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August 7, 1989

Elke Jordan
Human Genome Office
NIH
Bldg. 1, Room 201
Bethesda, MD 20892

Re: GENOMICS PN 480

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The Human Genome Program at the National Institutes of Health

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The Human Genome Program at the National Institutes of Health

JAMES D. WATSON AND ELKE JORDAN

National Center for Human Genome Research, National Institutes of Health, Bethesda, Maryland 20892

The Human Genome Initiative is a bold international effort to characterize all the genetic material in the human body. Goals of the project include mapping the 50,000 to 100,000 human genes, resulting in both genetic linkage and physical maps of the chromosomes; determining the nucleotide sequence of human DNA; and making this information available to the scientific community for research and medical applications. The National Institutes of Health (NIH), which has a long history of supporting research in genetics and molecular biology as an integral part of its mission to improve the health of the people of the United States, will play a major role in this vast undertaking. We here describe briefly the history of the genome program at NIH and the agency's plan to achieve the goals of the initiative.

During considerable discussion in 1986–1987 about the prospects of mapping and sequencing human DNA, the scientific community reached a consensus about the merit of the program, although there was concern that such a large-scale project might be funded at the expense of other important research programs. NIH participated in these discussions, and in October 1987, with the appropriation of funds earmarked for genome-related research, the NIH Human Genome Program was launched.

From the outset, NIH decided that any program of research on the human genome must be centrally coordinated. In February 1988, the Director of NIH convened the Ad Hoc Program Advisory Committee on the Human Genome, under the chairmanship of David Baltimore, to advise NIH on organizing its genome research activities. At that meeting, the panel developed a preliminary plan for the research and early cost estimates of the program. The Director also announced his intention to set up a central office at NIH to oversee the planning and conduct of NIH-supported genome research and to coordinate NIH's activities with those of other agencies, both domestic and international. The committee recommended that an eminent scientist be recruited to head the NIH program and a permanent advisory committee be established.

With regard to the science itself, the Ad Hoc Committee recommended that the NIH program proceed in phases. The initial efforts would concentrate on genetic linkage mapping; this would be expanded to include detailed physical mapping and, ultimately, determining the complete nucleotide sequence. At the same time, the committee recognized that, despite major technological advances in recent decades that have enabled science to progress to the point at which the genome project could even be considered, a considerable amount of technology must still be developed if scientists are to realize the goals of the Human Genome Initiative. These recommendations were similar to the conclusions arrived at in separate reports by the National Research Council of the National Academy of Sciences and the Office of Technology Assessment of the United States Congress.

Following the NIH Ad Hoc Committee's recommendations, the Office of Human Genome Research was formally established in October 1988. Its function is to plan, coordinate, and integrate research efforts, in collaboration with other agencies, industry, academia, and international efforts, and to provide for progress review of genomic analysis research. James Watson was appointed NIH Associate Director for Human Genome Research, in a part-time capacity, and Elke Jordan was appointed Director of the Office of Human Genome Research, with the responsibility of day-to-day administrative operation of the program. To provide ongoing advice from scientific experts, NIH also established a permanent Program Advisory Committee on the Human Genome. (A list of the members of the committee is given in Table 1.)

At its first two meetings, in January and June 1989, the Advisory Committee laid the ground for a detailed plan for the NIH genome program. The committee endorsed earlier recommendations that the NIH program be comprehensive. In addition to supporting efforts aimed at compilation of genetic linkage and physical maps of the human chromosomes, the sequencing of human DNA, and the development of the necessary technology, the NIH Human Genome Program will support mapping and sequencing of the DNA of important model organisms. Past experience has shown that information derived from studies of the biology of model systems is critical to understanding and interpreting human biology, and NIH believes that this will be equally true with respect to the human genome project.

At the January meeting, the committee concluded that certain aspects of the program needed thorough and immediate consideration. As a result, several working groups (composed of both committee members and outside experts) were set up to address these issues. One group considered training needs, to ensure that enough scientists with the necessary expertise are available to carry out genome-related research. A proposal for a new program of training grants and fellowships in genomics research was approved by the Advisory Committee in June.

A second working group is weighing important ethical, legal, and social issues that may arise from the sensitive information about ourselves that we can expect to learn from the genome project. Because the public has raised many such concerns about the possible applications of knowledge derived from the genome project, the committee urged NIH to fund studies of these issues along with the scientific research efforts. (A program announcement to solicit grant applications involving studies of ethical, legal, and social issues was published in the March 1989 edition of the "NIH Guide for Grants and Contracts.")

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TABLE 1

Program Advisory Committee on the Human Genome

Chairman, Norton Zinder, Ph.D.
Rockefeller University

Members

Bruce Alberts, Ph.D.
University of California, San Francisco

David Botstein, Ph.D.
Genentech, Inc.

Jaime G. Carbonell, Ph.D.
Carnegie-Mellon University

Joseph L. Goldstein, M.D.
University of Texas Southwestern Medical Center

Leroy E. Hood, Ph.D., M.D.
California Institute of Technology

Victor A. McKusick, M.D.
Johns Hopkins Hospital

Maynard V. Olson, Ph.D.
Washington University School of Medicine

Mark L. Pearson, Ph.D.
E. I. du Pont de Nemours and Company

Cecil B. Pickett, Ph.D.
Merck Frosst Centre for Therapeutic Research

Phillip A. Sharp, Ph.D.
Massachusetts Institute of Technology

Nancy C. Wexler, Ph.D.
College of Physicians and Surgeons

Liaison members

George F. Cahill, Jr., M.D.
Howard Hughes Medical Institute

C. Thomas Caskey, M.D., F.A.C.P.
Member, National Advisory General Medical Sciences Council
Baylor College of Medicine

Mary E. Clutter, Ph.D.
National Science Foundation

Robert M. Faust, Ph.D.
U.S. Department of Agriculture

Benjamin J. Barnhart, D.Sc.
U.S. Department of Energy

A third working group considered the need for research centers in the human genome program. Many of the research projects envisioned as part of the program can best be addressed by teams of investigators from many disciplines working cooperatively. For the research program to proceed efficiently, a sharing of resources will be necessary, both for actual investigation and to facilitate the collection, interpretation, and sharing of resulting information. This working group has developed guidelines for a center grant program, which were endorsed by the full committee at its June meeting.

Finally, a critical aspect of mapping and sequencing efforts will be the design of appropriate databases to handle the storage, data processing and analysis, and distribution of genome-related research information. Such databases must be comprehensive, up-to-date, and easily accessible to those who need the information. Although prototype databases exist for some kinds of data (e.g., GenBank), these were not designed with a view of the magnitude of demands now envisioned in relation to the human genome project. Thus, a working group on databases was set up to study this issue and to devise a plan for accommodating the database needs of the project. This working group will coordinate its activities with comparable database committees set up by other entities, such as the Department of Energy and the European Community. It is critical that databases be international in scope and compatible.

In its database development efforts, NIH is fortunate to be able to collaborate with the newly established Center for Biotechnology Information at the National Library of Medicine. The NCBI was set up to pursue research in information handling, particularly with respect to human molecular biology. Among the issues the Center will address initially is the development of improved formats for biological databases; one goal, for example, is the linking of various systems so that users can access them more conveniently and readily than is now possible.

Turning to the budget of the NIH Human Genome Program, the initial appropriation to NIH for genome research was $17.2 million for Fiscal Year 1988. The current fiscal year (1989) appropriation is $27.6 million. These funds, which were incorporated into the budget of the National Institute of General Medical Services, have been used almost exclusively to fund individual investigator-initiated research projects. (All grants and contracts funded as part of the genome program are approved in accordance with traditional peer review procedures.)

With the start of Fiscal Year 1990, the Office of Human Genome Research will become the National Center for Human Genome Research with an expanded staff and responsibility for awarding its own grants and contracts. A sizable increase in the budget for the NIH Human Genome Program is anticipated for Fiscal Year 1990. With this, the program will be able to enter a new phase and expand into other areas such as center grants, training grants, and contracts, while maintaining a solid core of investigator-initiated research.

While the NIH program is substantial, it certainly is not adequate to accomplish all the goals of the Human Genome Initiative. Furthermore, because the information from the program will be of very broad interest and applicability, it is essential that other agencies and organizations—representing different interests and approaches—be involved in funding and carrying out the human genome program. Cooperation and coordination between NIH and other groups involved in the Human Genome Initiative are essential.

Because the Department of Energy also has a major research interest in the Human Genome Initiative, NIH has established a formal Memorandum of Understanding regarding interaction between the two agencies. In addition to providing for regular joint meetings, the Memorandum calls

for creation of a joint advisory committee. To this end, a subcommittee of the NIH Program Advisory Committee on the Human Genome will meet several times a year with a subcommittee of DOE's Health and Environmental Research Advisory Committee. At the June meeting of the NIH Advisory Committee, it was agreed that the first task of this joint committee will be to draft an updated comprehensive plan for the genome project by the end of this year suitable for use by both agencies. This plan will be submitted to the advisory committees of both agencies for ratification.

NIH also is in frequent communication with other federal agencies and with the Howard Hughes Medical Institute, as well as with groups in Europe and Japan. To facilitate international coordination, NIH will be working closely with the Human Genome Organization (HUGO), a group of scientists from around the world who are interested in the genome initiative. They have organized with the express purpose of helping to make the Human Genome Initiative truly international in scope and ensuring that the data produced by the project are freely accessible to all who need them.

Clearly, the National Center for Human Genome Research at NIH has a challenging future. The tremendous resource of information, materials, and technology that will be produced by the genome program promises to revolutionize human biology and medicine by opening the way toward research and clinical possibilities hitherto unimaginable. The opportunity to develop a truly international program for the benefit of mankind is enormously exciting.

GENOMICS

International Journal of Gene Mapping and Nucleotide Sequencing
Emphasizing Analyses of the Human and Other Complex Genomes

July 24, 1989

Dr. Elke Jordan
Human Genome Office
NIH
Bldg. 1, Room 201
Bethesda MD 20892
USA

Re: Manuscript No. C128

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Authors: James D. Watson and ELKE JORDAN

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chemical shifts	chemical shifts, ^{14}N in cobalt(III) complexes

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Author(s) James D. Watson and ELKE JORDAN

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The Human Genome Program
at the National Institutes of Health

by James D. Watson and Elke Jordan

The Human Genome Initiative is a bold international effort to characterize all the genetic material in the human body. Goals of the project include mapping the 50,000 to 100,000 genes, resulting in both genetic linkage and physical maps of the chromosomes; determining the nucleotide sequence of all the base pairs of DNA; and making this information available to the scientific community for research and medical applications. The National Institutes of Health (NIH), which has a long history of supporting research in genetics and molecular biology as an integral part of its mission to improve the health of the people of the United States, will play a major role in this vast undertaking. In this paper we describe briefly the history of the genome program at NIH and the agency's plan to achieve the goals of the initiative.

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be addressed by teams of investigators from many disciplines working cooperatively. For the research program to proceed efficiently, a sharing of resources will be necessary, both for actual investigation and to facilitate the collection, interpretation and sharing of resulting information. The working group ~~is considering how such teams of investigators might be supported~~ has developed guidelines for a center grant program, which were endorsed by the full Committee at its June meeting.

Finally, a critical aspect of mapping and sequencing efforts will be the design of appropriate databases to handle the storage, data processing and analysis, and distribution of genome-related research information. Such databases must be comprehensive, up-to-date and easily accessible to all who need the information. Although prototype databases exist for some kinds of data that will be generated (e.g., Genbank), these were not designed with a view of the magnitude of demands now envisioned in relation to the human genome project. Thus, a working group on databases was set up to study this issue and to devise a plan for accommodating the database needs of the project. This working group will coordinate its activities with database committees set up by other entities, such as the Department of Energy and the European ~~Economic~~ Community. It is critical that databases be international in scope and compatibility.

In its database development efforts, NIH is fortunate to be able to collaborate with the newly established Center for Biotechnology Information at the National Library of

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The President's budget for Fiscal Year 1990 requests $100 million for the NIH Human Genome Program. With a sizable increase in the budget anticipated for next year, the program will be able to enter a new phase and expand into other areas such as center grants, training grants and contracts, while maintaining a solid core of investigator-initiated research. (All grants and contracts funded as part of the genome program are approved in accordance with traditional peer review procedures.)

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Because the Department of Energy also has a major research interest in the Human Genome Initiative, NIH has established a formal Memorandum of Understanding regarding interaction between the two agencies. Besides providing for regular joint meetings, the memorandum calls for creation of a joint advisory committee. To this end, a subcommittee of the NIH Program Advisory Committee on the Human Genome will meet several times a year with a subcommittee of DOE's Health and Environmantal Research Advisory Committee. ~~This joint committee will give particular attention to overlapping areas of interest.~~ At the June meeting of the NIH Advisory Committee it was agreed that the first task of this joint committee will be to draft an updated comprehensive plan for the genome project by the end of this year; suitable for use by both agencies. This plan will be submitted to the Advisory Committees of both agencies for ratification.

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Clearly, the National Center for ~~Office of~~ Human Genome Research at NIH has a challenging future. The tremendous resource of information, materials and technology that will be produced by the genome program promises to revolutionize human biology and medicine by opening the way toward research and clinical possibilities hitherto unimaginable. The opportunity to develop a truly international program for the benefit of mankind is enormously exciting.

PROGRAM ADVISORY COMMITTEE ON THE HUMAN GENOME

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Rockefeller University

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University of California, San Francisco

David Botstein, Ph.D.
Genentech, Inc.

Jaime G. Carbonell, Ph.D.
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Mary E. Clutter, Ph.D.
National Science Foundation

Robert M. Faust, Ph.D.
U.S. Department of Agriculture

David A. Smith, Ph.D.
U.S. Department of Energy

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Title: The human genome program at the National Institutes of Health

Pages: 10 Tables: 0 Figures: 0

Type of Article: Special Feature - Program description

The manuscript will be considered by our Editorial Board. Information concerning publication of this article will be sent as soon as possible.

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Editorial Office

Shannon
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May 19, 1989

Genomics
Editorial Office
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San Diego, California 92101

Dear Editor:

The enclosed manuscript is submitted in response to a request from Dr. Robert Mullan Cook-Deegan. A copy of the letter from Dr. Cook-Deegan is attached for your information. Please let me know if anything further is needed.

Sincerely yours,

Elke Jordan, Ph.D.
Director
Office of Human Genome Research

2 Enclosures

5/4/89

The Human Genome Program
at the National Institutes of Health

by James D. Watson and Elke Jordan

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and in October 1987, with the appropriation of funds earmarked for genome-related research, the NIH Human Genome Program was launched.

From the outset, NIH decided that any program of research on the human genome must be centrally coordinated. In February 1988, the director of NIH convened the Ad Hoc Program Advisory Committee on the Human Genome, under the chairmanship of David Baltimore, to advise NIH on organizing its genome research activities. At that meeting, the panel developed a preliminary plan for the research and early cost estimates of the program. The director also announced his intention to set up a central office at NIH to oversee the planning and conduct of NIH-supported genome research and to coordinate NIH's activities with those of other agencies, both domestic and international. The committee recommended that an eminent scientist be recruited to head the NIH program and a permanent advisory committee be established.

With regard to the science itself, the ad hoc committee recommended that the NIH program proceed in phases. The initial efforts would concentrate on genetic linkage mapping; this would be expanded to include detailed physical mapping and, ultimately, determining the nucleotide sequence. At the same time, the committee recognized that, in spite of major technological advances in recent decades that have enabled science to progress to the point at which the genome project could even be considered, a considerable amount of technology must still be developed if scientists

are to realize the goals of the Human Genome Initiative. These recommendations were similar to the conclusions arrived at in separate reports by the National Research Council of the National Academy of Sciences and the Office of Technology Assessment of the United States Congress.

Following the NIH ad hoc committee's recommendations, the Office of Human Genome Research was formally established in October 1988. Its function is to plan, coordinate and integrate research efforts, in collaboration with other agencies, industry, academia and international efforts, and to provide for progress review and genomic analysis research. James Watson was appointed NIH associate director for human genome research, in a part-time capacity, and Elke Jordan was appointed director of the Office of Human Genome Research, with the responsibility of day-to-day administrative operation of the program. To provide ongoing advice from scientific experts, NIH also established a permanent Program Advisory Committee on the Human Genome. (A list of the members of the committee follows.)

At its first meeting, in January 1989, the advisory committee laid the ground for a detailed plan for the genome program. The committee endorsed earlier recommendations that the NIH program be comprehensive. Besides supporting efforts aimed at compilation of genetic linkage and physical maps of the human chromosomes, the sequencing of human DNA and the development of the necessary technology, the NIH Human Genome Program will support mapping and sequencing of

important model organisms. Past experience has shown that information derived from studies of the biology of model systems is a critical key in understanding and interpreting human biology, and NIH believes this will be equally true with respect to the human genome project.

At the January meeting, the committee concluded that certain aspects of the program needed thorough and immediate consideration. As a result, several working groups (composed of both committee members and outside experts) were set up to address these issues. One group will consider training needs, to ensure that enough scientists with the necessary expertise are available to carry out genome-related research.

A second working group will weigh important ethical, legal and social issues that may arise from the sensitive information about ourselves that we can expect to learn from the genome project. Because the public has raised many such concerns about the possible applications of knowledge derived from the genome project, the committee urged NIH to fund studies of these issues along with the scientific research efforts. (A program announcement to solicit grant applications involving studies of ethical, legal and social issues was published in the March 1989 edition of the "NIH Guide for Grants and Contracts.")

A third working group will consider the need for research centers in the human genome program. Many of the research projects envisioned as part of the program can best

be addressed by teams of investigators from many disciplines working cooperatively. For the research program to proceed efficiently, a sharing of resources will be necessary, both for actual investigation and to facilitate the collection, interpretation and sharing of resulting information. The working group is considering how such teams of investigators might be supported.

Finally, a critical aspect of mapping and sequencing efforts will be the design of appropriate databases to handle the storage, data processing and analysis, and distribution of genome-related research information. Such databases must be comprehensive, up-to-date and easily accessible to all who need the information. Although prototype databases exist for some kinds of data that will be generated (e.g., Genbank), these were not designed with a view of the magnitude of demands now envisioned in relation to the human genome project. Thus, a working group on databases was set up to study this issue and to devise a plan for accommodating the database needs of the project. This working group will coordinate its activities with database committees set up by other entities, such as the Department of Energy and the European Economic Community. It is critical that databases be international in scope and compatibility.

In its database development efforts, NIH is fortunate to be able to collaborate with the newly established Center for Biotechnology Information at the National Library of

Medicine. The NCBI was set up to pursue research in information handling, particularly with respect to human molecular biology. Among the issues the center will address initially is the development of improved formats for biological databases; one goal, for example, is the linking of various systems so that users can access them more conveniently and readily than is now possible.

Turning to the budget of the NIH Human Genome Program, the initial appropriation to NIH for genome research was $17.2 million for Fiscal Year 1988. The current fiscal year (1989) appropriation is $27.6 million. These funds, which were incorporated into the budget of the National Institute of General Medical Services, have been used almost exclusively to fund individual investigator-initiated research projects.

The President's budget for Fiscal Year 1990 requests $100 million for the NIH Human Genome Program. With a sizable increase in the budget anticipated for next year, the program will be able to enter a new phase and expand into other areas such as center grants, training grants and contracts, while maintaining a solid core of investigator-initiated research. (All grants and contracts funded as part of the genome program are approved in accordance with traditional peer review procedures.)

While the NIH program is substantial, it certainly is not adequate to accomplish all the goals of the Human Genome Initiative. Furthermore, because the information from the

program will be of very broad interest and applicability, it is essential that other agencies and organizations--representing different interests and approaches--be involved in funding and carrying out the human genome program. NIH cooperation and coordination with other groups involved in the Human Genome Initiative is essential.

Because the Department of Energy also has a major research interest in the Human Genome Initiative, NIH has established a formal Memorandum of Understanding regarding interaction between the two agencies. Besides providing for regular joint meetings, the memorandum calls for creation of a joint advisory committee. To this end, a subcommittee of the NIH Program Advisory Committee on the Human Genome will meet several times a year with a subcommittee of DOE's Health and Environmantal Research Advisory Committee. This joint committee will give particular attention to overlapping areas of interest.

NIH also is in frequent communication with other federal agencies and with the Howard Hughes Medical Institute, as well as with groups in Europe and Japan. To facilitate international coordination, NIH will be working closely with the Human Genome Organization (HUGO), a group of scientists from around the world who are interested in the genome initiative. They have organized with the express purpose of helping to make the Human Genome Initiative truly international in scope and ensuring that the data produced by the project are freely accessible to all who need them.

Clearly, the Office of Human Genome Research at NIH has a challenging future. The tremendous resource of information, materials and technology that will be produced by the genome program promises to revolutionize human biology and medicine by opening the way toward research and clinical possibilities hitherto unimaginable. The opportunity to develop a truly international program for the benefit of mankind is enormously exciting.

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Robert Mullan Cook-Deegan, M.D.
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10 March 1989

Elke Jordan, Ph.D.
Deputy Director
Human Genome Office
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Building 1, Room 201
Bethesda, MD 20892
496-0844; FAX 496-4843

Dear Elke,

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I have included a copy of the instructions for authors. Please send the manuscript to the Genomics editorial office by June 1 if at all possible. This is a month earlier than I said in our phone conversation, and for this I apologise. I talked to you before speaking with the Academic Press folks, who explained the editorial process. July 1 is the date for the final copy, not initial receipt of the manuscript. If you cannot make the 1 June deadline, please let me know soon, and I can move your paper into a later issue and find another author for the premier issue.

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Thank you so much for fitting this into your schedule.

Sincerely,

Robert Mullan Cook-Deegan, M.D.
Special Sections Editor, Genomics

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cc: Victor McKusick
Evelyn Sasmor

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Robert Mullan Cook-Deegan, M.D.
7717 Goodfellow Way
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10 March 1989

Elke Jordan, Ph.D.
Deputy Director
Human Genome Office
National Institutes of Health
Building 1, Room 201
Bethesda, MD 20892
496-0844; FAX 496-4843

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1. MESSING, J. (1983). New M13 vectors for cloning. *In* "Methods in Enzymology" (R. Wu, L. Grossman, and K. Moldave, Eds.), Vol. 101, pp. 10–89. Academic Press, New York.
2. RAY, A., CHEAH, K-C., AND SKURRAY, R. (1986). An F-derived conjugative cosmid: Analysis of *tra* polypeptides in cosmid-infected cells. *Plasmid* **16:** 90–100.
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Short Communications. This section is open to succinct reports of important findings. They should not exceed six double-spaced typewritten pages including tables and illustrations. Do not use any section headings except Acknowledgments and References. All short communications must have abstracts. Illustrative material should be kept to a minimum (usually not more than two tables and figures). References should be in the same style as for full-length papers. This section does not provide an accelerated means of publication, but is designed to offer the opportunity to present in brief form noteworthy results of works in progress, confirming reports, and essential descriptions of original data submitted for peer review and archiving by the genetic databases.

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