Letters

Views of the Genome Project

There is nothing like a news account of one's opinions, performance, and even tone of voice to activate the juices. Leslie Roberts' description (Research News, 9 Nov., p. 756) of my role as a dissident at the November meeting of the Human Genome Project in San Diego forces me out of retirement (as a dissident) to present my views.

I like much of the science of the project and I admire the scientists involved. There is no doubt that the human genome will be mapped and, ultimately, sequenced, and what an important achievement that will be. I dispute the "top down" mechanism by which it is being administered. It is budgeted directly from Congress like a separate institute, with its own administration and council and even its own study sections. As a result, it is overbudgeted, overtargeted, overprioritized, overadministered, and micromanaged.

The genome project has become uniquely visible and placed on the defensive for three reasons: first, the earmarked nature of its administration and funding; second, its fairly large size and projected growth rate; and third, the current desultory state of extramural grant funding by the National Institutes of Health (NIH). It is likely that, if new and competing grants were being funded at the 1987 level of 6400 grants, instead of at the 1990 level of 4500 grants, the scientific community would not be reacting so strongly. The project is supposed to be an add-on to the NIH budget, but even genome administrators concede that its funding inevitably will compete with the rest of the NIH budget. If this is so, then its science should be considered in competition with the rest of NIH science.

It is possible to respect genome science but still ask whether it deserves to be or even benefits in the long run from being singled out. Mapping and sequencing are merely powerful tools, they are not the final goals of this project any more than the space station or the supercollider are the final goals of NASA and particle physicists. There are two goals for genome science: to identify genes that influence human health and to learn a lot of interesting biology about gene organization, expression, and evolution. The genome project would thus be better named the National Institute of Genetic Diseases and Biology.

A major expectation is that the map of the human genome will permit scientists to identify multiple genes involved in complex genetic disorders such as diabetes, heart disease, schizophrenia, Alzheimer's disease, and drug and alcohol dependency. However, methods in other areas of basic biological research are advancing right along with those for mapping and sequencing genomes. One or more of these methods may have an unsuspected impact on genome science, but "top down" management does not deal well with uncertainty.

In retrospect, who predicted 15 years ago at the start of the cancer program what would be learned about cancer or how it would be learned? The discovery of oncogenes and the elaboration of their functions have emerged from various sources funded by every institute of NIH and by other agencies, as well as from international research. The contributions to cancer research from just about every discipline of modern biology—genetics, biochemistry, cell biology, and developmental biology—have been essential. No one predicted 15 years ago that research on yeast, *Xenopus*, *Drosophila*, and *Caenorhabditis elegans* would have such a decisive role in elucidating the physiology of oncogenes. We are indeed fortunate that research on these organisms was not ignored over the past 10 years to target funds for cancer research.

I am admittedly a member of the NIH culture (perhaps "religion," as is suggested),

but there are strategic (policy) reasons why I believe that establishing a separate genome institute was inopportune. Congress has generally been sympathetic to NIH, but they have become understandably irritated at the cacophony, perceived as self-serving, that they have been hearing from different sectors of the scientific community. NIH should also get its act together and agree on priorities. Three priorities for NIH extramural funding exceed all others. First, there should be funding of individual investigator-initiated grants to about the 30th percentile. Currently, this means somewhere between 6000 or 7000 new and competing grants each year. The level should be stable, and it should be protected from earmarked projects. Second, there must be adequate funds for training of new scientists at the graduate and postdoctoral level. Third, there must be special attention to young scientists so that the best and brightest are launched on their independent careers as early as possible.

The genome project was the result of skillful persuasion on the part of distinguished scientists. I believe their resourcefulness was misdirected, and I regret that genome scientists did not see fit to add their powerful voices to strengthen the common enterprise with the full confidence that genome research would surely and inevitably progress right along with other exciting initiatives in the life sciences.

DONALD D. BROWN
Director,
Department of Embryology,
Carnegie Institution of Washington,
Baltimore, MD 21210

Two serious distortions in Roberts' recent Research News article require comment. First, it was implied that critics of the Human Genome Initiative (HGI) who support mapping the human genome, or various of its other "short term goals," actually support the initiative. This is incorrect. The relatively inexpensive and comparatively modest-scaled effort to map the human genome does not justify a $3-billion big science project; indeed, it is a project that can be completed without the need for any new "funding experiments." The predisposition of HGI supporters to claim that critics who support mapping have somehow diminished their opposition to the HGI is just one example of the distortion that the initiative's advocates have used in their campaign, a campaign whose tactics include the direct lobbying of Congress.

Many of us oppose brute force sequencing of the human genome because we believe it is an inefficient use of scarce research dollars. We have argued that biomedical research dollars are generally most efficiently spent on investigator-initiated research. We believe that innovation from scientists in the field produces better science than does narrowly targeted, top-down directed big science projects like the HGI. This is a position taken by many responsible scientists.

I must also protest the implication in Roberts' article that the opposition can be divided into two camps—one position represented by Bernard Davis and the other by myself and Martin Rechsteiner. My substantive position is virtually indistinguishable from that of Davis. The difference is only one of tactics—Rechsteiner and I have advocated writing to Congress as the only effective response to the direct lobbying efforts of the initiative's advocates.

It is an ominous development for American science when those who carry out not only their right, but also their obligation, to speak our freely on issues of such importance to science and society are subjected to unseemly personal attack by the leading general science journal in the United States.

MICHAEL SYVANEN
Department of Medical Microbiology and Immunology,
University of California,
Davis, CA 95616

Aging Studies

The cellular-molecular approach to the problem of the causes of aging received almost all the attention in Ann Gibbons' article "Gerontology comes of age" (Research News, 2 Nov., p. 622), and only one other approach was mentioned. However, not all of us believe that the main causes of aging will be found by studies of the molecular biology of cells. Cells do not exist in isolation in the body, and their functions are regulated by circulating hormones, nutrients, immunologic agents, blood gases, pH changes, waste products of metabolism, hemodynamic fluxes, and cell-to-cell communication. Studies of cells in vitro can tell us only of intrinsic changes, but not of the many important external factors that control cellular functions.

The late Nathan Shock, dean of American gerontology, expressed the view that aging is regulated principally by the integrative mechanisms of the body (*1*), which means mainly the brain, the endocrine glands, and the immune tissues, or what is now collectively termed the neuroendocrinimmune system. This system acts in coordination to control and integrate all body functions. We and others have presented evidence that dysfunctions that develop with age in the hypothalamic portion of the brain, a critical component of the neuroendocrinimmune system, lead to declines in body functions and to reduced ability to maintain body homeostasis (*2*). These result in cessation or reductions in reproductive functions, a decline in protein synthesis by body tissues (resulting from the decrease in growth hormone secretion), deficiencies in immune competence, and development of numerous mammary and pituitary tumors. Correction of neurotransmitter deficiencies in the hypothalamus of old rats has been shown to inhibit or reverse these and other aging declines in body functions and to even prolong their lifespan (*2*). The complex functions of the neuroendocrinimmune system cannot be explained by studying cells in vitro, least of all by studies of fibroblasts (connective tissue cells). I believe the knowledge gained thus far from studies of neuroendocrinimmune functions during aging has yielded far more basic information about the fundamental causes of aging than cellular studies have. They have also provided a basis for possible interventions to inhibit or reverse aging changes in elderly human subjects.

JOSEPH MEITES
Department of Physiology,
Michigan State University,
East Lansing, MI 48824–1101

REFERENCES

1. N. Shock, in: *Handbook of Biology of Aging*, C. E. Finch and L. Hayflick, Eds. (Van Nostrand Reinhold, New York, 1977), pp. 639–665.
2. J. Meites, R. Goya, S. Takahashi, *Exp. Gerontol.* **22**, 1 (1987).

Adaptive Optics

M. Mitchell Waldrop, in his Research News article "Astronomers try to put Mauna Kea 'into space' " (31 Aug., p. 987), describes the growing interest in adaptive optics in astronomy, as shown by our recent work in France (*1*) and in Chile (*2*). Nevertheless, a few quotes might mislead the reader.

The current prototype, in work on the European Southern Observatory (ESO) 3.6-meter telescope, functions with reference stars as faint as magnitude 10 to 13 (*3*) and is still being improved. The Hawaii approach also uses a reference star. The practical method of deriving from it the wavefront instantaneous distortion differs from ours, but this minor difference is not related to the system's sensitivity, which is set only by the particular photon detector being used. Because the use of adaptive optics in astronomy is still in its infancy, the proper evaluation of its capabilities and limits is of prime importance. It would be correct to state that there is no universal value for the magnitude of a reference star needed to inform the "rubber mirror." It all depends on the degree of correction one wants to achieve or, to put it differently, on the fraction of the total light