

lysate in a single chromatographic step because it forms only one homogeneous species. Second, because this obligate dimer has four carbohydrate binding sites, it binds gp120 and other glycoproteins with greater affinity than wild-type CVN. Third, Δ Q50-CVN shows an enhancing increase in efficacy in blocking viral entry in a quantitative HIV-1 envelope-mediated cell fusion assay. Thus, Δ Q50-CVN displays enhanced anti-HIV activity relative to the wild-type CVN monomer and offers a great advantage over wild-type CVN because it is extremely easy to purify large quantities to greater than 95% homogeneity. So, it may open the possibility that an effective drug treatment for HIV could reach underdeveloped countries.

Finally, the background of this invention is further described in J. Am. Chem. Soc. (2002) 124:3210-3211, J. Magn. Reson. (2002) 154:329-335, Structure (2001) 10:931-940, J. Am. Chem. Soc. (2001) 123:3892-3902, J. Am. Chem. Soc. 122: 6009-6016, and J. Mol. Biol. (1999) 288:403-412.

Methods and Compositions for Antagonizing Septic Shock

George Kunos (NIAAA).
DHHS Reference No. E-321-01/0 filed 15 Aug 2001.

Licensing Contact: Norbert Pontzer; 301/496-7736, ext. 284; e-mail: np59n@nih.gov.

Septic shock is an often fatal type of vasodilatory shock that may accompany microbial infections. Septic shock has therefore been an increasing problem in recent years because of the increasing number of individuals who are immunocompromised. Recent studies have indicated that the hypotension associated with hemorrhagic shock (Wagner *et al.*, Nature 1997; 390:518-521) or septic shock (Varga *et al.*, FASEB J. 1998; 12:1035-1044) may be mediated by macrophage-derived endogenous cannabinoids such as anandamide, acting at vascular cannabinoid receptors. In an earlier study (PNAS, 1999; 96:14136) the NIH inventor(s) presented several lines of evidence indicating the vasodilator effect of anandamide is mediated by a receptor distinct from the two known cannabinoid receptors, CB1 and CB2. In particular, anandamide-induced vasodilation persists in mice deficient in both CB1 and CB2 receptors. They postulated that a yet unidentified cannabinoid receptor was responsible for the observed effect. The invention described and claimed in the pending patent application provides compounds acting as agonists and antagonists at the newly described cannabinoid receptor

and methods for reversing pathological vasodilation of blood vessels observed during conditions such as septic shock.

Methods of Diagnosing and Treating Schizophrenia

Daniel R. Weinberger *et al.* (NIMH).
DHHS Reference No. E-247-01/0 filed 31 Aug 2001.

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Neurotrophins promote survival of neurons from both the central nervous system and peripheral nervous system in cell culture. More recently it has been shown that neurotrophins may serve as a new class of neuromodulators that mediate activity-dependent modifications of neuronal connectivity and synaptic efficacy. Brain derived neurotrophic factor (BDNF) is a neurotrophin that mediates LTP and hippocampus-related spatial memory. Schizophrenia and other mental disorders appear to involve deficits in verbal memory and reduced hippocampal—acetyl aspartate (NAA), a measure of hippocampal neuronal integrity. BDNF may thus play a role in memory function and human diseases of the hippocampus such as schizophrenia.

The human BDNF gene contains one known non-conservative SNP, producing a met66val substitution. The invention is related to the discovery that a met66val polymorphism in the gene for BDNF is correlated with verbal memory and risk for schizophrenia. The invention provides methods and kits for diagnosing and modulating verbal memory and risk for schizophrenia in an individual by determining the individual's BDNF genotype, and associating a met allele with impaired verbal memory and risk for schizophrenia and a val allele with enhanced verbal memory and protection from schizophrenia. The invention also provides methods of finding and using compounds which modulate BDNF function in order to treat human diseases of the hippocampus such as memory disorders and schizophrenia.

Retinoids Can Increase the Potency of Anti-Cancer Immunotoxins

You N. Wu and Richard J. Youle (NINDS).

U.S. Patent 5,942,230 issued August 24, 1999 and U.S. Patent 6,197,528 issued March 6, 2001.

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A unique method of potentiating the effect of anti-cancer immunotoxins has

been developed, thus offering to significantly improve the treatment of a number of cancers as well as autoimmune diseases. Prolonged treatment of human cancers with classical methods such as radiation and chemotherapy, or a combination of both, may cause greater damage than the underlying disease because healthy tissue is often damaged along with diseased tissue. More recently, immunotherapy has emerged as a new and promising therapy for treating cancer because it employs monoclonal antibodies specific for tumor cells coupled to protein toxins. Thus, cancer cells are selectively targeted for destruction. These immunotoxins are being examined in numerous clinical trials for the treatment of cancer and autoimmune diseases. However, often the protein toxin coupled to the monoclonal antibody does not pass as readily into the cytosol of the target cell as does the native protein toxin. This invention improves the effectiveness of such immunotoxins by employing retinoic acid, which disrupts the Golgi apparatus of the target cell and increases the cytosolic routing of specific protein toxins. Also included in this invention is an in vitro method for assessing the ability of a retinoid to potentiate the activity of immunotoxins.

Dated: July 29, 2002.

Jack Spiegel,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. 02-19866 Filed 8-6-02; 8:45 am]

BILLING CODE 4140-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Laboratory Animal Welfare: Change in PHS Policy on Humane Care and Use of Laboratory Animals

AGENCY: National Institutes of Health, DHHS.

ACTION: Amended Policy Statement.

SUMMARY: The NIH is changing the PHS Policy on Humane Care and Use of Laboratory Animals (PHS Policy) to permit institutions with PHS Animal Welfare Assurances to submit verification of Institutional Animal Care and Use Committee (IACUC) approval for competing applications subsequent to peer review but prior to award.

DATES: This change in PHS Policy is effective as of September 1, 2002 (*i.e.*, for all applications submitted for the May-June 2003 Advisory Council dates).

FOR FURTHER INFORMATION CONTACT: Anthony Demsey, Ph.D., Senior Advisor for Policy, Office of Extramural Research, National Institutes of Health, 301-496-5127, email: demsey@od.nih.gov.

SUPPLEMENTARY INFORMATION: In the March 28, 2002, *Federal Register* (67 FR 14956), the NIH proposed to change the PHS Policy to allow institutions to provide IACUC approval for competing applications subsequent to peer review but prior to award. This change would modify the PHS Policy, applicable to all PHS-conducted or -supported activities involving live, vertebrate animals, which currently provides institutions with a PHS-approved Animal Welfare Assurance the option of submitting verification of IACUC approval for competing applications (1) at the time of submission, or (2) subsequent to submission but within 60 days from the receipt date and in any case prior to peer review. Now, with this change in the PHS Policy, IACUC verification is no longer required to be submitted prior to NIH peer review, but instead is simply required prior to award. This process, already adopted as of May 1, 2000, for Institutional Review Board approval of applications involving human subjects, is often referred to as "just-in-time." The purpose of the change is to enhance the flexibility of institutions and reduce the burden on applicants and IACUCs, allowing resources to be focused on substantive review of applications likely to be funded. The change, however, permits funding components to require verification of IACUC approval at an earlier date if necessary.

Over 200 comments from the research community and institutional officials were received in response to the March 28, 2002, *Federal Register* solicitation for public comment on the proposed change. The comments were overwhelmingly in favor of the change; some included suggestions for NIH in its implementation of the change.

Consequently, NIH emphasizes the following principles and expectations:

- The fundamental PHS Policy requirement that no award may be made without an approved Assurance and without verification of IACUC approval remains in effect. This change only affects the timing of the submission of the verification of that review.

- This change is intended to permit flexibility and discretion on the part of the institution. It is not a requirement that IACUC approval be deferred. Institutional officials retain the discretion to require IACUC approval prior to peer review in certain

circumstances of their choosing if they so desire.

- Under no circumstances may an IACUC be pressured to approve a protocol or be overruled on its decision to withhold approval. NIH peer review groups will continue to address the adequacy of animal usage and protections in their review of an application and will continue to raise concerns about animal welfare issues. However, in no way is peer review intended to supersede or serve as a replacement for IACUC approval. An institution that elects to use IACUC just-in-time bears the responsibility for supporting the role of the IACUC.

- It remains incumbent upon investigators to be totally forthcoming and timely in conveying to their IACUCs any modifications related to project scope and animal usage that may result from the NIH review and award process. Should an institution find that one of its investigators disregards his/her responsibilities, the institution may, for example, determine that all animal protocols from that investigator be subject to IACUC approval before it will permit submission of an application from that investigator.

- The existing PHS Policy requirement that modifications required by the IACUC be submitted to the NIH with the verification of IACUC approval remains in effect, and it remains the responsibility of institutions to communicate any IACUC-imposed changes to NIH staff.

- The NIH understands its responsibility to ensure that institutions are given adequate notice to allow for timely IACUC review prior to award and will take appropriate internal measures to fulfill its responsibility to establish timely feedback.

For the reasons stated above, the NIH amends the PHS Policy on Humane Care and Use of Laboratory Animals as set forth below:

Amend the second sentence of Section IV.D.2. of the PHS Policy to delete the words "a time not to exceed 60 days after the receipt deadline date" and replace them with the words "any time prior to award unless specifically required earlier by the funding component" so that the sentence states: "For competing applications or proposals only, such verification may be filed at any time prior to award unless specifically required earlier by the funding component."

The NIH will modify the NIH Grants Policy Statement and instructions for the 398 Grant Application Form accordingly.

Dated: July 29, 2002.

Elias A. Zerhouni,

Director, National Institutes of Health.

[FR Doc. 02-19867 Filed 8-6-02; 8:45 am]

BILLING CODE 4140-01-P

DEPARTMENT OF THE INTERIOR

U.S. Geological Survey

Request for Public Comments on Information Collection Submitted to the Office of Management and Budget for Review Under the Paperwork Reduction Act

A request extending the collection of information has been submitted to the Office of Management and Budget for approval under the provisions of the Paperwork Reduction Act (44 U.S.C. Chapter 35). Copies of the proposed collection of information and related forms may be obtained by contracting the USGS Clearance Officer at the phone number listed below. OMB has up to 60 days to approve or disapprove the information collection but may respond after 30 days; therefore, public comments should be submitted to OMB within 30 days in order to assure their maximum consideration. Comments and suggestions on the requirement should be made directly to the Desk Officer for the Interior Department, Office of Regulatory Affairs, Office of Management and Budget, Washington, DC 20503 and to the USGS Clearance Officer, U.S. Geological Survey, 807 National Center, Reston, VA 20192.

As required by OMB regulations at CFR 1320.8(d)(1), the U.S. Geological Survey solicits specific public comments regarding the proposed information collection as to:

1. Whether the collection of information is necessary for the proper performance of the functions of the USGS, including whether the information will have practical utility;
2. The accuracy of the USGS estimate of the burden of the collection of information, including the validity of the methodology and assumptions used;
3. The utility, quality, and clarity of the information to be collected; and,
4. How to minimize the burden of the collection of information on those who are to respond, including the use of appropriate automated electronic, mechanical, or other forms of information technology.

Title: Ferrous Metals Surveys.

Current OMB approval number: 1028-0053.

Abstract: Respondents supply the U.S. Geological Survey with domestic production and consumption data on