

CUTTING-EDGE BASIC RESEARCH AWARDS (CEBRA)

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National Institute on Drug Abuse (NIDA)
(<http://www.nida.nih.gov>)

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PURPOSE OF THIS PA

The National Institute on Drug Abuse (NIDA) invites applications for Cutting-Edge Basic Research Awards (CEBRA) to foster highly innovative or conceptually creative research that advances our understanding of drug abuse and addiction and how to prevent and treat them. The CEBRA is a new mechanism designed by NIDA to foster novel research approaches and represents the high priority placed by NIDA on identifying such research. NIDA currently supports a great deal of innovative biomedical research. The CEBRA, however, is specifically designed to support research that is high-risk and potentially high-impact and that is underrepresented or not included in NIDA's current portfolio. It is not intended for incremental research or research extending ongoing programs. It is aimed at experienced drug abuse research investigators who wish to develop or adapt new methods or techniques and at new investigators or scientists with expertise in fields other than drug abuse who wish to establish innovative programs in drug abuse research. NIDA's CEBRA program will provide rapid review and funding decisions.

The R21 mechanism allows support for projects in the early, first stages of development (Stage I) where there are little or no preliminary data available, but which have a strong rationale and conceptual framework. Successful Stage I applicants will be eligible to apply for a Stage II award (R01) that will support the innovative research initiated in Stage I (R21). Specific features of the CEBRA include:

- o Focus on innovation.
- o Transition from feasibility stage to development stage.
- o Expedited review convened by NIDA for Stage I submissions.

This PA will replace, in its entirety, PAR-01-047, Cutting-Edge Basic Research Award announcement, published in the NIH Guide February 6, 2001 at <http://grants.nih.gov/grants/guide/pa-files/PAR-01-047.html>.

RESEARCH OBJECTIVES

Background

Over the past years, basic science discoveries have consistently been the basis for many major advances in both clinical and applied drug abuse research and have contributed to the implementation of successful drug addiction treatment strategies. Pharmacological, neurobiological, cell biological, and genetic research have provided insight into questions such as how each drug of abuse exerts its actions on the brain and other organs and produces addiction. Molecular, systems neurobiology, behavioral, and cognitive studies have shed light on how drugs of abuse affect both animal and human behavior. For example, research has elucidated aspects of the processes of acquisition and relapse, led to the development of new molecular markers, and provided a more fundamental understanding of the functioning of receptors and transporters. However, there is a need to increase our understanding of drug abuse in order to develop effective treatment and prevention interventions to alleviate the pain and devastation of addiction.

The goal of NIDA's CEBRA program is to accelerate the pace of discoveries that can advance addiction research by encouraging scientifically sound proposals that focus on innovation. The CEBRA seeks to encourage researchers to explore new approaches, test imaginative new ideas, and challenge existing paradigms in drug addiction research in both human and animal models. While NIDA currently supports many innovative and creative projects, the CEBRA is aimed at high-risk, high-impact research that is underrepresented or not included in NIDA's current portfolio. The proposed research should either: (1) test highly novel and significant hypotheses for which there is scant precedent or preliminary data and which, if confirmed, would have a substantial impact on current thinking; or (2) develop or adapt innovative techniques or methods for addiction research.

There is enormous potential for advances when knowledge is generated and combined in new and unexpected ways. Therefore, this announcement encourages applications from experienced drug abuse research investigators who wish to adapt new methods or techniques to study basic questions in drug abuse and addiction. Also encouraged to apply are new investigators or investigators with expertise in fields other than drug abuse to establish innovative programs in drug abuse and addiction research.

The CEBRA program is not intended for large-scale undertakings or to support or supplement ongoing research.

Recipients of the CEBRA R21 award (Stage I) will be eligible to apply for a Stage II R01 award that will provide support for successful, innovative exploratory and developmental research initiated in Stage I.

Areas of interest

Examples of relevant research include, but are not limited, to the following:

- o Applying novel or emerging technologies--such as biosensors, nanotechnology, proteomics, or transcriptome analysis--to address questions about the cellular biology of drug addiction or synaptic remodeling.
- o Developing new methods for in vivo regulation of gene and protein function, detection of protein-protein interactions, localization of proteins, or

measurement of synaptic activity.

- o Elucidating the role of cellular processes--such as regulation of mRNA translation, trafficking systems, cytoskeletal organization, protein degradation, autoregulatory cycles, etc. -- that have not been investigated extensively in studies of acute or persistent cellular responses resulting from acute or chronic exposure to drugs of abuse.
- o Discovering novel drug abuse-related signal transduction pathways or previously uncharacterized interactions between known pathways.
- o Applying molecular, neurochemical, and genetic approaches to explain gender-specific differences in the behavioral and biological response to drugs of abuse.
- o Improving methods for heterologous expression/overexpression of G-protein coupled receptors (opioid, cannabinoid, orphanin, etc.) in bacterial, yeast, insect, or mammalian cells.
- o Applying or developing new technologies for recording of neuronal activity, in animals or humans, that encode drug-related behaviors and/or stimuli.
- o Developing computational methods for interpreting or modeling neurophysiological, molecular, cognitive or behavioral data and processes relevant to drug abuse.
- o Developing innovative approaches for managing knowledge and integrating information from text, data, image, and other sources or files generated in addiction research.
- o Using novel methods for high throughput screening for new drug templates or receptor-specific ligands, and developing new and faster methods to design super-agonists and antagonists for various receptor types and subtypes.
- o Discerning functional interactions between non-opiate peptides and chemical neurotransmitters using methods other than anatomical or co-localization studies.
- o Developing multi-dimensional behavioral assays capable of detecting drug-seeking or drug-taking behaviors that are guided by a range of underlying psychological processes or states.
- o Exploring, in laboratory-based studies, the relationship between vulnerability to drug abuse/dependence and sensitivity to aversive consequences and/or initial subjective responses to drug effects.
- o Designing and validating unique apparatuses and paradigms for behavioral studies of, for example, behavioral choices, alternative behaviors or alternative reinforcers.
- o Developing measures to assess subjective experiences other than reward or hedonia that motivate the initiation or maintenance of drug abuse.

MECHANISM OF SUPPORT

Applicants are encouraged to consult with the appropriate NIDA staff listed under INQUIRIES for additional information to see if their research plans are

consistent with the objectives of the CEBRA PA.

Stage I Applications

For Stage I applications, this PA will use the R21 award mechanism with the following required instructions: (1) Stage I award will be limited to a 2-year effort and a maximum of \$100,000 in direct costs per year. (2) Applications are limited to a total of 10 pages for sections A-D.

Unsuccessful Stage I applications cannot be resubmitted to the CEBRA program, but may be submitted as a revised R21 or other mechanism for CSR review.

Stage II Applications

Applicants who receive a Stage I award will be eligible to submit a Stage II application, which will be a new (Type 1) award using the R01 mechanism. Stage II applications will extend and expand the research initiated under Stage I.

Responsibility for the planning, direction, and execution of the proposed projects will be solely that of the applicant.

This PA uses just-in-time concepts. It also uses the modular budgeting format. (see <http://grants.nih.gov/grants/funding/modular/modular.htm>). Specifically, if you are submitting an application with direct costs in each year of \$250,000 or less, use the modular format.

ELIGIBLE INSTITUTIONS

You may submit (an) application(s) if your institution has any of the following characteristics:

- o For-profit or non-profit organizations
- o Public or private institutions, such as universities, colleges, hospitals, and laboratories
- o Units of State and local governments
- o Eligible agencies of the Federal government
- o Domestic or foreign
- o Faith-based or community-based organizations

INDIVIDUALS ELIGIBLE TO BECOME PRINCIPAL INVESTIGATORS

Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.

WHERE TO SEND INQUIRIES

We encourage your inquiries concerning this PA and welcome the opportunity to answer questions from potential applicants. Inquiries may fall into three areas: scientific/research, peer review, and financial or grants management issues:

- o Direct your questions about scientific/research issues to:

Susan Volman, Ph.D.
Division of Neuroscience and Behavioral Research
National Institute on Drug Abuse
6001 Executive Boulevard, Room 4282, MSC 9555
Bethesda, MD 20892-9555
Telephone: (301) 435-1315
FAX: (301) 594-6043
Email: svolman@mail.nih.gov

o Direct your questions about peer review issues for Stage I to:

Teresa Levitin, Ph.D.
Office of Extramural Affairs
National Institute on Drug Abuse
6001 Executive Boulevard, Room 3158, MSC 9547
Bethesda, MD 20892-9547
Telephone: (301) 443-2755
FAX: (301) 443-0538
Email: tl25u@nih.gov

o Direct your questions about financial or grants management matters to:

Gary Fleming, J.D., M.A.
Grants Management Branch
National Institute on Drug Abuse
6001 Executive Boulevard, Room 3131, MSC 9541
Bethesda, MD 20892-9541
Telephone: (301) 443-6710
FAX: (301) 594-6847
Email: gf6s@nih.gov

SUBMITTING AN APPLICATION

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). The PHS 398 is available at <http://grants.nih.gov/grants/funding/phs398/phs398.html> in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

APPLICATION RECEIPT DATES: Applications submitted in response to this program announcement will be accepted at the standard application deadlines, which are available at <http://grants.nih.gov/grants/dates.htm>. Application deadlines are also indicated in the PHS 398 application kit.

SPECIFIC INSTRUCTIONS FOR MODULAR GRANT APPLICATIONS: Applications requesting up to \$250,000 per year in direct costs must be submitted in a modular grant format. The modular grant format simplifies the preparation of the budget in these applications by limiting the level of budgetary detail. Applicants request direct costs in \$25,000 modules. Section C of the research grant application instructions for the PHS 398 (rev. 5/2001) at <http://grants.nih.gov/grants/funding/phs398/phs398.html> includes step-by-step guidance for preparing modular grants. Additional information on modular grants is available at <http://grants.nih.gov/grants/funding/modular/modular.htm>.

The specific guidelines listed below on page limitations are for Stage I applications only (sections A-D) and supersede the PHS 398 instructions.

The research plan for Stage I applications should not exceed 10 pages. Information regarding specific aims, background and significance, preliminary studies, and research design and methods are all included in this 10-page limit. Tables and figures are also included in the 10-page limit. Photos and other graphics may be included in the appendix as instructed in PHS 398. Information about inclusion of women, minorities, and children are not part of the page limit of the Research Plan.

SENDING AN APPLICATION TO THE NIH: Submit a signed, typewritten original of the application, including the checklist, and three signed photocopies in one package to:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Room 1040, MSC 7710
Bethesda, MD 20892-7710
Bethesda, MD 20817 (for express/courier service)

To permit an expedited review of Stage I applications, applicants must simultaneously send two additional copies of the application to:

Director
Office of Extramural Affairs
National Institute on Drug Abuse
6001 Executive Boulevard, Room 3158, MSC 9547
Bethesda, MD 20892-9547
Rockville, MD 20852 (for express/courier service)
Telephone: (301) 443-2755
FAX: (301) 443-0538

APPLICATION PROCESSING: Applications must be received by or mailed on or before the receipt dates described at <http://grants.nih.gov/grants/funding/submissionschedule.htm>. The CSR will not accept any application in response to this PA that is essentially the same as one currently pending initial review unless the applicant withdraws the pending application. The CSR will not accept any application that is essentially the same as one already reviewed.

Stage I applications cannot be revised and resubmitted. Unsuccessful Stage I applications cannot be resubmitted to the CEBRA program, but may be submitted as a revised R21 or other mechanism for CSR review.

PEER REVIEW PROCESS

Applications submitted for this PA will be assigned on the basis of established PHS referral guidelines. An appropriate scientific review group convened by NIDA for Stage I applications and CSR for Stage II applications in accordance with the standard NIH peer review procedures (<http://www.csr.nih.gov/refrev.htm>) will evaluate applications for scientific and technical merit.

As part of the initial merit review, all applications will:

- o Receive a written critique
- o Receive a second level review by the National Advisory Council on Drug Abuse

REVIEW CRITERIA

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In the written comments, reviewers will be asked to discuss the following aspects of your application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals:

- o Significance
- o Approach
- o Innovation
- o Investigator
- o Environment

The scientific review group will address and consider each of these criteria in assigning your application's overall score, weighting them as appropriate for each application. Your application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. However, the CEBRA program is intended for high risk, high impact, innovative research, and reviewers will take this into account in their evaluations.

(1) SIGNIFICANCE: Does your study address an important problem? If the aims of your application are achieved, how do they advance scientific knowledge? What will be the effect of these studies on the concepts or methods that drive this field?

(2) APPROACH: Are the conceptual framework, design, methods, and analyses adequately developed, well integrated, and appropriate to the aims of the project? Do you acknowledge potential problem areas and consider alternative tactics? For Stage I a strong rationale and conceptual framework may be considered sufficient for establishing the feasibility of the project, in lieu of extensive preliminary data.

(3) INNOVATION: Does your project employ novel concepts, approaches or methods? Are the aims original and innovative? Does your project challenge existing paradigms or develop new methodologies or technologies?

(4) INVESTIGATOR: Are you appropriately trained and well suited to carry out this work? Is the work proposed appropriate to your experience level as the principal investigator and to that of other researchers (if any)?

(5) ENVIRONMENT: Does the scientific environment in which your work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

ADDITIONAL REVIEW CRITERIA: In addition to the above criteria, your application will also be reviewed with respect to the following:

PROTECTIONS: The adequacy of the proposed protection for humans, animals, or the environment, to the extent they may be adversely affected by the project proposed in the application.

INCLUSION: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects will also be evaluated. (See Inclusion Criteria included in the section on Federal Citations, below.)

DATA SHARING: The adequacy of the proposed plan to share data for Stage II projects.

BUDGET: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research.

AWARD CRITERIA

Applications submitted in response to a PA will compete for available funds with all other recommended applications. The following will be considered in making funding decisions:

- o Scientific merit of the proposed project as determined by peer review
- o Availability of funds
- o Relevance to program priorities

REQUIRED FEDERAL CITATIONS

MONITORING PLAN AND DATA SAFETY AND MONITORING BOARD: Research components involving Phase I and II clinical trials must include provisions for assessment of patient eligibility and status, rigorous data management, quality assurance, and auditing procedures. In addition, it is NIH policy that all clinical trials require data and safety monitoring, with the method and degree of monitoring being commensurate with the risks (NIH Policy for Data Safety and Monitoring, NIH Guide for Grants and Contracts, June 12, 1998: <http://grants.nih.gov/grants/guide/notice-files/not98-084.html>).

INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH: It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43).

All investigators proposing clinical research should read the AMENDMENT "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research - Amended, October, 2001," published in the NIH Guide for Grants and Contracts on October 9, 2001 (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html>); a complete copy of the updated Guidelines are available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm

The amended policy incorporates: the use of an NIH definition of clinical research; updated racial and ethnic categories in compliance with the new OMB standards; clarification of language governing NIH-defined Phase III clinical trials consistent with the new PHS Form 398; and updated roles and responsibilities of NIH staff and the extramural community. The policy continues to require for all NIH-defined Phase III clinical trials that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by

sex/gender and/or racial/ethnic groups, including subgroups if applicable;
and
b) investigators must report annual accrual and progress in conducting analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

INCLUSION OF CHILDREN AS PARTICIPANTS IN RESEARCH INVOLVING HUMAN SUBJECTS:
The NIH maintains a policy that children (i.e., individuals under the age of 21) must be included in all human subjects research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them. This policy applies to all initial (Type 1) applications submitted for receipt dates after October 1, 1998.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the inclusion of children as participants in research involving human subjects that is available at <http://grants.nih.gov/grants/funding/children/children.htm>.

REQUIRED EDUCATION ON THE PROTECTION OF HUMAN SUBJECT PARTICIPANTS: NIH policy requires education on the protection of human subject participants for all investigators submitting NIH proposals for research involving human subjects. You will find this policy announcement in the NIH Guide for Grants and Contracts Announcement, dated June 5, 2000, at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html>.

HUMAN EMBRYONIC STEM CELLS (hESC): Criteria for federal funding of research on hESCs can be found at http://grants.nih.gov/grants/stem_cells.htm and at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html>. Only research using hESC lines that are registered in the NIH Human Embryonic Stem Cell Registry will be eligible for Federal funding (see <http://escr.nih.gov>). It is the responsibility of the applicant to provide the official NIH identifier(s) for the hESC line(s) to be used in the proposed research. Applications that do not provide this information will be returned without review.

PUBLIC ACCESS TO RESEARCH DATA THROUGH THE FREEDOM OF INFORMATION ACT: The Office of Management and Budget (OMB) Circular A-110 has been revised to provide public access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with Federal funds and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm.

Applicants may wish to place data collected under this PA in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

URLS IN NIH GRANT APPLICATIONS OR APPENDICES: All applications and proposals for NIH funding must be self-contained within specified page limitations.

Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

HEALTHY PEOPLE 2010: The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This PA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at <http://www.health.gov/healthypeople>.

AUTHORITY AND REGULATIONS: This program is described in the Catalog of Federal Domestic Assistance No. 93.279, and is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. Awards are made under authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284 and administered under NIH grants policies described at <http://grants.nih.gov/grants/policy/policy.htm> and under Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92.

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.