THE CANCER LETTER INTERACTIVE

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President To Propose 2 Percent Increase In NIH Budget, Slowing Funding Growth

If the Clinton Administration prevails, the bridge that would carry biomedical research into the 21st century will be a rickety structure.

Sources said the budget proposal for fiscal year 2000 is expected to propose an increase of a little more than 2 percent for NIH, one of the lowest increases in recent memory.

Coming at the heels of several years of budgetary growth that

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In Brief:

BMS Chemistry Awards To Honor Fu, Wood; Grochow Joins NCI; Bowman Moves To TJU

GREGORY FU, the Firmenich associate professor of chemistry at Massachusetts Institute of Technology, and **John Wood**, professor of chemistry at Yale University, will receive the first Unrestricted Grants in Synthetic Organic Chemistry from Bristol-Myers Squibb Co. BMS said it plans to commit nearly $1 million annually to leading academic institutions and researchers through unrestricted grants and graduate fellowships in synthetic organic chemistry. . . . **LOUISE GROCHOW** was named chief of the Investigational Drug Branch in the NCI Cancer Therapy Evaluation Program. Grochow was associate professor of medicine at Johns Hopkins University School of Medicine, where she also served as laboratory director of the Pharmacology Analytic Core in the Oncology Center and associate director of the General Clinical Research Center. Grochow replaces Mario Sznol, who served as acting branch chief. . . . **BRUCE BOWMAN** was appointed director of the new Division of Medical Oncology and Medical Genetics in the Department of Medicine at Jefferson Medical College, Thomas Jefferson University, Philadelphia. He is also the first to hold the Robert L. Capizzi Professorship of Medicine at the medical college. Bowman was with Creighton University and the University of Nebraska Medical Center in Omaha, where he was director for Cancer Research and Hereditary Tumors at the Storz Cancer Institute. . . . **BRIAN SAUER** was appointed to head the new Developmental Biology Research Program at Oklahoma Medical Research Foundation. Sauer was senior staff fellow in the Biochemistry and Metabolism Laboratory of the National Institute of Diabetes, Digestive, and Kidney Disease. . . . **LEE BROWN** has joined the Leukemia Society of America as executive director of the Illinois Chapter, based in Chicago. Brown was vice president of development at the American Cancer Society Illinois Division.

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President Likely To Propose 2 Percent Increase For NIH

(Continued from page 1)

culminated in a spectacular 15 percent jump for NIH in the current fiscal year, the FY 2000 budget would leave the institutes scrambling for funds to cover their expanding multi-year commitments.

The President's budget proposal is scheduled to be made public Feb. 1.

Modest as it sounds, the expected increase is more than twice as high as the original figures proposed by the Office of Management and Budget, sources said. The original OMB proposal completed late last fall provided about a 0.8 percent increase for NIH.

After the first set of numbers is presented to the agencies, agency heads have the opportunity to appeal these numbers to OMB and the White House. Sources said the NIH funding was pushed above 2 percent after HHS Secretary Donna Shalala appealed to the White House to increase the NIH number.

The modest increase is consistent with the Administration's long-term plan to increase the NIH budget by 65 percent by the year 2003. That plan, proposed by the Administration last year, would have given NIH an 8.5 percent increase during the current year (**The Cancer Letter**, Feb. 6, 1998).

However, Congress last year was more generous than the Administration, giving NIH a 15-percent increase (**TheCancer Letter**, Oct. 23, 1998).

In effect, by proposing a nearly flat budget for FY 2000, OMB asserts that the government's biomedical research efforts received their year 2000 increase in fiscal 1999.

The Problem of Multi-Year Commitments

Be that as it may, the sudden halt in growth is likely to reverberate throughout biomedical research. During the period of expansion, NIH has been making multi-year commitments, particularly commitments to expand investigator-initiated research grants.

The research project grant pyramid at NCI has been expanding for several years. In FY 1998, NCI awarded 1,047 new grants for a total of $300 million and funded another $865 million worth of continuing grants. In the current fiscal year, the Institute plans to award 1,225 new grants worth $365 million, and put another $940 million into existing grants.

The weight of these obligations is great even at the time of rapidly expanding budgets. If the rate of budgetary increases drops suddenly, the grant payline would slip, and old obligations would force out new initiatives, officials said.

Last November, before the OMB target numbers came out, NCI Director Richard Klausner described the Institute's vulnerability to the Board of Scientific Advisors. "We certainly hope that we will continue to enjoy large increases, but we don't know for sure," Klausner said at the Nov. 12-13 meeting of the BSA.

"If we get something like a seven-and-a-half-percent increase next year—which we would have been very happy with—I don't know if we will be able to maintain the payline. We will not be able to do any new initiatives."

At the meeting, Klausner said NCI is trying to limit its out-year commitments in fiscal 1999, and is developing a series of one-year funding initiatives.

"What we will be doing this year, because of available funds, plus my concern about the uncertainty of exactly how long this rate of increase will be continued, will be to present a series of what I think you will find are very interesting one-shot funding initiatives," Klausner said.

Klausner said the initiatives could be issued as supplemental funds for grant awards (**The Cancer Letter**, Nov. 20, 1998).

Ironically, as members of the Administration, Klausner, along with NIH Director Harold Varmus and other institute directors, will be obligated to

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defend the President's budget proposal that is certain to cause great hardships for their grantees and their institutions.

Even before the appropriations process began in earnest, NIH has emerged as a likely target for Capitol Hill criticism over its ability to spend the 1999 budget wisely.

At this time, the issue of "absorption" of funds by NIH has been raised by Sen. Pete Dominici (R-NM), chairman of the Budget Committee.

Last month, NIH officials met with the staff of the Senate Appropriations Committee to discuss the institutes' financial needs and ability to spend money prudently, sources said.

Under the worst-case scenario for NIH, this perception of vulnerability could lead to Congressional inquiries and investigations that have been noticeably (and, some would say, mercifully) absent in recent years.

Appropriations Dysfunction

As biomedical research slips to a lower level on the President's list of priorities, buildup in defense spending is moving upward on that list. The budget proposal is expected to fund the largest defense buildup since the end of the Cold War. The proposal to boost defense is likely to be well received by the Republican majority on Capitol Hill—and would translate to a lower allocation for domestic spending.

On the other hand, the experience of recent years appears to point to a growing Congressional support for cancer research as well as a deepening dysfunction of the appropriations process, Capitol Hill observers say.

Consider the history of the FY 1999 appropriations bill. Last February, the Administration proposed an 8.5 percent increase for NIH through funds from what was then an expected settlement with the tobacco companies.

For months following the President's proposal, several key players on Capitol Hill repeatedly said they were puzzled by the plan. Before their puzzlement was resolved, the bill was loaded with "killer amendments," and, at the same time, Congress turned its attention to the President's sexual exploits.

Ultimately, when the appropriations deadlock was broken, an omnibus bill gave NIH a 15 percent increase.

If that experience is an indication, the outlook at the outset of the appropriations process could be a poor predictor of the outcome.

Klausner, Nathan Discuss Challenge Of Cancer Research In The "Post-Genome World"

The large scientific projects NCI established over the past three years, in particular, the Cancer Genome Anatomy Project, will provide structures to enable scientists to organize vast amounts of biologic information and act on that information to better understand, classify, prevent, and treat cancer, NCI Director Richard Klausner said.

As scientists complete the description of the human genome over the next several years, having these structures in place will help provide organizational principles for cancer biology in the same way that the periodic table drawn by 19th century Russian chemist Dmitri Mendeleev demonstrated rules that govern matter, Klausner said in a speech last month to the American Society of Hematology annual meeting in Miami.

"NCI must play a role in doing these large-scale scientific experiments to give the community the information and resources it needs to move from the promise of the genome to the reality of a post-genome world," Klausner said in a conference session titled "Clinical and Basic Investigation in the Post-Genome World."

Responding to Klausner's remarks, David Nathan, president of Dana-Farber Cancer Institute, said the NCI director's vision of cancer research in the future posed particular challenges for clinical investigation. Nathan said NIH has responded over the past few years to the need for greater training and resources in clinical research. He said it was now up to academic health centers to make organizational changes that will support and prepare clinical investigators for the future.

The edited text of Klausner's speech follows:

Certainly over the last 150 years, science or our conceptualization of science seems to always be in a state of revolution or of "paradigm shift." Darwin, Mendel, Watson and Crick, recombinant DNA. The "post-genome world" is perhaps the best catch-phrase for the paradigm shift we are now entering. But what is it? It is the shift to a systematic approach to biologic systems, processes, and phenomena, based upon, first, the knowledge of all the relevant components, and second, the ability to query, analyze and interpret these systematic data sets. The implications of that are enormous.

First, the advantages of playing with a full deck,

as opposed to one where many or most of the cards are missing, are obvious. It can actually finally bring rigor and meaningful affect to scientific exploration. Second, it raises the possibility of synthetic rather than purely reductionist approaches to medical research, enabling us to observe and intervene in the complex networks of pathways of cells and organisms that actually reflect biology. And, the promising insights of dealing with the complexity of networks are only now being glimpsed. Third, the principles of genomics, or systematic biology, can be generalized to produce new and productive interfaces between chemistry or computational sciences and biology. Finally, true scientific paradigm shifts alter how we think and they yield new insights.

The post-genome world, as Eric Lander has pointed out, is like chemistry after the periodic table. The periodic table of the 19th century gave us a data set, but more than that, it gave us an organization. It set the stage for applied chemistry on the one hand and the deep mysteries of quantum mechanics on the other. In short, it not only brought order out of chaos, but revealed the underlying rules that govern matter. Laying out the information packets of all biology will reveal organizational principles we are only beginning to appreciate. These principles are the manifest rules of three-plus billion years of evolution. These rules will begin to emerge, and those rules will be as powerful for biology and medicine as Mendeleev's table has been for chemistry.

So now let me illustrate a few examples of what we have put in place at the National Cancer Institute to help write that table for biology. I don't think it's parochial to posit that it is the very nature of cancer that demands that we rise to the challenge of helping to chaperone the entrance of the post-genomic world.

Cancer is biologically a strange and remarkable disease, best described as a disease of genomic instability, itself an amazing an very daunting problem. We know that cancer is always a genetic disease, not heritable, but genetic. It is due to the accumulation of a number of genetic changes that determine the nature of cancer, its development, the biology, and the actual manifestation of the disease. The central challenge of cancer biology is straightforward, and that is, to read and interpret the entirety of these genetic changes, and through that, to translate this Rosetta stone of altered genetic information that defines the disease. It's remarkable that we have come to that synthesis. Twenty years ago, one could not have gotten up here and said that. But that said, the challenge to fully describe and to fully interpret that genetic profile that defines the history, the development, the predisposition, the behavior, the response to therapy, of cancer is really a daunting challenge. How will we do that within this context of a post-genomic approach, this approach of having a full deck of cards to play with?

We have set out on an ambitious project to identify all, or as close to all as possible, human genes over the next few years, through the Cancer Genome Anatomy Project. This is different from the Human Genome Project. This is a post-genome project, although we are not waiting for the Genome Project to finish. That is to get the expressed genes, first through an EST sequencing project, and then to move, which we will this year, with the Genome Institute, to get full-length cDNAs, and to annotate where those genes are expressed and when. For our purposes, we are annotating them across all cellular lineages, during cancer development, and in cancer.

Just in the last year, we've achieved 350,000 sequences, about 30 percent of all sequences known in the public database. We are now up to 55,000 genes out of a total of presumably 80,000....

What will we do with all of this information?... It is time to move from a pathologic to a molecular classification and description of cancer, and that is exactly what we can do. Here is the NCI version 1.0 of the Lymphochip, containing about 7,000 genes. We have 50,000 sequences from lymphoma. We have 3,000 new genes discovered there, and 1,500 in the last several months, that are unique to these cells. We can now query the entirety of the array, and ultimately on this chip, which is 18 millimeters by 18 millimeters, we can simultaneously query the patterns of expression of all of these genes.... We can begin classifying these lymphomas....

We have announced that we will put out a $50-million challenge to provide all of these clones, arrays, technology to researchers who will apply to be part of this Director's Challenge to use this high-throughput analysis over the next few years to grab onto this momentum of the beginning post-genome world and move us in cancer from a pathologic or histologic definition to a new classification based on systematic analysis of gene expression [see **The Cancer Letter**, Dec. 4, 1998, for concept statement].

The process of the development of cancer, indeed, all biologic processes, take place within the context of a very complicated set of genetic filters,

the variations that distinguish one individual from another. Of course, we are all much more alike than we are dissimilar. But we know that approximately one out of every 900 bases in the genome is different between any two of us who are not identical twins. It is within that variation, those subtle differences, of who is going to respond to an environmental stimulus or a hormonal stimulus to get a particular disease, what is the outcome of that disease, etc., will likely be explained. This will represent the new post-genomic genetics.

Genetics is the biology of heredity, and especially the study of the hereditary transmission of variation. We have done a marvelous job at capturing simple heredity in the explosion of our understanding of genetic diseases by using paradigms of linkage analysis in single, Medelianly simple, usually dominant, though sometimes recessive traits, and to be able to identify the genes, a critical first step towards successfully intervening.

But what we will be moving to, is away from the paradigm of familial linkage, to population association. This will be profoundly transformative to medicine. How do we understand the biochemical pathways that impact on what happens to an individual when they are exposed to cigarette smoke, or estrogens, or androgens, or components of the diet, or what happens to one individual who inherits a BRCA1 mutation and never gets cancer versus another individual who gets multiple cancers by the time they are 30? It's the modification of these filters of genetic variability. Here is one example, attempting to understand why alcohol predisposes to nasopharyngeal carcinoma, in this case, in Puerto Rico. The answer in part is a polymorphism in the metabolism of alcohol, a polymorphism common to the population in alcohol dehydrogenase that determines the rate of production of acid aldehyde. In fact, not only explaining differences in risk, but yielding biologic insight, because we have no idea why alcohol would be a carcinogen. It probably isn't. This suggests that it is acid aldehyde, a perfectly good carcinogen, which, in fact, is the problem.

So for the first time, this variation will begin to illuminate countless decades of very difficult to pin down epidemiologic observations, which is why one day you read in the newspaper this is good for you, one day it's bad for you. We can't interpret exposures if we don't understand the genetic filter they come through. So what are we going to do about that? We have a new project called the Gene Annotation Index. We will systematically go through the genes we discover, through CGAP, beginning with an editorial board that will define "cancer-interesting genes"—we suspect that's going to be just about everything—and develop the technology for high-throughput discovery of the most useful approach to human variation and that is single nucleotide polymorphisms, SNPs. We will be looking for SNPs in actual genes that will guide us to experiments about individual variation that will be important in understanding almost every aspect of the process of disease, response to therapy, choice of therapy, risk, etc.

As with all of these projects, they are producing an enormous amount of information, which we put immediately into the public database, providing both information and reagents, clones, sequences, libraries, etc. This is a decision we made, that the NCI must play a role in doing these large-scale scientific experiments to give the community the information and resources it needs to move from the promise of the genome to the reality of a post-genome world....

How are we going to keep up with the possibilities of intervention with this rate of systematic and high-throughput discovery?

We will be able to, in other post-genome projects that I don't have time to talk about, map out rapidly with sequence, based upon expanding structural databases, the predicted structure and function of gene products, especially using one of the most surprising facts of biologic science of the last 20 years, and that is, the remarkable level of evolutionary conservation across all of life, across the entirety of life's history. It is really remarkable, but it allows us to assign function in ways that were unimaginable just a few years ago.

We will be able to map out a complete three-dimensional map of all of the interactions between any gene product and the gene products it interacts with. So how will we develop interventions, develop therapeutics, or preventives, that will finally be based on these explicit and exhaustive descriptions of the machines?

There are many approaches. I will show one that we have begun to fund through a series of new chemistry-biology centers around the country, which have a challenge, and that is, to apply simple principles of Darwinian biology to chemistry. That's not new. People have been doing this. It is the area of genetic chemistry, combinatory chemistry. The

principles are identical. They are biologic principles. Generate an enormous number of mutations or random structures, make sure that the quality of those mutations are high. The structures are interesting, they are natural-product-like, they have stereocenters, they are quite complex. And, have a high-throughput mechanism for Darwinian selection, in other words, screens that are smart with respect to the biology. And that is the challenge of these chemistry-biology centers, to actually recapitulate evolution with very high-quality mutations not yet available.

We need to challenge the synthetic-organic chemistry community to realize that scaling unbelievably clever and natural-product-like syntheses to create millions of compounds put on nanobeads, coated, that are able to be studied one bead at a time, but in a high-throughput way, so that we will create a series.... The goal is to learn to create this as a technology that is formatted to be compatible with basic laboratory research, the way we were able to format over the past 20 years recombinant DNA technology that at the beginning no one thought that every lab would do it just by ordering kits. We would like to have not only every gene for every cell, every expression pattern for every state, but small molecules that interact with and affect every gene product and all of their interactions. These centers are designing very clever high-throughput assays that will allow this sort of genomic analysis [see **The Cancer Letter**, Oct. 23, 1998, for list of funded chemistry-biology centers].

What began with, I will argue, the most important discovery that ever will be made in biology, the nature and structure of DNA, the thing that transformed biologic thinking from discussions about energy, which was the beauty of biology in the 1930s and 40s, to recognizing that biology is about information. We are the heirs of that generation of discoverers, finally able to capture or to envision capturing, not just the promise of more information, but the possibility of all information.

So what are the challenges? There are four I want to briefly comment on:

1. As with every change, there are enormous numbers of new technologies that we must learn how to support the development of, and to figure out how to export to the scientific community and the clinical research community and then to clinical applications. We need with this to be prepared to use this technology for new ways of thinking about experimentation, about describing populations, individuals, disease states, clinical trials. It is important, that with the marvelous potential amounts of dollars that could be assigned to these technologies, that these fundamental enabling technologies, which ought to be developed with academia and government and industry, are not tied up in short-sighted patents and licenses that take this information, which is our shared heritage, and hide it from the public good.

2. Informatics. As we move forward, one of the most powerful, important tools that will define biology is the need for a world of analytic approaches. How are we going to deal with all of this data? How are we going to understand it? How are we going to display it? How are we going to take it in? How are we going to communicate it? We will find that as we go on, I predict, that a tremendous fraction of actually doing biology and biomedical research will be in a new mathematics and a new set of analytic and informatics and communication approaches. We don't know how to do it. We need to figure out how to do it. We need to figure out how to train people, how to bring in other fields.

3. Capturing the promise of what I've talked about will involve bringing in multiple disciplines: computational mathematicians, computer scientists, material scientists—look at these chips, remote sensors, nanoprobes, molecular-sized robots that can go around and seek out these molecular changes—physicists, chemists. We need to examine our academic structures to make sure that those structures are not rigid and not frozen in a past history, but are able to respond to the multidisciplinary research that these will demand. Part of it is an incredible challenge, and that is, we need to reward people for collaborating and working together. We need to find a way to tell young people, anyone in research, that it will benefit you, that we will be able to evaluate contribution to collaboration, so that we can value it and link it to career development, and not penalize people for collaborating. This is an enormous challenge for our academic institutions.

4. The clinical research interface. There will be an enormous challenge of technology assessment and technology transfer. We need good mechanisms, which we are working on, for the rapid assessment of these new technologies, and to deal with the dissemination and the use of these technologies—genetic testing, new approaches to diagnosis, in clinical practice, only linked to evidence. This is a

remarkably critical and important role of professional societies such as ASH.

If we go back to the analogy of the periodic table, which I find very intriguing, I will point out something that I am often called upon to explain to the public and to the Congress, and that is, we are not at the end of science. As with the periodic table, it enabled the last century of chemistry, of the pharmaceutical industry, of molecular physics. It was the beginning and not the end. The application of the information to change medicine, we hope, will come as fast as possible. But there is an enormous amount of work to do. We are an impatient society. I fear that we will grow more impatient with, in fact, the extraordinary generosity of the Congress to the NIH, with expectations not just of moving in the right direction, not just of progress, but of product.

We should remember the periodic table. The last century of advances across an extraordinary number of fields would not have happened without that. But it has taken all that time and will take another century or more to continue to explore the myriad of applications and uses of the revolution we are all about to experience.

Excerpts from David Nathan's response:

Dr. Klausner, you pose a tremendous problem, as you know, for those of us who fancy ourselves clinical hemato-oncologists. Who is, now in your vision, a clinical hemato-oncologist? Well, she is first of all, a geneticist totally familiar with the CGAP chemistry. She is a protein chemist who understands protein-protein interactions and can measure them. She is a combinatorial chemist, a computational analyst, an imaging analyst, a population scientist, and above all, she is a superb clinician, a pharmacologist, a hematologist, an infectious disease expert, a radiotherapist, a surgeon, a psychologist, and she is available 24 hours a day.

How are we going to make that wonder? The panel on which I served spent a long time worrying about this and worrying about what the NIH and others should do about this. [The Report of the NIH Director's Panel on Clinical Research, December 1997, is available at http://www.nih.gov/news/crp/97report/1report.htm]

We went around the country to look at the cries of clinical investigators in the United States, beyond hematology an oncology. The universal complaint that makes it so difficult to train people to fit with the vision you just heard was lack of funding for free time. There was also lack of opportunity for free time because of excessive patient care demands, excessive administrative demands.... There were cries of insufficient personal compensation.... We noticed that there was poor training, particularly in biostatistics and epidemiology, and poor training in translational research, particularly to keep up with the kinds of translational research that Rick Klausner is talking about. To get that training, one has to be with someone who has a green thumb. There is relatively poor mentoring for training people to develop green thumbs, and if one doesn't develop the notion as an investigator that he or she will answer any question and learn the techniques necessary to answer that question, one risks developing what Joe Goldstein called "PAIDS," the Paralyzed Academic Investigator's Disease Syndrome, the person who is stuck with one technology, who can't get out of the periodic table, who can't move forward into this new period....

Recommendations of the report were that NIH should begin to train medical students in clinical research, and they are doing that; improve quality of training in clinical research, they are doing that. Develop new support mechanisms for clinical researchers, and NIH is doing that.

I feel that NIH has responded. But what about the academic health centers? What do we have to do to take care of this dangerous situation where in fact we may have brilliant ideas but no physicians to carry them out?

First of all, we need to establish disease-specific program teams in our hospitals, led by a clinical investigator, a population scientist, and a basic scientist. It's obvious that one cannot know everything and we have to work in teams.

We need to establish core laboratories that provide support for those disease programs, including the imaging cores that will permit investigators to do things like label dead and living cancer cells in the various solid tumors and actually measure the amount of cancer that a patient with a solid tumor has. That is a tremendous need, that is a really positive step we could take, and we need to develop the technology to do that.

We need to encourage collaborations among all the disciplines that I read within these specific disease programs, and use these cores as bait. Bring institutions together to develop a viable financial base. Single institutions can't do these things alone.

We need to collaborate, but that immediately

brings up the last point, our promotion system. This is hopeless. We can't just use the what-is-her-c.v. analysis anymore. We've got to be able to say, "What did the team do, and what did she do in the team?" We've got to change our way of thinking, because no one can learn everything,.

I think NIH is doing their thing, but I can tell you that academic medicine, in my view, has a long way to go. I believe we will get there, because the challenge is so wonderful.

Funding Opportunities:

Program Announcements

PAR 99-031: NCRR Shared Instrumentation Grant. Application Receipt Date: March 19

The National Center for Research Resources is continuing its competitive Shared Instrumentation Grant (SIG) Program initiated in FY1982. The program provides a mechanism for groups of NIH-supported investigators to obtain commercially-available, technologically sophisticated equipment costing more than $100,000.

Inquiries: Marjorie Tingle, Ph.D., Shared Instrumentation Grant Program, National Center for Research Resources, 6705 Rockledge Drive, Room 6154, MSC 7965, Bethesda, MD 20892-7965, phone: 301-435-0772, fax: 301-480-3659, email: SIG@ncrr.nih.gov.

PAR-99-032: Extramural Research Facilities Construction Projects. Application Receipt Date: Feb. 25.

The National Center for Research Resources is authorized by law to "make grants to public and nonprofit private entities to expand, remodel, renovate or alter existing research facilities or construct new research facilities." The facilities will be used for basic and clinical biomedical and behavioral research and research training.

Inquiries: W. Fred Taylor, Research Infrastructure, National Center for Research Resources, 6705 Rockledge Drive, Room 6142-MSC 7965, Bethesda, MD 20892-7965, phone 301-435-0766, fax 301-480-3770, email: taylorf@ncrr.nih.gov

PA-99-030: Aging And Old Age As Risk Factors For Multiple Primary Tumors

The National Institute on Aging and the National Institute of Dental and Craniofacial Research invite research grant applications for studies to define the magnitude and nature of the problem of multiple primary tumors and their association with advancing age and to develop biostatistical and etiologic methodologies for assessment of multiple primary tumors, with special emphasis in older-aged cancer patients. This solicitation is intended to stimulate research to build a knowledge base on occurrence of age-related multiple primary tumors. This PA encourages investigators to conduct research in epidemiology, methodology of disease classification (i.e., nosology), biostatistical methodology, gerontology, carcinogenesis, genetics, and environmental causes emphasizing the high-risk potential for people previously diagnosed with cancer to develop second primary tumors.

Inquiries: Rosemary Yancik, Ph.D., Cancer Section, Geriatrics Program, National Institute on Aging, 7201 Wisconsin Avenue, Suite 3E327, MSC 9205, Bethesda, MD 20892-9205, phone 301-496-5278, fax 301-402-1784, email: YancikR@exmur.nia.nih.gov or Ann Sandberg, Ph.D., Neoplastic Diseases Program National Institute of Dental and Craniofacial Research, 45 Center Drive, Room 4AN-24A, Bethesda, MD 20892, phone 301-594-2419, fax 301-480-8318, email ann.sandberg@nih.gov

RFA Available

RFA HG-99-001: Network for Large-Scale Sequencing of the Mouse Genome. Letter of Intent Receipt Date: March 1. Application Receipt Date: April 29.

The purpose of this RFA is to establish a Mouse Genome Sequencing Network that will support the mapping and sequencing of the mouse genome. The goals of the Network are to generate the necessary mapping resources and begin production of a working draft of the DNA sequence of the mouse genome. Applications for both pilot sequencing projects in new groups and the expansion of the capacity of existing sequencing centers are encouraged. Estimated funds available for the first year of support for awards under this RFA will be $21 million (total costs). It is expected that from one to four efforts will be funded for characterization of mouse BAC libraries, generation of a mapping resource and construction of a map of sequenced clones. For the sequence production component of the Network, it is anticipated that three to five new sequence production projects and up to four existing centers will be funded. One to three intramural projects may be funded. Applicants may request funding for any one or combination of the objectives.

Prospective applicants are invited to attend a briefing on Feb. 1 in the Natcher Building, Conference Room A, from 1-3 pm. NHGRI staff will explain the purpose of the program, provide detailed instructions about the application process and answer questions. For further information, contact the program staff listed below.

Inquiries: Dr. Jane L. Peterson (for sequencing) or Dr. Bettie Graham (for mapping resources), Division of Extramural Research, National Human Genome Research Institute, 38 Library Drive, Room 614, MSC 6050, Bethesda, MD 20892-6050, phone 301-496-7531, fax 301-480-2770, email Jane_Peterson@nih.gov or Bettie_Graham@nih.gov

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