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Diazeniumdiolates are a class of compounds which release nitric oxide (NO) under physiological conditions. Nitric oxide performs a number of regulatory functions in vivo such as controlling vascular tone and platelet function, but it can also combine with superoxide ion to produce peroxynitrite ion, as especially reactive species. Peroxynitrite-mediated cellular toxicity may have several therapeutic applications. Because of the relatively low amounts of superoxide ion present in some cells, the peroxynitrite mechanism of diazeniumdiolate toxicity is not uniformly available. In order to generate peroxynitrite ions in tissues or other media lacking adequate levels of superoxide ion, this invention provides a new class of compounds which release NO and superoxide ion simultaneously to generate peroxynitrite ions.

Molecules of this invention can be designed to generate peroxynitrite ion at specific biochemical targets. For one type of targeting, the release of NO is designed to be triggered by nucleophilic attack on the diazeniumdiolate drug while superoxide generation is simultaneously occurring at a quinone moiety elsewhere in the molecule. If the required nucleophilic attack is designed to be specifically catalyzed in the active site of glutathione S-transferase-pi, a cytoprotective enzyme overexpressed by certain tumors to render them drug-resistant, compounds of this invention could restore the susceptibility of tumor cells to chemotherapy by knocking out the excess enzyme, thereby preventing the tumor cells from inactivating the chemotherapeutic agents. Attachment of the compounds to polymeric compositions would physically localize the peroxynitrite activity. Physical localization in vivo may have utility against the recently recognized chronic infections caused by biofilms, and generation of peroxynitrite ions in vitro may have utility against infectious bilfilms on medical devices.

Dated: December 20, 2000.

Jack Spiegel,

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

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Heart, Lung, and Blood Institute; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2); notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Heart, Lung, and Blood Institute Special Emphasis Panel Program Project Reviews.

Date: January 12, 2001.

Time: 8 AM to 2 PM.

Agenda: To review and evaluate grant applications.

Place: Sheraton Columbia Hotel, 10207 Wincopin Circle, Columbia, MD 21044.

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Contact Person: Jeffrey H. Hurst, PhD, Health Scientist Administrator, 6701 Rockledge Drive, Room 7208, Bethesda, MD 20892, 301-435-0303.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

(Catalogue of Federal Domestic Assistance Program Nos. 93.233, National Center for Sleep Disorders Research; 93.837, Heart and Vascular Diseases Research; 93.838, Lung Diseases Research; 93.839, Blood Diseases and Resources Research, National Institutes of Health, HHS)

Dated: December 20, 2000.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 00-33084 Filed 12-27-00; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Neurological Disorders and Stroke; Notice of Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice

is hereby given of a meeting of the Board of Scientific Counselors, National Institute of Neurological Disorders and Stroke.

The meeting will be open to the public as indicated below, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the Contact Person listed below in advance of the meeting.

The meeting will be closed to the public as indicated below in accordance with the provisions set forth in section 552b(c)(6), Title 5 U.S.C., as amended for the review, discussion, and evaluation of individual intramural programs and projects conducted by the National Institute of Neurological Disorders and Stroke, including consideration of personnel qualifications and performance, and the competence of individual investigators, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: Board of Scientific Counselors, National Institute of Neurological Disorders and Stroke

Date: February 4-6, 2001.

Closed: February 4, 2001, 7:00 PM to 10:00 PM.

Agenda: To review and evaluate personal qualifications and performance, and competence of individual investigators.

Place: Bethesda Marriott Hotel, 5151 Pooks Hill Road, Bethesda, MD 20814.

Open: February 5, 2001, 8:15 AM to 11:10 AM.

Agenda: To discuss program planning and project accomplishments.

Place: National Institutes of Health, Natcher Building, Conference Room F-1/2, Bethesda, MD 20892.

Closed: February 5, 2001, 11:10 AM to 1:15 PM.

Agenda: To review and evaluate personal qualifications and performance, and competence of individual investigators.

Place: National Institutes of Health, Natcher Building, Conference Room F-1/2, Bethesda, MD 20892.

Open: February 5, 2001, 1:15 PM to 4:15 PM.

Agenda: To discuss program planning and program accomplishments.

Place: National Institutes of Health, Natcher Building, Conference Room F-1/2, Bethesda, MD 20892.

Closed: February 5, 2001, 4:15 PM to 5:15 PM.

Agenda: To review and evaluate personal qualifications and performance, and competence of individual investigators.

Place: National Institutes of Health, Natcher Building, Conference Room F-1/2, Bethesda, MD 20892.

Closed: February 5, 2001, 6:00 PM to 10:00 PM.