farfetched. The idea that a Hitler or a Stalin would prefer the engineering of Jews into Aryans or capitalists into communists as cheaper or more satisfying than killing them (as they did) is absurd. We must be vigilant about ethical concerns but not paralyzed by outlandish scenarios.

The belief of biologists that studying simple organisms such as *Escherichia coli*, flies, and rats is relevant to human physiology and behavior has been brilliantly confirmed. But there are differences. One cannot extrapolate carcinogenic potency from the mouse to the rat with precision, and even less to the human. Some diseases involve speech and mental states unique to man. Sequencing the human genome puts us on the threshold of great new benefits and some real but avoidable risks. There are immoralities of commission that we must avoid. But there is also the immorality of omission—the failure to apply a great new technology to aid the poor, the infirm, and the underprivileged. We must step boldly and confidently across the threshold.—DANIEL E. KOSHLAND, JR.