Curtis R. Altmann
1808 Martin Luther King Junior Way
Berkeley, California 94709

3/13/90

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Sir,

I am writing to you to voice my opposition to the human genome project (HGP). A copy of a letter written by Martin Rechsteiner, soon to appear in the FASEB Journal, has prompted me to take action as I agree with the arguments and the conclusions.

I am a graduate student at the University of California at Berkeley in the Department of Molecular and Cellular Biology and have been following the debate concerning the HGP. I believe that there is little to no direct medical benefit of the effort and fear that the funds thus wasted will compromise both our competitive advantage in biotechnology and our educational system. We need more money for training graduate students and post-docs, and increased support of university research; not "Big Science" projects.

I hope that my opposition and that of others will be vocal enough to curtail this dangerous waste of national resources.

Thank you for your time and attention,

Curtis R. Altmann

Curtis R. Altmann

THE JOHNS HOPKINS UNIVERSITY
BALTIMORE, MARYLAND 21218

DEPARTMENT OF BIOLOGY

27 March 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub:

I would like to join a rather large number of my colleagues in the biosciences in questioning the real value of the human genome project, the extremely expensive proposal that is now beginning to emerge from the National Institutes of Health. The program, even in its early stages, would require more than $200 million, and I gather that the estimate for a more-or-less complete job would be closer to $3 billion. There are a number of questions of a scientific nature that make the project of questionable interest. It is well-known that about 95% of the genetic material in the human genome is basically "filler" and a total sequencing of the genome would involve a great deal of wasted time and effort. I do believe that the approach favored by individuals such as Dr. Victor McKusick at Johns Hopkins, aimed at locating and sequencing specific portions of the genome related to human disease, would make a much more sensible beginning.

Sincerely yours,

C.B. Anfinsen

Christian B. Anfinsen
Professor of Biology

CBA:djh

MEDICAL COLLEGE OF WISCONSIN

Department of Biochemistry

February 28, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub:

I strongly agree with the enclosed letter by Professor Dr. Rechsteiner and should like to request that you take these suggestions under advisement in future decisions concerning support for the human genome project.

Sincerely,

H. Ankel

Helmut Ankel, Ph.D.
Professor
Dept. of Biochemistry

HA:cs

Enc.

8701 Watertown Plank Road
Milwaukee, Wisconsin 53226
(414) 257-8435 / 8257 / 8259
FAX: (414) 257-2008

RICE

April 16, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126 Building 1
9000 Rockville Pike
Bethesda MD 20892

Dear Sir,

I am a research biologist of some 23 years research experience. I have worked as a molecular biologist for the last 13 years. I am writing to express my deep disapproval of the human genome project and to urge you to do whatever you can to prevent this foolish waste of government research funds.

Although a case can be made for generating a **linkage map** of the genome, there are no grounds on which actually sequencing the genome can be defended. The vast majority of the DNA in the human genome (95%) is junk DNA, the sequence of which will yield no useful information. In addition the work is exceedingly labor intensive, incredibly expensive and totally lacking in any kind of creativity. In other words not only is it useless work - it's expensive, tedious, boring, useless work.

Up to this point, the style of government research funding in biological science has been to support modestly, and on a competitive basis, research into a great diversity of biological problems. The recent brilliant advances (recombinant DNA technology, oncogenes, understanding of cholesterol metabolism) that have come out of this work are a tribute to the creativity of the scientists involved and to the effectiveness of this approach. Using government funds in this way (that is to let the excellence of the research dictate the funding) is the only way to ensure high quality, creative research and a decent training in research for the next generation.

The human genome project is the exact antithesis of this approach. A debilitating fraction of the government research funds available will be set aside for this project which represents some of the dullest, most useless, work imaginable. It will attract the least able, least creative, scientists, who are unable to find other support and who will be attracted by the guaranteed funding of this project. If any young scientists in training are sucked into this project, it will ultimately be their ruin. They could only emerge from working on this project as the worst kind of mindless technician with no experience or potential in creative research.

The human genome project is an ill-conceived, foolish idea that will damage the research efforts of the country. At a time when the great need for decent training in science in this country is being recognized it seems even more inappropriate. I urge you to do what you can to prevent this folly.

Sincerely,

K.M. Beckingham
Associate Professor of
Biochemistry and Cell Biology

Department of Biochemistry and Cell Biology • Wiess School of Natural Sciences
Rice University • P.O. Box 1892 • Houston, Texas 77251 • (713) 527-4015 • FAX (713) 285-5154

$3.00

UNIVERSITY OF MINNESOTA
TWIN CITIES

Hematology-Oncology Division
Department of Pediatrics
Box 484 UMHC
420 Delaware Street S.E.
Minneapolis, Minnesota 55455
(612) 626-2778

90 APR 12 P2:55

5 April 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub:

Few scientific proposals have been greetedwith as much media coverage as the Human Genome Project. Although I consider the effort noble, I feel that the Human Genome Project (HGP) is not a sound scientific undertaking. Moreover, in a period of severe budget restraint at the national Institutes of Health, it is foolish to invest $3 billion to sequence the entire genome. Our dollars would be more wisely spent on cancer and AIDS research for the following reasons:

1) We were told that the resulting information will have great impact on major human diseases. Although this could be true, significant advances in heart disease and cancer were made independent of HGP. Most oncogenes have revealed themselves by their dominant effects, not by sequence analysis of human genomes.

2) Knowing a map location or amino acid sequence of a mutant gene product does not insure the development of rational therapies.

3) The HGP is a costly, wasteful, and inappropriate allocation of research funds. The $3 billion total assumes no delays or no cost overruns, but already there have been delays on the project.

4) The HGP will provide little useful training and no intellectual stimulation to young scientists. This could be the most tragic of the consequences of funding. Spending $3 billion at a time when our country is falling further and further behind in the quality of its science is foolish. The education value of this project is nearly nihil.

5) Finally, 95% of DNA does not code for proteins and is thought my many, including of the advocates of the HGP, to be junk.

Please curtail this tremendous waste of scientific resources at a time when research dollars could be put to better use.

With best regards,

Bruce R. Blazar, M.D.
Associate Professor
Department of Pediatrics
Division of Hematology/Oncology

BRB/tc

23815

SCRIPPS CLINIC
AND RESEARCH FOUNDATION

RCH INSTITUTE
OF SCRIPPS CLINIC
10666 NORTH TORREY PINES ROAD
LA JOLLA, CALIFORNIA 92037
619 455-9100

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, M.D.
20892

May 8, 1990

Dear Sir,

This letter is in reference to the Human Genome Project (HGP). The goal of this project, as you know, is to obtain the DNA sequence of the human genome. Technicians in biological sciences feel that this project is a waste of time and money and should not be funded for the following reasons:

1) At 200 million dollars a year, for a minimum of 15 years, the HGP will prevent at least 1000 scientists a year from recieving RO1 grants from the NIH.
2) Scientists who are not funded do not employ technical help. Technicians rely on grants for our jobs.
3) Research institutes in San Diego, for example, employ an estimated 15,000 technicians skilled in biological research. When primary investigators lose their funding technicians lose their jobs! Unemployment is not somthing which should result from a scieintific endevor.
4) The HGP will require technicians to have only one skill-sequencing DNA. This task is tedious and uneducational. Technicians thrive on knowledge and information that will enable them to become more aware of the needs and problems in science. Sequencing DNA will not help their education.

Please take notice of my concern and voice my opinion, and that of others like me, in the appropriate circles. Don't forget-legislative action is the voice of the people!

Sincerely,

Jonathan M. Blevitt M.S.

84089

UNIVERSITY OF VIRGINIA
HEALTH SCIENCES CENTER
DEPARTMENT OF ANATOMY AND CELL BIOLOGY

June 1, 1990

Dr. William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, Maryland 20892

Dear Dr. Raub,

I am a biomedical scientist at the University of Virginia School of Medicine and I am writing to express my considerable concern about the impact that funding the Human Genome Project will have on the rest of biomedical science and, in particular, on the funding of individual research grants (RO1s). I do not feel that the Human Genome Project is at heart a scientific project; it might be considered more akin to the Kennedy Administration's drive to put a man on the moon or a later administration's War on Cancer. I do support the development of an improved map of the human genome (although I feel this could be done through the normal research funding channels) but I have serious reservations about the actual wholesale sequencing. I would rather see the money spent on individual research labs for projects focused towards specific scientific or medical questions than as big block grants to industry and major centers that would primarily do wholesale assembly line sequencing work performed by technicians. We face a serious dilemma: a decline in interest in entering science as a career at the same time as projected major manpower needs in the 1990s due to faculty retirements. The decline in the availability of individual research grants is driving existing scientists out of the laboratory at the same time as it is discouraging potential future scientists from entering the field. We must lure smart young people into careers in science; one way to do this is to increase the money put into training scientists (training grants, individual fellowships and positions for graduate students and postdocs on individual research grants) and to increase the supply of individual research grants (RO1s); I believe that this is the way to plan for a healthy, productive scientific enterprise and I believe that massive expenditures on the Human Genome Project are likely to compromise these goals, without necessarily giving us a significant return for the investment.

Sincerely,
Robert A. Bloodgood

Robert A. Bloodgood, Ph.D.
Associate Professor

SCHOOL OF MEDICINE, BOX 439, CHARLOTTESVILLE, VIRGINIA 22908, 804-924-2731

8-1622

University of Pittsburgh
SCHOOL OF MEDICINE
DEPARTMENT OF RADIATION ONCOLOGY
JOINT RADIATION ONCOLOGY CENTER

April 23, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear William F. Raub:

The enclosed letter was sent to me for comment. I heartily agree. The money to be spent on the genome project would be much better spent on R01-type grants. Many of these grants include plans to clone a gene. The difference is that they know why, and what use the information will be put to. The data will not be just catalogued.

A better approach might be simply to make cloning and sequencing facilities available to assist non-molecular scientists that have a specific need for this. If such facilities were available at reasonable cost, we would not all have to become molecular biologists.

Sincerely,

Sallie S. Boggs, Ph.D.
Associate Professor

SSB/caa

PRESBYTERIAN-UNIVERSITY HOSPITAL
230 LOTHROP STREET, PITTSBURGH, PA 15213 (412) 647-3600

Charles R. Buck, Ph.D.
Department of Anatomy
University of Utah, Sch. of Med.
50 N. Medical Drive
S.L.C., UT 84132
April 25, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub:

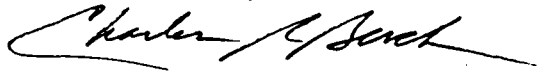
I am a young biomedical research scientist writing to you to express my profound reservations about the practicality, feasibility and rationale of the Human Genome Project (HGP). Initially, my basic curiosity about the complexity of the human genome (or of any genome) made the prospect of a complete sequence seem very attractive. Indeed in the best of times, in the best of all possible worlds, such information is potentially important. Obviously however, neither of the above conditions exist. I believe the human genome project to be ill-conceived, ill-timed and potentially disastrous to the scientific enterprise of this country.

The HGP is a bad idea because of the following: 1) It is far too expensive. Particularly in these times of NIH cutbacks, spending three billion dollars (or more) on a project such as this will effectively eliminate thousands of productive scientists from our population. Additional monies are desparately needed for the NIH, a funding level of 10% of approved grants in this country is a national disgrace. However, funding should be channeled to independent investigators throughout the country. These are the scientists who have established this nation as the world leader in biomedical research, not large groups of scientists myopically contemplating a single approach or a single project. 2) The project will not assist in the desparately-needed training of young scientists. Sequencing is incredibly tedious and time consuming (I have done it, I know). The HGP will not attract scientists or scientists-in-training. In addition, the drain on the NIH budget created by this project will eliminate

grant money which is currently used to support graduate students and post-doctoral fellows. 3) A complete sequence of the human genome is of questionable value. As you are no doubt aware, more than 90% of our genome is thought to be completely useless as a template for RNA and, subsequently, protein synthesis. This "junk" DNA is unlikely to provide important information and sequencing the junk will occupy much of the effort of the HGP. The much-espoused argument that the HGP wil provide vital material in our search for the causes of genetic disease does have merit. However, the phenomenal strides made in our understanding of cancer, muscular dystrophy and cystic fibrosis, all argue that such diseases are approachable without the aid of sequence information of the entire genome.

I believe that there are many other reasons why the HGP should not continue. I would be most happy to discuss this with you further, at your convenience. Thank you in advance for your attention to this matter.

Sincerely yours



Charles R. Buck, Ph.D.

MICHIGAN STATE UNIVERSITY

DEPARTMENT OF BIOCHEMISTRY
BIOCHEMISTRY BUILDING

EAST LANSING • MICHIGAN • 48824-1319 • USA

April 20, 1990

Dr. William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub:

I am writing with regard to the proposed human genome DNA sequencing project (HGP), which is currently being considered for federal funding. I am an Assistant Professor of Biochemistry at Michigan State University. My research project is the cloning, sequencing and manipulation of genes encoding human transcription factors.

The HGP is a poor use of federal funds. Sequencing the human genome will be a tremendous technical feat, but the scientific value of the accomplishment will be small. The portions of the human genome that are of particular interest are currently being identified, cloned and sequenced--by people like me. There is no real need, and certainly no cost-effective need, to determine DNA sequences for which the biological relevance has not been established. As a basic scientist interested in the mechanisms by which life works, I look at HGP as another triumph of huge-scale, technical science over smaller academic science. Smaller science is a much better investment for federal funds.

It is unclear to me how the federal government can justify such a large expense on HGP, when basic science is so badly underfunded. In the Molecular Biology Study Section at the National Institutes of Health (NIH), where my grant is currently being considered for funding, only 13 to 14% of the grants will be paid. For NIH to make an adequate contribution to basic science, 30 to 40% of these grants must be paid. This is particularly true in such a competitive Study Section, where the average quality of proposals is always high. Under the current funding regime, the NIH is not supporting enough quality basic research.

The time has come when Americans must be clever to advance this Country economically, strategically and spiritually. America's scientists are striving to do important research, teach undergraduates and train the next generation of scientists. The federal government is giving us little encouragement, and at the same time, our government is considering spending huge sums of money on projects of little interest or value.

I suspect that the majority of my colleagues agree with my position on this subject, but may be too busy to write.

Very Sincerely;

Dr. Zachary Frontie Burton
Department of Biochemistry
Michigan State University
East Lansing, MI 48824
(517) 353-0859

33516

University of Idaho
College of Letters and Science
Department of Biological Science
Moscow, Idaho 83843
208-885-6280
FAX 208-885-7905

90 MAY 18 PM 9:50

Senator Steve Symms
U.S. Senate
Washington, D.C. 20510

Dear Senator Symms:

A radical policy change is occurring in the National Institutes of Health. It is being implemented without proper debate, and is adversely affecting the progress of medical research. Furthermore, it is reversing a policy that was established by Congress to ensure that each region of the country receive its share of NIH funding. I am referring to the Human Genome Project, which is, as you are probably aware, an effort to sequence the entire human genome. I strongly urge you to keep this project out of the N.I.H.

Although sequencing the entire human genome is certainly harmless in itself, it is far less important than other ongoing and potential new lines of research. Since new funds are not being appropriated for the human genome project and this money is currently being derived from existing programs, the project will actually impede medical research. The problem is not really too technical to explain to the non-scientist.

Somewhere between 95 and 98% of the human genome consists of what biologists commonly call "junk" DNA. This is DNA which does not transmit information to the cell, and which most likely serves no function at all. Genetic defects related to disease are, of course, found in about 2% of the human genome which contains functional genes. Most genes involved in disease can be located and sequenced without sequencing the entire genome -- in fact, this is already being done, and does not require an "initiative" or a massive diversion of funds. More importantly, locating and sequencing genes involved in disease does <u>not</u> automatically lead to a cure for disease. For example, the location and sequence3 of the sickle cell anemia gene has been known for over 20 years, and no cure has been developed. In order to cure disease, all aspects of the structure and function of the genome, the cell and the organism must be understood. It is not enough to know the sequence of the gene. And as funds are being diverted from other avenues of inquiry in order to sequence the <u>mostly irrelevant</u> DNA sequences of the entire human genome, the conquest of disease and other important technological advances will be hindered.

The diversion of funds to the human genome project, and hence away from the broader biological research projects, has additional undesirable national policy implications. First, the hundreds of millions of taxpayer dollars that have been invested in training today's scientists -- arguably the best in the world -- will be wasted as productive, promising laboratories are unfunded. It is important to point out that these scientists who are so important to our technological competiveness cannot merely redirect their research into the human genome project. The human genome project is a massive scientific assembly line which requires very few scientifically trained minds and an army of specialized technicians. It cannot make use of a fraction of our country's investment in highly trained and talented scientists.

use of a fraction of our country's investment in highly trained and talented scientists. Secondly, the human genome project, by its nature, involves unimaginative, repetitive and routine tasks. If we can't offer our brightest, most creative young minds the promise that they will be able to engage in challenging, innovative research, they will simply leave science.

Third, the human genome project is threatening to change the American system of support for biomedical research. Sequencing the human genome will tend to concentrate research in large laboratories in a small number of elite locations. The concentration of funds in a small number of centers will be a setback to developing a geographically broad-based high technology economy, and will have a long-term negative impact on regional and local economic development.

There is some disagreement among responsible scientists about whether the human genome project would be worth doing in the hypothetical case that it could be funded in addition to normal science funding. But among those scientists whose personal power is not enhanced by this diversion of funds, there is an unusual degree of consensus that the scientific knowledge gained by the monumental and routine task of sequencing the human genome would not measure up to the amount of scientific and medical knowledge which will be lost by the curtailment of the more diverse, inspired and problem-oriented medical research. In fact, given the amount of money realistically available to biomedical research, there is an unusual consensus among responsible scientists that the very goals that the human genome initiative purports to attain -- the curing of human disease - will be actually hurt because more medically relevant and effective research programs will be unfunded. We, the silent majority of the scientific community, urge you to help us defeat the human genome initiative, unless it can be funded with new money.

Sincerely,

John A. Byers

John A. Byers
Associate Professor of Zoology

UNIVERSITY OF KENTUCKY
Chandler Medical Center

College of Medicine
Department of Biochemistry
800 Rose Street
Lexington, Kentucky 40536-0084
(606) 233-5549
FAX (606) 258-1037

March 29, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9600 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub:

I am writing to inform you that I am deeply troubled by the news I hear of plans to proceed with the Human Genome Project. The proposals which favor the brute force approach do not have much appeal for me or my colleagues. The problem with this stems from the fact most of the sequencing work will not be creative or innovative and will not allow students or postdoctoral fellows to generate knowledge that will further their own careers. We already read of reports of students refusing such projects because they do not wish to spend their graduate or postdoctoral time in the repetitive process of sequencing some miniscule part of the genome which in all likelihood will yield no interesting biological information.

The Human Genome Project is simply a bad idea. Science in the United States is strong precisely for the reason that basic research is competitively reviewed and funded and that innovative, creative ideas are what drives research. I believe that we should fund scientists who are targetting interesting segments of DNA for study. Using this approach we will generate the information we need to understand the human genome. If instead we divert funds from the best scientists to projects that simply generate endless sequence information, we will damage the scientific enterprise.

I urge you to oppose the Human Genome Project and support biomedical research through its traditional funding mechanisms.

Sincerely yours,

Mary Sue Coleman

Mary Sue Coleman, Ph.D.
Professor

MSC/dk

02948

UNIVERSITY OF CALIFORNIA, RIVERSIDE

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO

SANTA BARBARA • SANTA CRUZ

DIVISION OF BIOMEDICAL SCIENCES

RIVERSIDE, CALIFORNIA 92521-0121

March 19, 1990.

William F. Raub
Acting Director,
National Institute of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Mr. Raub :

I am writing to express my extreme concern with the policy of science funding in the USA. I have recently learned that my grant application to the National Institute of Health (NIH) scored 155, which is the score given to outstanding-excellent projects. Nevertheless, I was very sorry to learn that my application is not going to be funded because of the lack of resources from NIH. I am an assistant professor struggling with tenure and all implications inherent to this process. With this lack of support to my project I will not be able to train postdoctoral scientists. I will not be able to attract and direct to scientific research talented graduate students. I will not be able to strengthen the areas of science and research which made this country big, serious and respected. I will not be able to prevent the evasion of talented students that do not want to remain in the Universities, Research Institutes because of the lack of support and opportunities and stimulus. I will not be able to continue my studies that modestly contribute to the progress of human knowledge. I will not be able to teach medical students at a level that made Medicine in this country the most advanced one in the world. I will not be able to contribute to revert the decline in the USA competitiveness.

At the same time that I am frustrated, depressed and sad about my news from NIH, I learned that a controversial project of Human Genome Project is being launched. This is being called the "*Big Science Project*". It amounts to $200,000,000 per year for the next 15 years. And of course, this figure will be severely inflated in the close future. The rationale for this project is controversial. Its goals are highly questionable and several scientific articles had raised serious objections. What is this project going to do ?

The Human Genome Project will provide little or no creative intellectual training. It will simply result at most, in the formation of an army of technicians skilled only in obtaining DNA sequences and entering the results in data bases. It is a mechanical, boring task that not only do not praise creativity, dedication and the progress of scientific knowledge but also, will not necessarily promote the understanding of human diseases as the advocates of the project claim. Also, the money involved in the Project will be diverted to companies to develop (not to create concepts or reasoning) equipment !

In my specific grant application I requested on average less than $100,000 a year. I would be training two postdoctoral fellows, two graduate students and paying 25% of my salary in addition to a technician's salary. Not only the allocation of funds to "*small*" science has always produced important insights in biomedical

research but, the multiplicative effect of forming generations of intelligent human beings is more efficient. Each postdoctoral fellow coming out of my laboratory will in his/her turn fecundate other areas of science and

other brains. This small, rigorous, efficient process explains the success of the US. Unfortunately, there is not much money involved in it and so it lacks the title of "*BIG*" science.

The process of intellectual formation of a scientist is not and cannot be industrialized. Each mind has its own pace. Each mind has its own process of development, maturity and creativity.

Try to imagine: with less than $100,000/year I would be able to direct and form four intellectually independent scientists. Could you figure out how many people could be attracted to science with the $200,000,000/year from the Human Genome Project.

As a person that wakes up every morning and goes to the laboratory to work, I can tell you that the perspectives for science in our country are not good. We fight to attract students to a scientific career. We spend a lot of time in looking for funding sources. We spend a lot of time in writing grant applications. And all this, on behalf of an ideal, a dedication and an intellectual satisfaction.

I urge you to analyze in detail the origins, objectives and the importance of the Human Genome Project for the scientific development of the nation. I also urge you to study its implications to human disease. Our progress in understanding human disease had been very successful without having a data bank of human genes. Moreover, there is a huge step in identifying the defective gene and the cure of a disease. Several examples illustrate this last statement (Cystic Fibrosis, Muscular Distrophy, etc.). Those illness had their gene identified a long time ago. Yet, we do not know the physiology of those illness.

If you dedicate some time to the meditation of some points that I have barely scratched in this letter I will feel myself fully justified in having written it.

Thank you for reading this letter.

Yours sincerely.

Samuel Cukierman, M.D., Ph.D.

UNIVERSITY OF MINNESOTA
TWIN CITIES

Office of the Dean
Medical School
Box 293 UMHC
420 Delaware Street S.E.
Minneapolis, Minnesota 55455

Office at 3-120 Owre Hall
(612) 626-4949
FAX (612) 626-5657

March 28, 1990

William F. Raub, Ph.D.
Acting Director
National Institutes of Health
9000 Rockville Pike
Building 1, Room 114
Bethesda, MD 20892

Dear Dr. Raub:

I wish to express my concern and reservations regarding the magnitude of the Human Genome Program. I say this with considerable appreciation for the advances that have been made in molecular biology and its applications both to genetics and to the many facets of biomedical research. However, it is clear that the planned increases will have deleterious effects upon the financial support for the infrastructure of biomedical research.

Broadly-based biomedical research has been the infrastructure and the strength of the programs supported by the National Institutes of Health and of the extraordinary network of scientists within academic institutions in the United States. The wealth of knowledge upon which our current information has developed has accrued primarily through non-directed research.

Scientists trained and working in several facets of biology have gained from working with their colleagues across multiple disciplines in order to achieve their scientific objectives. An electrophysiologist seeking to understand organ function may learn how to use simple cell systems in conjunction with cell or developmental biologists. The latter may seek to understand the mechanisms of an ion transport system in conjunction with a biochemist, who in turn may seek expertise from a molecular biologist working with applied systems, who in turn may seek technical input from a fundamental molecular biologist working with bacterial systems. Finally, this sequence of information transfer will require reinsertion within systems of increasing complexity to test the original hypothesis within the intact organ system. The application of this knowledge to the human with disease is essential and represents the ultimate product of the research. All of these systems and scientists working both independently and interdependently are critical to achieve the final product.

The financial reality of funding of the NIH does not permit both a massive increment of expenditures for the Human Genome Program and continuation of a strong, broadly-based and deep biomedical research infrastructure. The erosion in the latter that has evolved in the past two years has reached catastrophic proportions. Almost every NIH institute director has clearly stated this result of competitive funding from a limited source and has predicted even worse outcomes in the near future. Most academic institutions with major investments in research have seen the negative impact of multiple factors upon the research funding of their faculty. Individual investigators and would-be scientists are discouraged with the future of their efforts. The manifestations of those impacts was recently reported

in the New England Journal of Medicine (322:739-742,1990) in which declines of American authorship of research is documented.

My request not to fund the magnitude of designated research projected for the Human Genome project is not intended to diminish the potential significance of its product. It is, however, intended to emphasize that, as has been the case with most other very expensive and targeted research programs undertaken in either the physical or biological sciences, it will occur at the expense and sacrifice of other equally vital work. The latter can be put on hold only at the jeopardy of its being dismantled. Furthermore, I must emphasize that unidirectional attempts to deal with human biology and disease have usually been misleading, not from false information but from the inadvertent exclusion of other concepts or methods of experimentation.

I hope that the NIH will neither actively nor passively seek nor support the funding of the Human Genome project in the magnitude planned for the next fiscal year. I hope that the NIH would not respond favorably to external pressures but will maintain its steadfast position to seek increased support for its primary non-directed or designated investigator-initiated research without compromise. To do otherwise will lead invariably to further politicization of the NIH and its supporters and potentially to its dismantling.

Sincerely,

David M. Brown, M.D.
Dean
Professor, Laboratory Medicine
and Pathology and Pediatrics

DMB:pat

Dr. William F. Raub, Acting Director
National Institues of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub;

March 15, 1990

The enclosed letter is from my colleague and friend, Dr. Marty Rechsteiner. I agree with the principles that he has outlined and would encourage you and your colleagues to hold more hearings on this important matter for biomedical research in the United States. The HGP as now organized is setting a precedent for biomedical research and many aspects of it may not be productive either for the intended goals of the HGP specifically or the biomedical research community at large.

Sincerly,

Kyle A. Dethlefsen

Kyle A. Dethlefsen
Dept. of Radiology
University of Utah
School of Medicine
Salt Lake City,UT 8413

Tulane University Medical Center

School of Medicine
Department of Biochemistry
1430 Tulane Avenue
New Orleans, Louisiana 70112

Cable TUMED

February 26, 1990

William F. Raub
Acting Director
National Institute of Helth
Room 126, Building I
9000 Rockville Pike
Bethesda, MD 20892

Dear Mr. Raub:

Please read the enclosed letter with which I, as a Principal Investigator of an N.I.H. grant, heartily concur. The morale among U.S. academic scientists now is dreadful because of the shockingly inadequate percentages of unsolicited grant applications funded by the major divisions of the N.I.H. This despair with the scientific enterprise at the basic research level filters down to poor science education at the high school level. The money for the Human Genome Project should be immediately funneled into 1000 more competitive research grants which will help, but not totally alleviate, the previous drastic decreases in percentage of grants funded over the last decade.

Yours truly,

Melanie Ehrlich

Melanie Ehrlich, Ph.D.
Professor

ME/lo

cc: Martin Rechsteiner
Department of Biochemistry
University of Utah School of Medicine
Salt Lake City, UT 84132

THE OREGON
HEALTH SCIENCES UNIVERSITY
611 S.W. Campus Drive Portland, Oregon 97201 (503) ~~225-8774~~ 279-8774

School of Dentistry
Department of Biochemistry

March 14, 1990

William F. Raub, Acting Director
National Institute of Health
Room 126, Building 1
900 Rockville Pike
Bethesda, MD 20892

Dear Mr. Raub:

I am not in favor of the Human Genome Project (HGP) for the following reasons:

1. There is no urgent need for the information that would be derived. There are pressing needs for additional support in other areas of biological research such as brain disorders, ageing, and cancer.
2. The information will not lead to a solution of any problem. The information, though interesting, in many cases will be superfluous. Large segments of DNA are spacers, etc., and there is no urgent need to determine the sequence of these areas.
3. Much of the work to be done could be classed as idiot work - repetitive without being challenging. The money would be better spent educating young people in problem solving.
4. It will create a few super centers while eliminating many small but superb research laboratories. The purported 3 billion dollar price tag could support 5,000 $600,000 projects, or 5,000 researchers with 5-year grants at $60,000 per year. I think the money could be better spent that way.

I would appreciate it if you would reconsider your support of the HGP. This is not a trivial matter. The strength of our place in science depends on the competitive support of many laboratories and not the few. I hope the glamour of such a project will not sway your decision.

Thank you for your continued support of science. To maintain our competitive position in the world requires even more support.

Sincerely,

Walter L. Gabler, D.D.S., Ph.D.
Professor and Chairman
Department of Biochemistry

Committee on Cancer Biology

THE UNIVERSITY OF
ARIZONA
HEALTH SCIENCES CENTER

1501 North Campbell Ave.
Tucson, Arizona 85724
(602) 626-7479
FAX (602) 626-2284

March 22, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Mr. Raub:

I am writing to express my reservations regarding the Human Genome Project (HGP), which has been highlighted in several recent articles in Science and other scientific and lay publications. I agree with the arguments put forth by Marty Rechsteiner of the University of Utah (see attached letter).

As chairman of a graduate education program, I am very aware of the current limitations in training funds for young scientists in this country. As an independent investigator who has served on NIH study sections, I also know that many scientists, both junior and senior level, have been forced to stop or curtail their research activities due to current budget restrictions. The net effect of limiting training and resources available for funding the best science has been, in my opinion, to dramatically injure our country's leadership position in research and development. Allocating resources to fund the HGP, which by the opinion of many is not the best science, should at least be delayed until enough money is available to restore training and support for the best research to at least maintenance levels.

I hope you will seriously consider this issue in the light of the arguments raised by Dr. Rechsteiner.

Sincerely,

Eugene W. Gerner, Ph.D.
Professor of Radiation Oncology and Biochemistry
Chair, University Committee on Cancer Biology

82722

Anatrace
1280 DUSSEL DRIVE
MAUMEE, OHIO 43537
(419) 891-3030

April 25, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Bldg. 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Mr. Raub:

I'm writing to express my concern over the funding of the human genome project (HGP). My feelings are simply this. It's not the best use of NIH research funds.

The HGP project appears to have been suggested as a "good thing to consider" and then became a vehicle for a shrinking and hard pressed department (DOE) to grab some headlines and hence some funds. H&HS (via NIH) rightly thought that DOE was invading their turf and if anyone was going to do it, they (NIH) were. This was the turning point, because although there were, and are, many competent scientists in NIH that are not in favor of HGP, the momentum had gathered under DOE and the NIH had to carry it forward and their reputation gave it credibility. Even then there was sniping from the academic community so a scientific saint figure in the person of nobelist Dr. James Watson was brought in to calm the waters.

NIH research monies should be used to research, not the automated molecular bookkeeping of HGP. So many truly worthy, innovative grant requests, with high study section scores, from young investigators are not funded because of lack of money. Such a waste. Not only immediately but in the failure of the bright, committed young people launch their careers. The estimated three (3) billion dollars for HGP would help may good people if used properly. HGP is not good for America's future. There is no stewardship here.

Be assured that many members of the technical, scientific and academic community have similar views. Let's use our resources wisely. Wind down HGP in a with all judicious haste.

Sincerely,

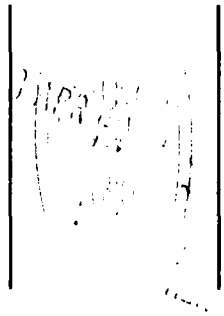
Don N. Gray

Don N. Gray, PhD
President

83617

SCHOOL OF MEDICINE IN SHREVEPORT
Louisiana State University
Medical Center
1501 Kings Highway
Post Office Box 33932
Shreveport, LA 71130-3932
Telephone: (318) 674-5160

Department of Biochemistry
and Molecular Biology



April 16, 1990

Dr. William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub:

I wish to voice my strong opposition to the Human Genome Project (HGP). In a period of severe budget restraint at the National Institutes of Health, I believe it is foolish to invest 3 billion dollars (or more) to sequence the entire human genome. I say this for the following reasons:

[1] *The HGP has questionable goals.* Most U.S. bioscientists do not support brute-force sequencing of genomes. In the case of the human genome, up to 95% of the DNA does not code for proteins and is thought by many, including some of its advocates, to be "junk." Thus, elucidation of the complete sequence is an extremely inefficient use of NIH funds. Far more reasonable and useful at this time would be a comprehensive gene mapping project that would focus the effort on the "cream" (i.e., the genes) of the human genome. In other words, it would be far better to target specific diseases using an enhanced human genetic map than to sequence yards of DNA on the chance that a medically important locus is present.

[2] *The HGP is a costly, wasteful, and inappropriate allocation of research funds.* Its boosters say the the HGP will cost $200 million per year for 15 years. This assumes no delays and no cost overruns--but already delays are occurring. In addition, up to 20% of the cost of the project has been earmarked for creation of computer databases--$600 million to computer-warehouse junk DNA sequences! As an assistant professor of biochemistry and molecular biology with a nationally funded research program, I am deeply disturbed by this extravagant use of federal research funds. Wouldn't it make more sense to disburse the $200 million as 1000 individual RO1 grants, thereby funding laboratories in universities, rather than 10 or so block grants to major sequencing centers?

[3] *The HGP will provide little useful training and no intellectual stimulation to young scientists.* Because the HGP provides so little intellectual excitement for graduate students or postdoctoral fellows, it would have to be accomplished by technicians. As already mentioned, $200 million translates into 1000 individual research grants that support a diverse collection of undergrads, graduate students, and postdoctoral fellows at universities throughout the country.

Besides the actual scientific product from these grants, there is a tremendous educational benefit to the nation. By contrast, diversion of the same funds to the HGP will result in armies of technicians skilled only in obtaining DNA sequences and entering the results into data bases. Since the future of scientific research depends upon vigorous training programs, it is bad science policy to fund cadres of technicians at the expense of university laboratories.

In closing, let me be very clear: I support continued refinement of the human genome map, for *this* will have a significant impact on our understanding of major human diseases. What I strongly oppose is the brute-force, shotgun sequencing of the DNA of every human chromosome. Such effort is not only costly but is unlikely to yield much beneficial information beyond that of the vastly more cost-effective genetic mapping endeavor. It is not too late to focus the HGP on the latter goal. Such curtailment would serve the dual purpose of making the entire project more cost-efficient as well as preserve sufficient NIH funds for traditional biomedical research in individual research laboratories.

Thank you for your consideration of my viewpoint. I would be interested in hearing your response to the objections I've raised above, if your time permits.

Sincerely,

David S. Gross

DAVID S. GROSS, Ph.D.
Assistant Professor of Biochemistry
and Molecular Biology
(318) 674-5027

John G. Hildebrand, Ph.D.
629 North Olsen Avenue
Tucson, AZ 85719

16 March 1990

Dr. William F. Raub
Acting Director
National Institutes of Health
R00m 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub:

As a professional biological scientist and senior professor in a university biological sciences faculty, I wish to express my views on the Human Genome Project (HGP).

I join the chorus of other scientists who believe that the HGP is a flagrant waste of Federal research funds. In my view, the HGP is mediocre "science" that represents appalling science policy.

The HGP did not arise from a broad consensus that the sequence information is badly needed. In fact, it is my sense that a very large majority of biomedical and biological scientists in this country believe the HGP to be a bad idea. There is no reason to subscribe to the specious argument that information obtained through the HGP will have a major impact on human diseases. Indeed, even the most stunning successes of the genetic-mapping approach -- discovery of the genes responsible for cystic fibrosis and muscular dystrophy -- did *not* require the kind of detailed sequence information toward which the HGP is directed.

The HGP is projected to cost at least $3,000,000,000 over 15 years. Of that amount, no less than $600,000,000 is expected to be required for computer databases to computer-warehouse sequences most of which will be those of so-called "junk" DNA! Our society cannot afford that kind of price tag on such an ill-considered initiative. At this very moment, our academic-science enterprise is in a very precarious state. Having been second to none elsewhere in the world, basic research in the USA is threatened by diminishing ability and interest on the part of students, decaying research infrastructure, and especially sharply reduced availability of research funds. At a time when many outstanding investigator-initiated, peer-reviewed research projects are going unfunded because of the worst paylines in the history of NIH and NSF, how can we justify wasting *billions* of dollars on work that has not been adequately rationalized and is not even respectable science?

One of the most important issues before you in your important leadership role in American science is the mistake that we call the HGP. It is not too late to take a strong stand and acknowledge that this bad idea need not inevitably be implemented.

Yours respectfully,

John G. Hildebrand, Ph.D.

MEDICAL
COLLEGE OF
WISCONSIN

Department of Biochemistry

March 2, 1990

Dr. Wm F Raub
NIH acting Director
Bethesda, MD.

Dear Dr. Raub:

I am writing in regard to my concerns about the proposed human genome project (HGP). I feel strongly that the money could be better spent elsewhere and without going into all the scientific reasons do not feel the HGP will yield the expected results. As colleague after colleague returns from NIH study sections with horror story after horror story I am concerned the US will lose its competitive edge in Science. Our advances have come through the support of individual investigators

8701 Watertown Plank Road
Milwaukee, Wisconsin 53226
(414) 257-8435 / 8257 / 8259
FAX: (414) 257-2008

not through funding hundreds of ... technicians to perform sequencing chores, yielding data of dubious value. Why not sequence the many pure proteins known that have important biological functions? As I will be retiring at the end of our present grant I do not have a personal "axe-to-grind." I am however very concerned about the effect of the HGP if funded, on the future of research in this country.

Sincerely,

M Claire Kennedy
Research Prof.

Human genome project 2-19-90

SIR: $200 million per year for the human genome project may be peanuts to Norton Zinder and James Watson (C&EN, Dec. 11, 1989, page 4), but it would represent 1000 National Institutes of Health-funded grants at $200,000 each per year. Certainly this would be very welcome peanuts to those scientists whose NIH grants were approved but not funded. I agree

It is incredible what greed, selfishness, and egotism these people have in pushing their human genome project. The NIH funding or funding by any other agency of this highly questionable project will ensure that the diversity of science research and technology in the U.S. will be retarded and suspended for several years to come.

John F. Robyt
Pro[illegible] a State U[illegible]

ANDRAS G. LACKO
5834 B WESTHAVEN DR.
FORT WORTH TX. 76132
(817) 292-8188

February 28,1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building I
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub,

I identify with and support the views of Dr. Rechsteiner eloquently stated in the enclosed letter. Cosequently I am strongly opposed to the human genome project. From the available evidence, it is clear that this project has very questionable potential for meaningful payoffs in either the basic sciences or medicine. The program is aimed to accomplish a goal simply because it is there and because it is a monumental task. Many people attempted to climb Mount Everest for the same reasons but at a much lower cost.

The N.I.H. peer reviewers routinely reject proposals for the lack of well identified and specific goals. The human genome project would be high on the list of such disapprovals had it been subjected to a thorough evaluation. The program is clearly over funded and it is likely to gobble up what is equivalent to about 20% of the support allotted for investigator initiated research; supposedly the primary goal of the N.I.H.

As a scientist with over 20 years of experience in conducting and reviewing research projects, I couldn't be more disappointed if the funding of this project will go forward as projected. I urge you to take action against it!

Sincerely

Andras G. Lacko Ph. D.
Professor of Biochemistry
Texas College of Osteopathic Medicine

Dartmouth Medical School HANOVER • NEW HAMPSHIRE • 03756

Department of Biochemistry • TEL. (603) 646-7616

March 14, 1990

Dr. William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub:

I am a biochemist engaged in basic biomedical research. I am writing to urge that the human genome project not be funded. The reasons for this position are cogently presented in the enclosed statement of Dr. Martin Rechsteiner. At this time only a modest effort to map the human genome is warranted. The funds for the genome project should instead be used to increase the number of research grants to individual investigators.

Sincerely,

Gustav E. Lienhard

Gustav E. Lienhard
Professor of Biochemistry

GEL/erj

PURDUE UNIVERSITY

DEPARTMENT OF CHEMISTRY

March 16, 1990

Dr. William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub:

I am writing to relay my concerns on the state of federal funding for biomedical research. I am a Professor of Biochemistry in our Chemistry Department at Purdue University, and I have been performing fundamental research for close to 30 years. Fundamental research has a very low priority today and funding is very difficult to obtain from the National Institutes of Health and the National Science Foundation. In addition to the obligation the federal government has to many agencies, the very large budget deficit, and finally the negative attitude toward raising taxes, it is becoming impossible for research scientists to train American students for future opportunities in academic positions and industry.

The funding program is further complicated by a new plan for a ten year multi-billion dollar budget for the human genome structure. The human genome project is mission orientated and similar to other biomedical missions now pursued. These projects waste money, utilize an enourmous manpower reserve, and depend on a "shot gun approach" to reach their goal. The answers to the genome project, cancer research, heart problems, AIDS, neurological disorders, and a host of other problems and projects, will be understood and progress made by the individual investigator doing his thing and doing it best.

The past history of science depended on the unexpected breakthrough of a single experiment and describes how our greatest advances took place. These advances came from the abilities of many outstanding scientists. Creative genius is developed at an early stage and is a rare commodity. Mission oriented research wastes these talents and delays the progress that should be possible with freedom to pursue individual goals.

I express these concerns to you and hope they will be valuable in your further deliberations of funding the human genome project. The United States Government cannot afford to risk funding a project that may or may not be successful after the expenditure of the time and money it will require. I hope you appreciate the merit of indivdual research projects chosen by peer review and allow American scientists to perform fundamental research to the best of their abilities.

Sincerely yours,

Albert Light,
Professor of Chemistry
(317) 494-5293

AL:jh

HERBERT C. BROWN LABORATORY OF CHEMISTRY • RICHARD B. WETHERILL LABORATORY OF CHEMISTRY
WEST LAFAYETTE, IN 47907-3699 • FAX (317) 494-0239

Department of Biochemistry and Biophysics

Oregon State University

Weniger Hall 535
Corvallis, OR 97331-6503

(503) 754-4511

March 20, 1990

Dr. William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, Maryland 20892

Dear Dr. Raub:

I am writing to question the wisdom of the goal to determine the entire DNA base sequence of the human genome. Superficially, the Human Genome Project (HGP) sounds like a marvelous idea--a biologist's equivalent of the Manhattan Project, involving armies of scientists and machinery, with coordinated progress toward a defined goal. The project would generate voluminous amounts of data, whose analysis could solve major medical problems.

However, this goal would be achieved at the expense of dollars and manpower diverted from more creative research to what many of us consider drudgery. The data in the aggregate will be less useful, in my opinion, than that which could continue to flow from thousands of laboratories carrying out untargeted basic research. The value of this latter approach has been shown repeatedly--from the discovery of antibiotics, through the spectacular successes of the recombinant DNA era.

If the genome project is to consume $200 million per year for fifteen years, as proposed, the bulk of that money must be diverted from traditional investigator-initiated project grants, the backbone of our biomedical research enterprise. Proponents of the HGP claim that the project is being funded independently of individual project grants, but virtually no one in the research community believes that--particularly the growing legions of us whose NIH applications are being regularly stamped "Approved but not funded." The present funding situation is causing talented graduate students to reassess their career goals and move away from basic research and academic careers, at precisely the time when shortages of academic scientists are being forecast. The HGP is one of several elements that help make this situation ripe for disaster.

The recent success of medical geneticists in isolating genes for cystic fibrosis and Duchenne muscular dystrophy was achieved with high-precision genetic mapping techniques; massive DNA sequencing was unnecessary to achieve these stunning successes. Many of us believe that the aims of the HGP could be met admirably with the modified goal of creating a high-resolution map of the human genome; sequencing of interesting regions could follow, but need not be scheduled on a crash basis.

82740

Such curtailment would (1) allow the continued support of most high-quality individual and small-group collaborative biomedical research through the proven project grant mechanism; (2) continue to allow bright young scientists to engage in exciting research, rather than being recruited to the drudgery of massive sequencing in the absence of hypotheses or heuristic models; and (3) would allow the research community to still move briskly toward the control of diseases that have a genetic component, as well as gaining the numerous additional benefits that would flow from detailed understanding of the human genome.

Yours sincerely,

Christopher Mathews

Christopher K. Mathews
Professor and Chairman

CKM:sc

Department of
Biochemistry and
Biophysics

Oregon State University

Weniger Hall 535
Corvallis, OR 97331-6503

(503) 754-4511

March 21, 1990

Dr. William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, Maryland

Dear Dr. Raub:

I am writing to express my opinion that biomedical research will suffer if large chunks of the NIH budget continue to be diverted to the ill-conceived human genome sequencing project. The danger of supporting a large centralized project of dubious merit is illustrated by an historical example. For decades, biological research in the Soviet Union was stifled by imposition of an unsound scientific idea promulgated by Soviet health secretary Lysenko. Although not as damaging or widespread in its effects as Lysenkoism, the genome initiative is nontheless a bad idea that will destroy smaller projects of far greater scientific merit and relevance to human health. The human genome sequencing project should not be funded.

Sincerely,

Gary Merrill

Gary Merrill
Assistant Professor

92674

WAKE FOREST

The Bowman Gray

School of Medicine

March 14, 1990

Department of Microbiology and Immunology
(919) 748-4471

Steven B. Mizel, Ph.D.
Chairman

Gary A. Brewer, Ph.D.
Henry M. Drexler, Ph.D.
Eugene R. Heise, Ph.D.
Arnold S. Kreger, Ph.D.
Louis S. Kucera, Ph.D.
Douglas S. Lyles, Ph.D.
Charles E. McCall, M.D.
Quentin N. Myrvik, Ph.D.
Brian A. Pollok, Ph.D.
Stephen H. Richardson, Ph.D.
Rosanne J. Spolski, Ph.D.
D. Denee Thomas, Ph.D.
Ivo van de Rijn, Ph.D.

Dr. William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub:

The major goal of biomedical science in the United States is the improvement of human health. The National Institutes of Health has done an outstanding job in providing the leadership and funds that have been necessary to undertake the battle against infectious diseases, cancer, AIDS, heart disease, and autoimmune diseases. Through the NIH funding system, a relatively large number of laboratories in universities and medical centers around the country have made tremendous strides in the discovery of the causes and cures for many diseases. Today we are confronted by a new type of proposal that has serious consequences for the future of biomedical research in the United States.

The proposed human genome project (HGP), which is dedicated to sequencing the entire human genome at a projected cost of three billion dollars, has received a great deal of attention, but very little debate on its actual merits. I would argue that it is a bad idea on several grounds. First, most of the human genome contains "junk" or filler genetic material (DNA) that does not encode the blueprints for making proteins. To sequence the entire genome means wasting a great deal of time and money on gathering meaningless information. Success in biomedical research has always come from more targeted efforts. For example, recently the genes associated with cystic fibrosis and muscular dystrophy were identified by such a directed approach.

The difficulty in obtaining NIH support for research is driving many biomedical scientists away from independent research in academic centers and acting as a deterrent for students who are considering a career in biomedical science. We must insure that there will be a next generation of biomedical scientists in the United States. These individuals can only be trained in universities and medical centers in active, creative research environments.

300 South Hawthorne Road, Winston-Salem, North Carolina 27103
TELEX 806449 BGSM WSL TELEFAX (919) 748-4204

Sequencing the human genome requires no intellectual effort--it is the work of technicians. Three billion dollars spent on the human genome project would fund approximately 3000-5000 laboratories for a period of 3-5 years. Many of these laboratories would serve as outstanding environments for biomedical research training.

We stand at a crossroads in biomedical science. If we choose wisely, we will continue our proven record of success in responding to the many diseases that afflict mankind. If we choose poorly--if we committ our funds and energy to projects like the human genome project--we will damage our efforts in the here and now as well as in the future.

I urge you to oppose the human genome project. We can and should do better than to throw money away on such an inefficient and potentially harmful approach to biomedical research.

Sincerely,

Steven B. Mizel, Ph.D
Professor and Chair

John E. Morris
6315 N.W. Ponderosa
Corvallis, Oregon 97330

4/12/90

Dear Dr. Rowley,

I am writing to express my opposition to the Human Genome Project (HGP) as presently proposed. Not that the goal is unworthy, but quite simply, it would absorb too much funding from more innovative & potentially more valuable science. Already, in recent years scientists have seen targeted programs greatly reduce the number of NSF & NIH basic research grants. This has the potential to significantly harm American science leadership. More valuable genome information will be gained by supporting imaginative individual projects.

Sincerely,

John E. Morris,
Professor of Zoology &
Associate Dean of Science,
Oregon State University

83253

Department of Physiological Chemistry
University of Wisconsin Medical School
587 Medical Sciences Building
1300 University Avenue
Madison, Wisconsin 53706
Department Office: (608) 262-1347

March 13, 1990

Mr. William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Mr. Raub,

I am writing to voice my deep opposition to the human genome project. I believe that the project is both a waste of research funds and a misguided and ill-thought scientific project. I am certain that most of the sequence information that is generated will never prove to be of any scientific value (especially since probably greater than 90% of the sequences are non-coding or "junk" DNA sequences). The human genome project is a "brute-force" and indeed, stupid, way to determine those sequences that will be of biological interest. It would be much more reasonable to support the analysis of just the sequences of interest.

There are other reasons for my opposition to this project, too. Although its supporters say otherwise, I think that it is quite likely to divert funds from much more important and reasonable areas of research. Also, the work itself is sheer drudgery, and will provide little or no intellectual stimulation. We are already feeling the effects of a lack of promising young scientists in our undergraduate and graduate programs, and the human genome project can only worsen this problem. We need to provide our young scientists with important, stimulating problems to be addressed.

I am a molecular biologist, and am well versed in both the techniques of DNA sequencing and the analysis of DNA sequences. I understand quite well the problems inherent in the human genome project, and the limitations of the usefulness of the sequence information that will be generated by this project. Please consider my objections (and those of many of the finest researchers in my area) and put a stop to the human genome project. Thank you.

Sincerely,

Mary Anne Nelson

Dr. Mary Anne Nelson

82457

University of Illinois
College of Medicine at Urbana-Champaign

190 Medical Sciences Building
506 South Mathews
Urbana, IL 61801

March 28, 1990

Mr. William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Mr. Raub:

As a biochemist and molecular biologist, I am worried about what has been happening recently to science in America. America's great success in the general arena of biochemistry/molecular biology has been through efforts of individual investigators in their own, mostly university, scientific laboratories following their instincts about what is important. In our system, research grants, in large part from the National Institutes of Health, have made much of this possible. However, now money is being taken away from the regular grant system ("RO1" grants) and being funnelled into projects like the human genome project (HGP). I will list some of the bad consequences of this reallocation of money and will ask you to do what you can to block it.

1. The HGP is costly and will probably require much more than the $200 million now being requested.

2. This money will inevitably come from the money otherwise given scientists in universities and elsewhere.

3. Many laboratories will close down for lack of funding. This is already starting.

4. Many of these laboratories are productive.

5. Most human DNA does not code for anything; only a little does. Thus there will be a lot of waste in sequencing useless DNA.

6. Sequencing is mindless. It will require lots of technicians. The resources spent on this will be diverted away from graduate students and postdoctoral fellows, who see and solve problems. We need to continue to develop "thinking" manpower, for they will give this society the innovations needed for our future.

7. Merely knowing where a gene is and its sequence does not provide the degree of scientific advance that investigations of the psychology and cellular functions of proteins do.

In sum, spending all this money in the HGP will divert money from funding good quality biochemistry and molecular biology. These are very difficult times, and good laboratories are going under for lack of funds. A shortage of good scientists is forecast even under times of adequate funding. Funding the HGP will only worsen matters. I urge you to vote to block this.

Sincerely,

George W. Ordal

George W. Ordal
Associate Professor
Department of Biochemistry/
School of Basic Medical Sciences

GWO/sak

DEPARTMENT OF
PHARMACOLOGY
THE UNIVERSITY OF MICHIGAN MEDICAL SCHOOL

March 8, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Mr. Raub:

I am writing to make you aware of the arguments contesting the rationale behind the human genome project summarized by Martin Rechsteiner in the enclosed letter to the Journal of the Federation of American Societies for Experimental Biology. Many of us employed in scientific research feel that this incredibly costly effort will draw badly needed funds from the R01 grants that fund the truly creative science that has given the United States its preeminent position in biomedical discovery. I feel strongly that the human genome project should be curtailed.

Sincerely,

William B. Pratt

William B. Pratt, M.D.
Professor of Pharmacology

WBP:mef

6322 Medical Science Building I • Ann Arbor, Michigan 48109-0626
(313) 764-8165 • FAX (313) 763-4450

UNIVERSITY AT BUFFALO
STATE UNIVERSITY OF NEW YORK

Department of Biological Sciences
Faculty of Natural Sciences and Mathematics
Cooke Hall
Buffalo, New York 14260
(716) 636-2363

March 5, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Mr. Raub:

A convincing letter soon to appear in FASEB Journal indicates clearly and for good reasons that the human genome project is a waste of federal research funds. The letter is authored by Martin C. Rechsteiner, Professor of Biochemistry, University of Utah. I support his letter. Please read it and you may well be convinced.

Sincerely yours,

C. A. Privitera
Professor, Biol. Sciences
SUNY at Buffalo

CAP:rms

UNIVERSITY OF MINNESOTA
DULUTH

Department of Biochemistry and Molecular Biology
School of Medicine
10 University Drive
Duluth, Minnesota 55812-2487

(218) 726-7922
FAX: (218) 726-6235

March 29, 1990

William F. Raub
Acting Director
National Institutes of Health
Building 1, Room 126
9000 Rockville Pike
Bethesda, MD 20892

Dear Mr. Raub:

I don't often write to public officials to state my opinions—not because I don't have them, but because I recognize that you, too, are a busy person with many duties and concerns. In this instance, however, I feel compelled to write.

Enclosed is a copy of a letter sent to me by Professor Martin Rechsteiner from Utah, a person I do not know personally. I do share his opinions for the most part, however. I am deeply concerned that basic science research in this country is being jeopardized by the funneling of precious and limited research dollars into a few selected areas. The human genome project is one area; AIDS research is another. There has to be a more rational way to sustain and stimulate American biomedical research than that.

I hope that you will continue to do what you can to increase resources for education and research and to support broad-based research throughout the country, rather than the focused and expensive projects that may not be worth the risk. Reducing the number of investigator-initiated NIH grant awards by more than 1000 is a poor move for the country.

At this time in our history, it is critical that we allocate resources effectively to support both science and the health of our nation.

Sincerely,

Joseph R. Prohaska
Professor of Biochemistry and Molecular Biology

JRP:bcb

Enclosure

UNIVERSITY OF CALIFORNIA, RIVERSIDE

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO SANTA BARBARA • SANTA CRUZ

DIVISION OF BIOMEDICAL SCIENCES RIVERSIDE, CALIFORNIA 92521-0121

March 21, 1990

William F. Raub
Acting Director
National Institute of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, Maryland 20892

Dear Mr. Raub:

As a biomedical scientist deeply interested and involved in work in a genetic disease, I would like to join a group of my colleagues who vigorously oppose the human genome project. I agree with my colleagues that this project is diffuse and inefficient. It is divisive to the medical scientific community and represents an emphasis which badly unbalances our endeavors to understand biology and disease.

I seriously urge a reconsideration of the purposes and objectives of this project and a reorientation of human gene mapping, which is disease specific.

Sincerely yours,

Paul M. Quinton, Ph.D.
Professor
Biomedical Sciences, UCR
Physiology, UCLA

PMQ:np

82.661

University of Colora[redacted]ealth Sciences Center

Hepatobiliary Research Center

Campus Box B158
4200 East Ninth Avenue
Denver, Colorado 80262
(303) 270-8566

March 26, 1990

William F. Raub
Acting Director National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Sir:

I am writing you regarding the human genome project which has been proposed to the NIH for funding. For the past several years I have read several articles regarding the goals, function and funding for the human genome project. After much consideration I have come to the conclusion that at this time in our country's state of knowledge and financial condition, it is a very poor project into which we should invest so much money. Firstly, the premise on which the human genome project is based is conceptually erroneous. There is no reason to believe that understanding the primary structure of the human genome will in any way lead to the new insights into disease processes. This concept is risky for reasons that are obvious to most biomedical scientists. It is not reasonable to ask the NIH to make a major gamble with a large amount of money at a time when more practical research programs are in dire need of funding. Frankly, I believe the history of science and medicine clearly indicates that truly profound understanding is gained from diligence, hard work and a commitment towards understanding diseases one step at a time. Taking this risky "leap-frog" approach might lead to new understanding, but this success will require a large amount of luck. While lucky breaks may accelerate scientific accomplishments, it should not be the premise of investigation. Finally, there are very few diseases that are the result of single gene defects. While many times single gene defects have given us an understanding of one of many causes for a particular disease expression, this only leads to a partial understanding. Undertaking the huge task of sequencing the entire human genome and then taking particular DNA sequences that may or may not be the direct cause of the human disease and using these sequences to find areas of the genome that may be responsible for a particular disease is by no means a trivial matter. Even if one were to uncover these specific areas of a human genome, which may correlate to genetic markers of specific diseases, we are still left with the task of understanding the biochemistry and physiology through which these sequences lead to disease mechanisms. It is not apparent how information on the structure of the human genome will advance our understanding of these processes.

There are additional concerns regarding the funding of the human genome project. It is my understanding that the human genome project will be accomplished by about twenty large laboratories. This large team effort will allow the tedious mechanics of sequencing and storing the sequences of the human genome to be accomplished. Because there is

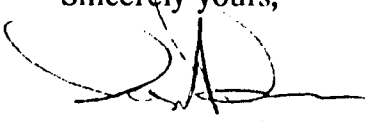
82784

nothing intellectually challenging regarding the sequencing of the human genome, it is unlikely that graduate students or post-doctoral fellows can be trained on this project. This is quite different from the situation in which small grants are given to individual laboratories where graduate students and post-doctoral fellows work on understanding several different aspects of different human diseases. Thus, supporting the human genome project as proposed will likely have a deleterious effect on educating young scientists. It is my understanding from reading several articles on the demographics of our society, that we will have a dramatic shortage of scientists in the near future. It seems reasonable that this issue be addressed when considering the impact of funding the human genomic project.

In conclusion, I believe that supporting the human genome project will risk an enormous expenditure of money to obtain information that is unlikely to yield new insights into understanding disease processes. Furthermore, it is likely that diverting money to the human genome project will exacerbate the potential problems we face concerning the shortages of young scientists. I hope that this letter serves to allow you to look further into the dramatic impact that this risky program may have on our society.

If I may be of further assistance to you in this matter, please do not hesitate in asking. Thank you for your attention to this matter.

Sincerely yours,



Roger A. Davis, Ph.D.
Professor
Biochemistry, Biophysics, Genetics/
Medicine/Physiology

RAD:ps

February 26, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pick
Bethesda, MD 20892

Dear Dr. Raub:

The human genome project is mediocre science and terrible science policy. In a period of severe budget restraint at the National Institutes of Health, I believe it is foolish to invest three billion dollars (or more) to sequence the entire human genome. Below, I briefly discuss five reasons for thinking the HGP is an ill-conceived idea. Despite an abundance of articles in Science, Nature and JAMA on the human genome project (HGP) and ample reference to its critics, the basis for our opposition has not found its way into print. I hope you will consider my arguments carefully.

The HGP has questionable origins.

This statement may sound like back-fence gossip, but it is meant to convey the fact that the HGP did not arise from a broad consensus among scientists that the sequence information was badly needed. Rather the idea seems to have emanated from somewhere within the Department of Energy; most evidence points to the deserts of New Mexico. Formally, the idea was presented by Charles DeLisi (1); a bill to fund the HGP was subsequently introduced by New Mexico Senator Domenici (2). This led to a squabble over which government agency, DOE or NIH, should direct the project. Sadly, the NIH won adding an air of medical legitimacy to the venture. Had DOE prevailed, I believe we would see much more vigorous opposition from the biomedical and biological community. As it is, I believe an overwhelming majority of the latter consider the HGP a bad idea.

The HGP has questionable goals.

The original aim of the HGP was simple enough. Determine the sequence of all the base pairs in the human genome. Never mind that 95% of the DNA doesn't code for proteins and is thought by many, including some of its advocates, to be "junk" (1). The goal has shifted recently to include sequencing of plant, worm, yeast and bacterial genomes as well (3,4). This move, reminiscent of political maneuvers by defense contractors to spread manufacturing among several states, has generated a few more enthusiasts for the project. But as noted above, I believe that most U.S. bioscientists do not support brute force sequencing of genomes.

What is the justification for all of this sequencing? We are told that the resulting information will have great impact on major human diseases. This is a specious argument for several reasons. First, significant advances in understanding the two major diseases in the U.S., heart disease and cancer, were made independent of the HGP. The seminal work of Brown and Goldstein on cholesterol metabolism did not require their knowing the map positions of HMG Co A reductase or the LDL

receptor. Likewise, most oncogenes have revealed themselves by their dominant effects, not by sequence analysis of human genomes (5).

Second, even the two stunning successes of the human mapping approach, discovery of the genes responsible for cystic fibrosis and muscular dystrophy, did not require detailed sequence information. To be sure, a reasonable linkage map was needed to identify the CF and MD genes, and I support continued refinement of the human genome map. But a map was available and was being refined in the absence of the HGP. It would be far better to target specific diseases using a better human genetic map than to sequence yards of DNA on the chance that a medically important locus is present.

The HGP is a costly, wasteful and inappropriate allocation of research funds.

Its boosters say that the HGP will cost $200 million per year for 15 years. This three billion dollar total assumes, of course, no delays and no cost overruns. But already we are apprised of delays in the project (6). How do we know it will only take 15 years? And what response could be raised at that time to a claim that "we're only half-finished?" The open-ended nature of the venture is disturbing. The HGP may become the first NIH project to compete with defense's C5A transport as a drain on federal coffers.

Of this projected three billion dollar outlay, Cantor estimates that 20% will be used for computer databases alone (7). Imagine that! Six hundred million dollars to computer-warehouse junk DNA sequences. Apparently, the rest of the money will be disbursed to several sequencing centers, to companies for developing sequencing equipment and perhaps to a few individual labs. The thrust is big science, not small science, so no doubt most of the cash will go to centers and/or industry.

Watson is quoted in Science as saying "Two hundred million dollars is not all that much money" (8). Clearly, that is a matter of opinion. Granted, it is not a lot of money by defense department standards. Perhaps that was Watson's frame of reference since so much about the HGP smacks of defense department mentality. As one of a large number of PI's with a current NIH priority score between 10 and 15%, I can assure Watson that 200 million dollars seems like a lot of money to me. For a struggling young assistant professor facing tenure, it might appear to be all the money in the world. However, the key issue is not one's perception of wealth, but whether $200 million should be disbursed as 1000 R01 grants, thereby funding laboratories in universities, or as 10 or so block grants to sequencing centers. For me, there is simply no doubt the proper choice is the former.

The HGP will provide little useful training and no intellectual stimulation to young scientists.

Headline in the January 8 issue of The Scientist--"Researchers, discouraged by mapping's drudgery, doubt that a five-year plan to finish high resolution image is now feasible." If mapping is drudgery, what word applies to sequencing? Because the HGP provides so little intellectual excitement for graduate students or post-doctoral fellows, it will be accomplished by technicians. Two hundred million dollars translates into 1,000 ROIs that support a diverse collection of undergrads, graduate students and post-doctoral fellows at various universities. Besides the actual scientific product from these grants, there is a tremendous educational benefit to the nation. By contrast, diversion of the same funds to the HGP will result in

armies of technicians skilled only in obtaining DNA sequences and entering the results into data bases. At a time when a scientific career looks bleak enough, it makes no sense to compound the problem of recruiting scientists by restricting university grants. Since the future of U.S. biomedical research depends upon vigorous training programs, **it is bad science policy to fund cadres of technicians at the expense of university laboratories.**

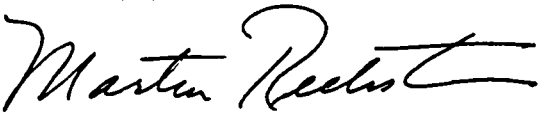
The HGP is divisive.

The concept of big science versus little science, new to biology, is frankly quite distasteful. The words conjure up big leagues versus little leagues, serious versus trivial, important versus unimportant. True, these terms have long been applied to physics where they apparently do not cause rancor. The same cannot be said of their recent introduction into biology. It has been proposed that big science is bad science (9). The spirited debate that followed on whether big science, defined as 20-30 post-docs per lab, is anywhere near as efficient as the typical smaller research group takes on a whole new dimension when applied to the HGP.

The HGP should be curtailed.

In short, the HGP is a waste of national resources and is detrimental to the training of young scientists. The demise of Mohole, a similar grandiose, costly and ill-conceived project to drill deep into the earth, proves that bad ideas are not inevitably implemented. I urge you to take the steps necessary to curtail the human genome project.

Sincerely yours,



Martin Rechsteiner
Department of Biochemistry
University of Utah School of Medicine
Salt Lake City, UT 84132

References

1. JAMA 258:1131-1132 (1987)
2. JAMA 259:15-16 (1988)
3. Nature 339:648 (1989)
4. Science 245:131 (1989)
5. Science 235:305-311 (1987)
6. Science 247:281-282 (1990)
7. AAAS Observer, November 3, 1989
8. Science 239:725-726 (1988)
9. Cell 41:337-338 (1985)
10. Science 246:576-578 (1989)

February 26, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pick
Bethesda, MD 20892

Dear Dr. Raub:

The human genome project is mediocre science and terrible science policy. In a period of severe budget restraint at the National Institutes of Health, I believe it is foolish to invest three billion dollars (or more) to sequence the entire human genome. Below, I briefly discuss five reasons for thinking the HGP is an ill-conceived idea. Despite an abundance of articles in Science, Nature and JAMA on the human genome project (HGP) and ample reference to its critics, the basis for our opposition has not found its way into print. I hope you will consider my arguments carefully.

The HGP has questionable origins.

This statement may sound like back-fence gossip, but it is meant to convey the fact that the HGP did not arise from a broad consensus among scientists that the sequence information was badly needed. Rather the idea seems to have emanated from somewhere within the Department of Energy; most evidence points to the deserts of New Mexico. Formally, the idea was presented by Charles DeLisi (1); a bill to fund the HGP was subsequently introduced by New Mexico Senator Domenici (2). This led to a squabble over which government agency, DOE or NIH, should direct the project. Sadly, the NIH won adding an air of medical legitimacy to the venture. Had DOE prevailed, I believe we would see much more vigorous opposition from the biomedical and biological community. As it is, I believe an overwhelming majority of the latter consider the HGP a bad idea.

The HGP has questionable goals.

The original aim of the HGP was simple enough. Determine the sequence of all the base pairs in the human genome. Never mind that 95% of the DNA doesn't code for proteins and is thought by many, including some of its advocates, to be "junk" (1). The goal has shifted recently to include sequencing of plant, worm, yeast and bacterial genomes as well (3,4). This move, reminiscent of political maneuvers by defense contractors to spread manufacturing among several states, has generated a few more enthusiasts for the project. But as noted above, I believe that most U.S. bioscientists do not support brute force sequencing of genomes.

What is the justification for all of this sequencing? We are told that the resulting information will have great impact on major human diseases. This is a specious argument for several reasons. First, significant advances in understanding the two major diseases in the U.S., heart disease and cancer, were made independent of the HGP. The seminal work of Brown and Goldstein on cholesterol metabolism did not require their knowing the map positions of HMG Co A reductase or the LDL

receptor. Likewise, most oncogenes have revealed themselves by their dominant effects, not by sequence analysis of human genomes (5).

Second, even the two stunning successes of the human mapping approach, discovery of the genes responsible for cystic fibrosis and muscular dystrophy, did not require detailed sequence information. To be sure, a reasonable linkage map was needed to identify the CF and MD genes, and I support continued refinement of the human genome map. But a map was available and was being refined in the absence of the HGP. It would be far better to target specific diseases using a better human genetic map than to sequence yards of DNA on the chance that a medically important locus is present.

The HGP is a costly, wasteful and inappropriate allocation of research funds.

Its boosters say that the HGP will cost $200 million per year for 15 years. This three billion dollar total assumes, of course, no delays and no cost overruns. But already we are apprised of delays in the project (6). How do we know it will only take 15 years? And what response could be raised at that time to a claim that "we're only half-finished?" The open-ended nature of the venture is disturbing. The HGP may become the first NIH project to compete with defense's C5A transport as a drain on federal coffers.

Of this projected three billion dollar outlay, Cantor estimates that 20% will be used for computer databases alone (7). Imagine that! Six hundred million dollars to computer-warehouse junk DNA sequences. Apparently, the rest of the money will be disbursed to several sequencing centers, to companies for developing sequencing equipment and perhaps to a few individual labs. The thrust is big science, not small science, so no doubt most of the cash will go to centers and/or industry.

Watson is quoted in Science as saying "Two hundred million dollars is not all that much money" (8). Clearly, that is a matter of opinion. Granted, it is not a lot of money by defense department standards. Perhaps that was Watson's frame of reference since so much about the HGP smacks of defense department mentality. As one of a large number of PI's with a current NIH priority score between 10 and 15%, I can assure Watson that 200 million dollars seems like a lot of money to me. For a struggling young assistant professor facing tenure, it might appear to be all the money in the world. However, the key issue is not one's perception of wealth, but whether $200 million should be disbursed as 1000 R01 grants, thereby funding laboratories in universities, or as 10 or so block grants to sequencing centers. For me, there is simply no doubt the proper choice is the former.

The HGP will provide little useful training and no intellectual stimulation to young scientists.

Headline in the January 8 issue of The Scientist--"Researchers, discouraged by mapping's drudgery, doubt that a five-year plan to finish high resolution image is now feasible." If mapping is drudgery, what word applies to sequencing? Because the HGP provides so little intellectual excitement for graduate students or post-doctoral fellows, it will be accomplished by technicians. Two hundred million dollars translates into 1,000 ROIs that support a diverse collection of undergrads, graduate students and post-doctoral fellows at various universities. Besides the actual scientific product from these grants, there is a tremendous educational benefit to the nation. By contrast, diversion of the same funds to the HGP will result in

armies of technicians skilled only in obtaining DNA sequences and entering the results into data bases. At a time when a scientific career looks bleak enough, it makes no sense to compound the problem of recruiting scientists by restricting university grants. Since the future of U.S. biomedical research depends upon vigorous training programs, **it is bad science policy to fund cadres of technicians at the expense of university laboratories.**

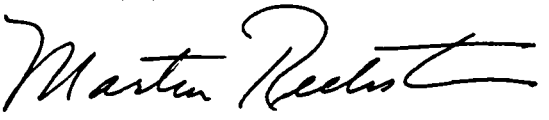
The HGP is divisive.

The concept of big science versus little science, new to biology, is frankly quite distasteful. The words conjure up big leagues versus little leagues, serious versus trivial, important versus unimportant. True, these terms have long been applied to physics where they apparently do not cause rancor. The same cannot be said of their recent introduction into biology. It has been proposed that big science is bad science (9). The spirited debate that followed on whether big science, defined as 20-30 post-docs per lab, is anywhere near as efficient as the typical smaller research group takes on a whole new dimension when applied to the HGP.

The HGP should be curtailed.

In short, the HGP is a waste of national resources and is detrimental to the training of young scientists. The demise of Mohole, a similar grandiose, costly and ill-conceived project to drill deep into the earth, proves that bad ideas are not inevitably implemented. I urge you to take the steps necessary to curtail the human genome project.

Sincerely yours,



Martin Rechsteiner
Department of Biochemistry
University of Utah School of Medicine
Salt Lake City, UT 84132

References

1. JAMA 258:1131-1132 (1987)
2. JAMA 259:15-16 (1988)
3. Nature 339:648 (1989)
4. Science 245:131 (1989)
5. Science 235:305-311 (1987)
6. Science 247:281-282 (1990)
7. AAAS Observer, November 3, 1989
8. Science 239:725-726 (1988)
9. Cell 41:337-338 (1985)
10. Science 246:576-578 (1989)

THE UNIVERSITY OF UTAH

March 23, 1990

William F. Raub, Ph.D.
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, Maryland 20892

Dear Dr. Raub:

I am writing to express my concern over the funding of the Human Genome Project (HGP) and the potential consequences of this decision.

In 1990, we Americans face an existing and worsening crisis within our scientific community. With the recent profound reduction in numbers of grants funded by the National Institutes of Health, the U.S. scientific community is dangerously, and perhaps mortally threatened. For many years, the U.S. has led the world in biomedical research, contributing to a long series of stunning advancements in the understanding of human biology and in the medical care of people worldwide. Now, we are witnessing a decline in our research community, as established and productive investigators go unfunded and as funds and positions for the training of new investigators have evaporated. This is creating a dramatic "brain drain" of the most discouraging kind: the demise of a hard-won public asset due to neglect. Compounding the tragedy is the fact that once the scientific community is dismantled, it will not be easy to return to our previous high standard, even if more money is infused. No, those ejected from the system will be disillusioned, and a period of inactivity will render them unproductive, uncompetitive and out of touch. In addition, with a depleted scientific community, we will have to resort to training new American scientists out of the country, just as the English, Japanese, French, Italians and Germans previously relied upon America.

The recent commitment of the sum of two hundred million dollars per annum to the HGP has contributed to reduced support for other important biomedical science in the U.S.A. If funding for the HGP is left in place, this will divert funds for approximately 1,000 grants per year from general NIH support. In my opinion, this is a misplaced emphasis.

Division of Human Development and Aging

School of Medicine
50 No. Medical Drive
Salt Lake City, Utah 84132
(801) 581-2628

First, although highly focused study of the human genome is meritorious (and already being conducted under funding allocated on the basis of scientific merit), the determination of the sequence of nucleotide bases for the entire genome will be largely "busy work", endowing relatively few centers nationwide. In addition, a large portion of the work will be, of necessity, rote technology and not science. Consequently, one questions whether these will be desirable sites for training of creative new scientists. Finally, the practical return of such work, not focused upon relevant human disease or biologic mechanisms, is highly questionable at best. For these reasons, I am seeking your help in redirecting the HGP funds to the general NIH fund, where they could be distributed according to merit, whether related to the human genome or not. Such action is badly needed to save America's scientific community.

I and many others will be most grateful for your assistance in supporting American Science. If I can be of any help to you, please let me know.

Sincerely,

Gerald Rothstein

Gerald Rothstein, M.D.
Professor of Medicine and Pediatrics
Chief, Division of Human Development and Aging

GR/kl

February 27, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Director Raub,

I am writing to you to make known my opposition to the Human Genome Sequencing Project. As a young Assistant Professor, struggling for NIH grant support, it is disturbing to me that a significant amount of money ($200 million!) is being drained from the NIH budget each year to support this speculative, ill conceived project, thus diverting funds from many capable, innovative and hard-working scientists. At a time when U.S. science, technological, and biomedical leadership is under increasing pressure from countries such as Japan and W. Germany, it seems unwise to undermine that leadership even further by supporting a project which is both controversial and bad science policy.

I am not alone in my opposition to this project, as I'm sure you've learned from the many other letters you've received regarding this project. I hope this letter will help stimulate you into taking action to help stop this project. U.S. science and scientists need your help!

Thank you for your time and consideration.

Sincerely,

Patrick N. Shaklee, Ph.D.
Assistant Professor of Biochemistry
University of North Texas and Texas
College of Osteopathic Medicine

PENNSTATE

(814) 865-5497

Department of Molecular & Cell Biology
College of Science

Paul M. Althouse Laboratory
The Pennsylvania State University
University Park, PA 16802

April 13, 1990

William F. Raub, Acting Director
National Institutes of Health
Rm 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub:

I am writing to suggest that you take a strong stand against expanded investment into the Human Genome Project. I have been studying the molecular basis of cancer (oncogene research) for ten years and, like most molecular biologists, have made extensive use of sequencing techniques and sequence information. These projects have involved sequencing of targeted objectives and the benefit/cost ratio has been high. Even so, a relatively small percentage of our effort, time and budget (and similarly for other labs in this research area), has been devoted to sequencing. This is not because there were not other interesting regions to sequence, or because we were limited by technological reason but simply because other experiments were more important. This is the case is most areas of biological research. To take another critical example, while certain DNA sequences are certainly important in AIDS research, the important questions require other biochemical and cell biological approaches for their solution.

In talking with colleagues at national meetings, I find little enthusiasm for the HGP. For the most part, creative scientists are not interested in it. Frankly, I am surprised that the idea has received as much federal support as it has, and shocked at the possibility that, if its budget continues to grow, the HGP will compete with funds for the truly important work that is being done by intelligent individual scientific groups. While there are those who thrive on creating the sort of "big science" empires that the HGP will generate, I suspect that the final benefit/cost ratio of the project will be at least an order of magnitude below that of currently funded NIH research programs.

As you know, biological and medical research is currently in a "golden period" of great opportunity and progress. In a world of unlimited resources, it would be nice to support all feasible approaches. But, in our world of limited resources, grandiose, but essentially scientifically inefficient projects like the HGP can not be tolerated. I have just returned from serving on one of the NIH Study Sections which evaluates the scientific merit of research grant proposals. I was sorry to see that, because of the current "funding crunch", many proposals of much higher merit than the HGP will probably not be funded. The effect of the HGP will be to exacerbate this situation and I suspect that its net effect will be to hinder, not to advance medical research. Please recommend reduction of the HGP budget commensurate with a dramatic narrowing of its focus (e.g., genome mapping, not sequencing).

Sincerely,

David Shalloway

David Shalloway
Associate Professor of
Molecular Biology

#3244

May 8, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, M.D.
20892

Dear Sir,

This letter is intended to voice my opposition to the support of funding for the Human Genome Project (HGP), the massive expenditure of federal funds to be used to determine the base pair seqeunce of human DNA. As a young research scientist already facing a bleak funding situation for research and teaching, the HGP appears as a tremendous waste of funds and a threat to the foundations of basic scientific research. Please find enclosed a detailed analysis of the problems associated with funding of the HGP prepared by Dr. Martin Rechsteiner and which recently appeared in the FASEB Journal. I agree with Dr. Rechsteiner's concerns and strongly urge you to curtail support for the Human Genome Project. Thank you for your consideration.

Sincerely yours,

James R. Lerner PhD.
RESEARCH INSTITUTE OF SCRIPPS CLINIC
10666 N. TORREY PINES RD.
LA JOLLA, CA. 92037

NIH

62 : ON 02 MAY 90

84343

ALBERT EINSTEIN COLLEGE OF MEDICINE
OF YESHIVA UNIVERSITY

1300 MORRIS PARK AVENUE • BRONX, NEW YORK 10461

DEPARTMENT OF CELL BIOLOGY
Phone: (212) 430-2815
FAX #: (212) 823-5877

Jonathan R. Warner, *Chairman*	430-3022
Barbara K. Birshtein	430-2291
Margaret C. Kielian	430-3638
Kenneth S. Krauter	430-3508
Joseph J. Maio	430-3084
Lorraine Marsh	430-2841
Matthew D. Scharff	430-3527
Carl L. Schildkraut	430-2097
Arthur I. Skoultchi	430-2169
Pamela Stanley	430-3346

March 29, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Mr. Raub,

A major reason that America leads the world in biotechnology and medical science is that the government has had a policy of funding good projects in extremely diverse subject areas. This policy has allowed small laboratories typically comprising a principal investigator (faculty member), technicians (1-2) graduate students (2-3) and post-doctoral fellows (2-3) to flourish, producing work of high quality, that often leads to major advances in a field.

Because of the enormous complexity of biological science, it is critical to foster small groups and diversity since a major leap in understanding can come from any direction at any time and often occurs in the stimulating environment of an intensive group. Unfortunately, the future looks bleak for small group science. At current funding levels, many grants with excellent proposals are not being funded. This is resulting in many people who are already trained (i.e. a major investment of the government) leaving research. Perhaps, more importantly, the current funding situation is terrifying to new graduates, who are therefore not embarking on research careers. (I am currently training a Chinese graduate student and two Indian post-doctoral fellows - no Americans. It is typical that many science trainees in laboratories at this major American medical school are foreign nationals). The situation will only get worse if funding of the human genome project is approved.

The idea of blindly sequencing all the DNA in the genome is intellectually bankrupt and also useless as a training exercise for creative science. This would not be a

major problem if it were to be privately funded. However it is proposed to divert major funds ($200 million dollars per year, equal to ~ 1000 new grants equal to ~ 8000 brains working on NEW problems) into this technological exercise. Surely Americans (and especially politicians) have realised that their strength and leadership derives from diversity. The sequencing of the human genome is a good project for the Japanese - let them do it. They have the resources and the technological capabilities. Let American scientists use their resources more wisely - by sequencing mapped regions of the human genome associated with disease states and by funding creative, innovative research in a wide variety of areas. Please do everything in your power to stop funding of the human genome project so American science can continue to lead the world in major medical advances.

Yours sincerely,

Pamela Stanley

Pamela Stanley, Ph.D.
Professor of Cell Biology

PS/rl

UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL
Department of Molecular Genetics and Microbiology
55 Lake Avenue, North, Worcester, MA 01655 (508) 856-2292

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, Maryland 20892

March 17, 1990

Dear Mr. Raub:

I am writing to tell you what a bad Idea I think the human genome project is. In a period of severe budget restraint at the National Institutes of Health, it is foolish to invest three billion dollars (or more) to sequence the entire human genome. Most of the genome (about 95%) doesn't encode proteins and is junk as far as we can tell. Sequencing the genome is not an efficient way to understand human disease. As examples, understanding the genes involved in cancer and cholesterol metabolism was achieved without the human genome project. The two successes of the DNA mapping approach, discovery of the genes responsible of cystic fibrosis and muscular dystrophy, did not require detailed sequence information. It would be better to target diseases using a better human genetic map than to sequence tremendous amounts of DNA hoping to recognize a medically important locus.

A much better use of this money would be to increase the number of RO1 grants. One thousand RO1's could be funded from the 200 million dollars per year that is targeted for this project. The best science is funded by RO1 grants because they are subjected to a critical review by peers on the basis of scientific merit, and areas the government wants targeted do receive more money. The human genome project involves doing drudgery type of science and thus will require the hiring of many technicians, because students and postdocs will not want to do it. Students and post-docs want to do interesting work, where a question is being asked. RO1's support

graduate students and postdoctoral fellows, who will become the scientists of the future. Because it is so difficult to get grants many young people do not want to enter science. The future of U.S. biomedical research depends upon vigorous training programs and thus it is bad science policy to fund large numbers of technicians rather than university laboratories. I do not know any scientists who think the human genome project is a good idea. (In fact, we know that if we can get ourselves named a Center for anything, money is easy even if the science isn't too good! However, it often takes politicking, which is abhorent to some of us and others of us feel we don't have the time or means to succeed at it.)

In short, the human genome project is a waste of national resources and is detrimental to the training of young scientists.

Yours truly,

Janet Stavnezer

Janet Stavnezer, Ph.D.
Associate Professor

UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL
Department of Molecular Genetics and Microbiology
55 Lake Avenue, North, Worcester, MA 01655 (508) 856-2292

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, Maryland 20892

March 17, 1990

Dear Mr. Raub:

I am writing to tell you what a bad Idea I think the human genome project is. In a period of severe budget restraint at the National Institutes of Health, it is foolish to invest three billion dollars (or more) to sequence the entire human genome. Most of the genome (about 95%) doesn't encode proteins and is junk as far as we can tell. Sequencing the genome is not an efficient way to understand human disease. As examples, understanding the genes involved in cancer and cholesterol metabolism was achieved without the human genome project. The two successes of the DNA mapping approach, discovery of the genes responsible of cystic fibrosis and muscular dystrophy, did not require detailed sequence information. It would be better to target diseases using a better human genetic map than to sequence tremendous amounts of DNA hoping to recognize a medically important locus.

A much better use of this money would be to increase the number of RO1 grants. One thousand RO1's could be funded from the 200 million dollars per year that is targeted for this project. The best science is funded by RO1 grants because they are subjected to a critical review by peers on the basis of scientific merit, and areas the government wants targeted do receive more money. The human genome project involves doing drudgery type of science and thus will require the hiring of many technicians, because students and postdocs will not want to do it. Students and post-docs want to do interesting work, where a question is being asked. RO1's support

graduate students and postdoctoral fellows, who will become the scientists of the future. Because it is so difficult to get grants many young people do not want to enter science. The future of U.S. biomedical research depends upon vigorous training programs and thus it is bad science policy to fund large numbers of technicians rather than university laboratories. I do not know any scientists who think the human genome project is a good idea. (In fact, we know that if we can get ourselves named a Center for anything, money is easy even if the science isn't too good! However, it often takes politicking, which is abhorent to some of us and others of us feel we don't have the time or means to succeed at it.)

In short, the human genome project is a waste of national resources and is detrimental to the training of young scientists.

Yours truly,

Janet Stavnezer

Janet Stavnezer, Ph.D.
Associate Professor

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD. 20892.

1406 Grady Avenue
Charlottesville
VA 22903

6 March 1990.

Dear Dr. Raub:

It is my belief that the "Human Genome Project", predicted to cost at least $200 million per year, is an inappropriate use of scientific research funds.

As a nation, we need to maintain a steady supply of scientists. Currently money for training post doctoral fellows is very hard to obtain and, when these fellows have achieved a faculty position it is even harder for them to obtain research funds. I think that the $200 million would be better spent in maintaining a diverse supply of talent rather than putting all our eggs in one basket. Especially as, in the last few years, the molecular biologists have discovered that they need scientists from other disciplines to help them characterize and test their products.

As a tax payer and a scientist I am against spending $200 million on the "Human Genome Project" at this time.

Yours sincerely

Frances A. Stephenson

Research Associate in
Physical Biochemistry

Dartmouth Medical School HANOVER • NEW HAMPSHIRE • 03756

Department of Biochemistry • TEL. (603) 646-7616

March 23, 1990

Dr. William F. Raub
Acting Director, National Institutes of Health
Room 126, Building 1, 9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub,

I am writing to express my strong objection to the proposal to sequence the human genome. This is mediocre science, bad science policy, and in the current fiscal climate, extremely damaging to the strength of biomedical research in this country.

The human genome sequencing is mediocre science in the sense that it is unlikely to yield new and significant information relevant to major human diseases, at least at any level compatible with the extremely high cost of the project. It is also mediocre science in that it is pedantic, a completely inadequate format in which to train new, young science investigators and is not an approach likely to elucidate fundamental understandings of human genetics.

It is poor science policy in that the proposals to sequence the human genome have originated not from an informed national debate among the scientific community, but rather as a political back room activity, advanced by a small group of scientists who have a clear vested interest in the project. I would strongly encourage you to support an open dialogue among informed scientists at national scientific meetings, such as the American Society of Biological Chemists, the Cell Biology meetings, the Biophysical Society meetings, the American Chemical Society meetings, and the Genetics Society meetings, in order that you and individuals in a position to make such policy decisions should hear the opinions of the scientific community regarding the value of this extremely expensive undertaking. To date, no such dialogue has taken place, and this is in large part responsible for the very poor decision-making surrounding this project that has taken place to date.

That the human genome sequencing project is extremely damaging to the strength of biomedical research in this country stems directly from the fact that this multi-billion dollar project is competing for individual research awards (RO1) at the National Institutes of Health, where funding for approved and highly meritorious projects has also been severely curtailed. Although my own research continues to be supported by the NIH, I am extremely distressed to observe that my colleagues, and especially very talented and committed younger scientists, are unable to gain funding for their proposed research projects, even when these projects are receiving very favorable comments from the peer reveiw process. The continued shortfall in funding individual research awards can have nothing but a damaging effect on the strength of biomedical research for the remainder of this century and well into the next. Aside from the loss of new and important information relevant to human diseases, we are propagating a situation where it is impossible to train highly talented young people who are essential to continue the research work so necessary to the health of our nation.

With the above considerations in mind, I urge you strongly to curtail any further funding of the human genome sequencing project, and to move to hear a debate on the merit of this proposal, a debate best held in the format of the national scientific meetings. I would appreciate your response to my comments, and will look forward to hearing from you.

Yours truly,

Bernard L. Trumpower

Bernard L. Trumpower
Professor of Biochemistry

BLT/erj

UNIVERSITY OF MINNESOTA
TWIN CITIES

Department of Therapeutic Radiology-Radiation Oncology
Medical School
Box 494 University of Minnesota Hospital and Clinic
Harvard Street at East River Road
Minneapolis, Minnesota 55455
(612) 626-6700

March 28, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Raub:

Few scientific proposals have been greeted with as much media coverage as the Human Genome Project. Although I consider the effort noble, I feel that the Human Genome Project (HGP) is not a sound scientific undertaking. Moreover, in a period of severe budget restraint at the National Institutes of Health, it is foolish to invest $3 billion to sequence the entire genome. Our dollars would be more wisely spent on cancer and AIDS research for the following reasons. 1) We were told that the resulting information will have great impact on major human diseases. Although this could be true, significant advances in heart disease and cancer were made independent of HGP. Most oncogenes have revealed themselves by their dominant effects, not by sequence analysis of human genomes. 2) Knowing a map location or amino acid sequence of a mutant gene product does not insure the development of rational therapies. 3) The HGP is a costly, wasteful, and inappropriate allocation of research funds. The three billion dollar total assumes no delays or no cost overruns, but already there have been delays on the project. 4) The HGP will provide little useful training and no intellectual stimulation to young scientists. This could be the most tragic of the consequences of funding. Spending $3 billion at a time when our country is falling further and further behind in the quality of its science is foolish. The educational value of this project is nearly nihil. 5) Finally, 95% of DNA does not code for proteins and is thought by many, including some of the advocates of the HGP, to be junk.

Please curtail this tremendous waste of scientific resources at a time when research dollars could be put to better use.

Sincerely,

Daniel A. Vallera, Ph.D.
Professor and Director
Section on Experimental Cancer Immunology
Department of Therapeutic Radiology

DAV/kej

May 8, 1990

William F. Raub
Acting Director
National Institutes of Health
Room 126, Building 1
9000 Rockville Pike
Bethesda, M.D.
20892

Dear Sir,

This letter is intended to voice my opposition to the support of funding for the Human Genome Project (HGP), the massive expenditure of federal funds to be used to determine the base pair seqeunce of human DNA. As a young research scientist already facing a bleak funding situation for research and teaching, the HGP appears as a tremendous waste of funds and a threat to the foundations of basic scientific research. Please find enclosed a detailed analysis of the problems associated with funding of the HGP prepared by Dr. Martin Rechsteiner and which recently appeared in the FASEB Journal. I agree with Dr. Rechsteiner's concerns and strongly urge you to curtail support for the Human Genome Project. Thank you for your consideration.

Sincerely yours,

Joanne M. Weskendorf, PhD.

84/17