COLUMBIA UNIVERSITY

GSAS News&Views

A PUBLICATION OF THE GRADUATE SCHOOL OF ARTS AND SCIENCES SUMMER 1994

The New Biology: Getting Ahead of the Curve

Robert Pollack

Professor of Biological Sciences

On the 18th of June, 1940, Winston Churchill spoke to the House of Commons on the disastrous course of the war of England and France against Germany. He ended with the famous peroration:

"Let us therefore brace ourselves to our duties and so bear ourselves that, if the British Empire and its Commonwealth last for a thousand years, men will say, 'This was their finest hour.'"

Many will recognize this sentence today, but few may recall an earlier phrase it refers to; the reason for "therefore:"

"But if we fail, then the whole world, including the United States, including all that we have known and cared for, will sink into the abyss of a new Dark Age made more sinister, and perhaps more protracted, by the lights of perverted science."

What could Churchill have meant in 1940 by "the lights of perverted science?" While he could have been guessing at the coming use of rockets, jet planes, napalm or nuclear bombs, he did not have to imagine any future weapons to call upon the intersection of science and government in pre-war Nazi Germany. This had already led to the orderly, scientifically-planned and executed euthanasia of many Germans, and by 1940 these operations had been extended to the East, in occupied Poland. By the time Churchill spoke, the major organizations of German genetics, biology, anthropology and medicine and many of the best scientists and physicians in the Reich had joined for more than five years in murder of what the German government and its scientists had agreed to call "Ballastexistenzen," lives not worth life.

Fifty years later those "lights of perverted science" still have the power to cast a shadow over the laboratories and hospitals in which biology and medicine come together. In the last third of the century, a new biology – built on the discovery that DNA is the genetic material – has provided medicine with a research agenda and a set of tools and techniques drawn from basic research on the human genome. These have recently given us such notable successes as the isolation and characterization of the genes responsible for cystic fibrosis, Huntington's Disease and hundreds of other inherited diseases; the restoration of function by insertion of absent genes in tissues of patients with inherited diseases; and technologies of early warning for late-onset diseases such as Alzheimer's, cancer and heart disease.

"...a knowledgeable woman will be able to get the information she needs to decide whether or not to carry to term a child that would be, for instance, a boy, or a girl, or short, or deaf, or gay."

While these successes and others like them are welcome, they have come to us entwined with less desirable consequences. For every late-onset disease that can be diagnosed in advance of symptoms by a tell-tale difference in DNA, considerable numbers of healthy people find they are paying large sums only to confront news that often brings them little to do but wait for the inevitable. The widening gap between diagnosis and treatment has had a second consequence, one that touches one of the most sensitive issues facing us today. Prenatal DNA diagnosis coupled with termination of pregnancy provides a rational way to avoid bearing a child with a life-threatening inherited disease; more and more diagnoses of variant alleles can be made in a first-trimester fetus, providing a woman with a new and ever-growing set of reasons for early termination of her pregnancy.

Before molecular diagnostic techniques can be properly used on the DNA of either adults or fetuses, all interested parties must agree which alleles of any gene are to be considered normal, and which may be taken as markers of childhood or adult disease. In the near future these techniques will allow pregnant women to decide whether or not they want to bear a child whose physical and mental states today fall well inside the boundaries of "normal." With time, computer technology will allow the simultaneous analysis of PCR-derived DNA data on dozens or hundreds of different genes. At that moment, a knowledgeable woman will be able to get the information she needs to decide whether or not to carry to term a child that would be, for instance, a boy, or a girl, or short, or deaf, or gay.

Taken together, these and many other two-edged developments at the boundary of medicine and basic science have defined a new sort of privacy, one that all other definitions of privacy are dependent upon: the right to control the information contained in one's own genome. Both law and politics move slowly; the technology is moving much faster than either. As a result, issues of genetic privacy, left to grow in the dark of legal and political neglect, have developed the capacity to present us with unexpected and nasty surprises. If the "perverted science" that the Allies and the people of occupied Europe rightly feared and hated is still nowhere on the horizon, the tools and capacity for its reappearance are, unfortunately, nevertheless in our hands today.

The public knows this. Advances in human genetic analysis have been met by a widespread fear that aspects of molecular medicine somehow are – or will soon become – a shadow on every person's future. The negative reaction to the contributions of genomic science to medicine manifests itself in many ways, from Congressional hostility to further increases in basic research budgets at the NIH, to legal skirmishes based on the supposition that techniques to elucidate a person's genetic status will be used by government for non-therapeutic purposes.

How should the scientific community itself respond to these matters? If we confuse what is possible with what is so, we slow the progress of medicine, and reduce everyone's chance of benefiting from such progress – including our own. If we ignore the past, and claim the risk is too small to worry about, we will lose control of our own futures and share responsibility for a future burdened with avoidable consequences. The answer, obviously, is for us to approach the problem as scientists: to ask perceptive questions about the technologies we have developed, gather data carefully, test our hypotheses, draw our conclusions, and publish our results so that our colleagues and others may know what we have found. Our obligation is sharpened by the fact that the most powerful technologies for violating genetic privacy come from the best – not the worst – of our nation's laboratories. It would be wrong to simply cull out the risks and attribute them to "bad" science; these problems are ours, precisely because they derive from excellent science.*

The discovery of genomic markers that correlate with a propensity to develop a disease late in life, and the performance of prenatal tests of genomic DNA, mean that we can now gather data on individual human genomes that is the informational equivalent of nuclear fuel: once obtained, it cannot be safely buried or forgotten, but must be constantly guarded lest it damage the lives of future generations. If we do not plan to deal with their consequences, these two contributions of basic molecular biology to medical diagnosis will put us at risk of losing – in the name of a better future – our hopes for that future and our freedom to enjoy it.

What should scientists do to get ahead of the curve? A group of scientists and other thoughtful people might meet, first, to establish a common base of understanding of the current state of knowledge of human genetics. Then, second, with that base of understanding, they might attempt through discussion and study to anticipate some of the legal, political and scientific accommo-dations that might allow basic research to proceed unfettered by misapplication of its discoveries. Subsequently, such groups might hope to study and report on one or more examinations of specific issues, their possible consequences, and the alternative accommodations that society might employ to balance the needs of individual privacy with the imperatives of basic research and the entrepreneurial opportunities that are emerging with the new knowledge about the human genome.

"...we can now gather data on individual human genomes that is the informational equivalent of nuclear fuel: once obtained, it cannot be safely buried or forgotten..."

A number of colleagues here and elsewhere have expressed an interest in making these initial efforts, and we would welcome the suggestions and contributions of GSAS alumni.

Professor Pollack worked for several years with Dr. James Watson, co-discoverer of DNA's structure, at Cold Spring Harbor Laboratory. For many years a professor at Columbia, Pollack also served as Dean of Columbia College through much of the 1980s. A recent winner of a Guggenheim writing fellowship, he is the author of "Signs of Life: the Language and Meaning

Prof. Robert Pollack (L) with Dr. Thomas Watson

*There is no need to confuse these issues with, for instance, ones arising from experiments that get announced at press conferences instead of being published, journals that will not publish a result that runs counter to a prevailing view, senior colleagues whose only contribution to a paper are their names below the title, or short-lived papers with exciting results but missing controls and incomplete methods sections.