EXECUTIVE OFFICE OF THE PRESIDENT OFFICE OF SCIENCE AND TECHNOLOGY POLICY WASHINGTON, D.C. 20506 April 16, 1990

Dear Dr.

This Office is receiving a large number of letters addressed to expressing opposition to the Human Genome Project. Many of these letters are based on valid differences of opinion, but many others seem to reflect premature judgments, and

I am responding in a general letter even though your letter may not have raised all of the specific points addressed.

The general theme seems to be that the Human Genome Project (HGP) is diverting funds from small science into big science, and that the project is of questionable value. Many letters imply that support for the HGP is at the expense of the writer's interest, or of investigator-initiated research projects in general, and that the HGP will have a deleterious effect on young scientists.

Since some of the objectives clearly reflect concerns over the NIH budget as a whole, let me comment on that situation first. Despite inevitable annual variations, the NIH budget held up quite well through 1987. The next three years the increase was only 6 to 7 percent each year, including AIDS, 3 to 4 percent excluding AIDS. These figures clearly do not cover biomedical inflation, which runs 1.5 to 2 percent ahead of the Consumer Price Index. Nevertheless, the National Institutes of Health (NIH) budget still represents about 40 percent of the Federal non-defense R&D, and about 63 percent of the NIH budget supports work that is classified as basic science. The fraction of submitted applications actually funded held fairly steady at about 33 to 35 percent during the 80s, figures very similar to those of the past few decades. There were, of course, variations among Institutes, each of which has a separate, non-transferable budget, and each of which is subject to differing levels and types of earmarks.

What has changed in the last few years relates largely to the growing concern over the deficit, and the Gramm-Rudman approach, plus major political decisions regarding science funding, of which the Human Genome Project has become the surrogate for the basic biomedical science community. In the total scheme of things, it is not a major player.

In the construction of the annual Federal budget, items that the President has addressed get first call on new funds. commitments are always larger in the first year following a Presidential campaign than later on. This year such items as the superconducting supercollider, the manned flight to Mars, the space station, AIDS, environmental issues, education, and others in that category received preferential budgetary treatment. Several of these are very big ticket items. The President's budget proposal for 1991 contains an overall increase of about 12.2 percent for non-defense related R&D. The budget proposed for the National Aeronautics and Space Administration goes up 24 percent, for the National Science Foundation 17 percent, for NIH (the non-AIDS portion) 3.7 percent. That latter figure is essentially the same throughout the entire Federal government as a cost of living adjustment.

All of the special priority items mentioned above, and many others, influence the funds available to NIH, but perhaps the largest easily identifiable influence has been funding for AIDS activities. The AIDS budget is now about 10 percent of the total Only about \$220 million of the \$800 million budget NIH budget. is available for investigator initiated research. Some of the same arguments raised in connection with the Genome Project have been raised in connection with AIDS. One of the principal ones is that such projects divert funds from other meritorious NIH The question of diversion of funds is very hard to activities. Funds provided by the Congress for such specific purposes prove. might not have come to NIH at all, absent the political decisions to fund the designated activities.

In the case of the Human Genome Project, NIH moved forward with specific plans only after considerable public debate on the subject, involving several national meetings, and a report by the National Academy of Sciences recommending a concerted long-term program. The report of the Academy committee was followed by a special meeting convened by NIH in Reston, Virginia, involving a number of key figures and opinion leaders in the field of genetics including three Nobel Laureates. There continues to be very strong support for the HGP from important segments of the biomedical community.

Some letters have expressed apprehension about the advent of big science at the NIH. The Genome Project is not really big science. Two-thirds of the present Genome budget is in RO1 and PO1 awards, which stress mapping, general methodological improvements that will have broad use in biology, and beginning work on regulatory segments. Even the creation of a few Centers is no real departure from established NIH practices. Everyone is agreed that systematic sequencing of non-coding regions is some

years away, and will await methodological improvements including automation, and a considerable reduction in average cost per nucleotide.

Other letters have stressed the negative impact on training and intellectual development of young scientists. This criticism stresses the mundane nature of sequencing, and assumes that graduate students and young scientists would be asked to do it. I do not know of anyone who has proposed that. Rather such work probably awaits automation, and could well be done commercially under contract.

Still other letters have stressed that sequencing is not likely to contribute to the understanding of genetics, that 95 percent of the human genome is merely spacer, junk DNA, with "meaningless information." That strikes me as a premature judgment and begs the question, "How do we know that?" Many scientists would hold that if it is meaningless, it would not have been preserved over the millennia. We will only learn the answer to such questions by additional research, evaluating as we proceed. Perhaps the approach should be to do one or a few model chromosomes and see what we have learned, but even that type of approach is years away and awaits methodological improvements and cost reductions.

There is, in addition, worldwide interest in this Project and funding is developing in many foreign countries, as well as our own. The prospects of effective international coordination are growing. Such collaboration should reduce the cost of the Genome Project to the U.S.

and I have repeatedly stated in public addresses and in testimony that the strength of the research system is in small science, in the investigator-initiated research project grant or program project grant. In my view the Human Genome Project fits that description in its emphasis on ROls and POls and training.

I would like to add a final word about the write-in campaign on the Human Genome Project. This reminds me of some of the factional disputes during the period of 1979 to 1982, when NIH funding was also very tight, when young scientists were not getting support and some were leaving the field. Such activities were divisive then and they are becoming divisive now. The real issue is the level of support of science that this country will make, and whether it is more important to allocate \$100 billion

or more to bail out the Savings and Loan industry, or to add 1 percent that much to the NIH and other research budgets. House and Senate Appropriations Subcommittees have told me for several years that our competitors in those particular Subcommittees, namely education and labor, get behind a single budget, whereas the biomedical community operates like a cottage industry with each small component advocating for itself. When things get tight as they now are, we fall to advocating our own parochial interest over those of someone else. A much more effective strategy is to join forces in supporting a single budget proposal at the level of the Congress, such as the one developed and supported by 140 scientific organizations, under the leadership of the Association of the American Medical Colleges. I view that as a constructive approach. It speaks to the issues of foregone opportunities in health related research, of the underpinnings of the biotechnology industry, and of the signals sent to young people whom this country must continue to attract into science if we are to preserve our position of world leadership.

Thank you for writing.

Sincerely,

/a/ James B. Wyngaarden

James B. Wyngaarden, M.D. Associate Director for Life Sciences

cc: Senator Edward Kennedy Senator Albert Gore Dr. William F. Raub

Department of Biological Chemistry Hahnemann University Broad & Vine Philadelphia, Pennsylvania 19102-1192