

Imidazoacridones With Anti-Tumor Activity

Description of Invention: The present invention relates to novel bifunctional molecules with potent and selective activity against colon, liver and pancreatic tumors. Compounds have low animal toxicity, excellent PK/PD characteristics and proved to be very effective in several preclinical animal models of cancer. Extensive mechanistic studies have demonstrated that compounds inhibit tumor growth through a novel mechanism. These agents are composed of an imidazoacridone moiety linked by a nitrogen containing aliphatic chain of various length and rigidity to another aromatic ring system capable of intercalation to DNA.

Previous studies on related symmetrical bis-imidazoacridones revealed that only one planar imidazoacridone moiety intercalates into DNA. The second aromatic moiety, which is crucial for biological activity, along with the linker resides in DNA minor groove, and is believed to interact with DNA-binding proteins (most likely, transcription factors and/or repair proteins). The symmetrical bis-imidazoacridones arrest the growth of sensitive cancers (especially colon cancers) but do not kill the tumors. It was hypothesized that the growth arrest was due to the inability of the affected tumor cells to repair DNA damage caused by the compounds. Remarkably, bis-imidazoacridones are very well tolerated, are very tissue selective and do not appear to damage normal tissues.

Since the binding of the symmetrical bis-imidazoacridones to DNA was unsymmetrical, the inventors have developed unsymmetrical compounds in which one imidazoacridone moieties was replaced by other intercalating groups, with the expectation that this would enhance biological activity while retaining the remarkable tissue selectivity and low systemic toxicity. The new compounds contain intercalating moieties such as 3-chloro-7-methoxyacridine or naphthalimide along with the original imidazoacridones.

These new compounds, especially those containing naphthalimide moiety, are extremely cytotoxic against a variety of tumor cells in vitro (IC₅₀ at low nanomolar range) and kill tumor cells by inducing apoptosis. In vivo, in nude mice xenografted with human tumors, the compounds significantly inhibited the growth of such tumors as colon tumor HCT116 and Colo205 as well as pancreatic tumors (lines 6.03 and 10.05 freshly established from a patient).

These compounds are extremely potent agents against hepatocellular carcinoma as evidenced by their ability to eradicate liver cancer in an orthotopic liver cancer model in rats. Remarkably, no toxicity was observed at the therapeutic doses. These are among the most potent agents known against cancers of the GI tract and appear to be tolerated very well.

Inventors: Wieslaw M. Cholody *et al.* (NCI)

Patent Status:

- U.S. Patent 6,664,263 issued 16 Dec 2003 (HHS Reference No. E-289-1999/0-US-07) and related international patents/patent applications.

- U.S. Patent 6,541,483 issued 01 Apr 2003 (HHS Reference No. E-065-1996/2-US-25) and related international patents/patent applications.

Licensing Status: Available for licensing.

Licensing Contact: Betty B. Tong, PhD; 301-594-6565; tongb@mail.nih.gov.

Collaborative Research Opportunity: The National Cancer Institute, Center for Cancer Research, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize imidazoacridones as therapeutic agents for cancer treatment. Please contact John Hewes, PhD at 301-435-3121 or hewesj@mail.nih.gov for more information.

Dated: April 29, 2011.

Richard U. Rodriguez,

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

[FR Doc. 2011-11055 Filed 5-4-11; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Eunice Kennedy Shriver National Institute of Child Health & Human Development; Notice of Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. App.), notice is hereby given of a meeting of the National Advisory Child Health and Human Development Council.

The meeting will be open to the public, 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 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/or contract proposals 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 and/or contract proposals, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Advisory Child Health and Human Development Council.

Date: June 2, 2011.

Open: 8 a.m. to 12:20 p.m.

Agenda: (1) A report by the Director, NICHD; (2) Report of the Subcommittee on Planning and Policy; (3) NICHD Scientific Visioning update; and other business of the Council.

Place: National Institutes of Health, Building 31, 31 Center Drive, C-Wing, Conference Room 6, Bethesda, MD 20892.

Closed: 12:20 p.m. to 5 p.m.

Agenda: To review and evaluate grant applications and/or proposals.

Place: National Institutes of Health, Building 31, 31 Center Drive, C-Wing, Conference Room 6, Bethesda, MD 20892.

Contact Person: Yvonne T. Maddox, PhD, Deputy Director, National Institute of Child Health, and Human Development, NIH, 9000 Rockville Pike MSC 7510, Building 31, Room 2A03, Bethesda, MD 20892, (301) 496-1848.

Any interested person may file written comments with the committee by forwarding the statement to the Contact Person listed on this notice. The statement should include the name, address, telephone number and when applicable, the business or professional affiliation of the interested person.

In the interest of security, NIH has instituted stringent procedures for entrance onto the NIH campus. All visitor vehicles, including taxis, hotel, and airport shuttles will be inspected before being allowed on campus. Visitors will be asked to show one form of identification (for example, a government-issued photo ID, driver's license, or passport) and to state the purpose of their visit.

Information is also available on the Institute's/Center's home page: <http://ww.nichd.nih.gov/about/nachhd.htm>, where an agenda and any additional information for the meeting will be posted when available.

In order to facilitate public attendance at the open session of Council, reserve seating will be made available to the first five individuals reserving seats in the main meeting room, Conference Room 6. Please contact Ms. Lisa Kaeser, Program and Public Liaison Office, NICHD, at 301-496-0536 to make your reservation. Additional seating will be available in the meeting overflow rooms, Conference Rooms 7 and 8. Individuals will also be able to view the meeting via NIH Videocast. Please go to the following link for Videocast access

instructions at: <http://www.nichd.nih.gov/about/overview/advisory/nachhd/virtual-meeting.cfm> The meeting is partially closed to the public.

(Catalogue of Federal Domestic Assistance Program Nos. 93.864, Population Research; 93.865, Research for Mothers and Children; 93.929, Center for Medical Rehabilitation Research; 93.209, Contraception and Infertility Loan Repayment program, National Institutes of Health, HHS)

Dated: April 29, 2011.

Jennifer S. Spaeth,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 2011-11034 Filed 5-4-11; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Diabetes and Digestive and Kidney Diseases; Notice of Closed Meetings

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

The meetings 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 Institute of Diabetes and Digestive and Kidney Diseases Special Emphasis Panel, PAR-09-247: NIDDK Ancillary Studies to Major Ongoing Clinical Research Studies in CKD (R01).

Date: May 27, 2011.

Time: 2 p.m. to 5 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, Two Democracy Plaza, 6707 Democracy Boulevard, Bethesda, MD 20892. (Telephone Conference Call.)

Contact Person: Najma Begum, PhD, Scientific Review Officer, Review Branch, DEA, NIDDK, National Institutes of Health, Room 749, 6707 Democracy Boulevard, Bethesda, MD 20892-5452. (301) 594-8894. begumn@nidk.nih.gov.

Name of Committee: National Institute of Diabetes and Digestive and Kidney Diseases Special Emphasis Panel, Periodontitis and Glycemic Control.

Date: June 15, 2011.

Time: 2 p.m. to 4 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, Two Democracy Plaza, 6707 Democracy Boulevard, Bethesda, MD 20892. (Telephone Conference Call.)

Contact Person: D. G. Patel, PhD, Scientific Review Officer, Review Branch, DEA, NIDDK, National Institutes of Health, Room 756, 6707 Democracy Boulevard, Bethesda, MD 20892-5452. (301) 594-7682. pateldg@nidk.nih.gov.

Name of Committee: National Institute of Diabetes and Digestive and Kidney Diseases Special Emphasis Panel, Studies Related to Diabetes.

Date: June 17, 2011.

Time: 2 p.m. to 4 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, Two Democracy Plaza, 6707 Democracy Boulevard, Bethesda, MD 20892. (Telephone Conference Call.)

Contact Person: D. G. Patel, PhD, Scientific Review Officer, Review Branch, DEA, NIDDK, National Institutes of Health, Room 756, 6707 Democracy Boulevard, Bethesda, MD 20892-5452. (301) 594-7682. pateldg@nidk.nih.gov.

(Catalogue of Federal Domestic Assistance Program Nos. 93.847, Diabetes, Endocrinology and Metabolic Research; 93.848, Digestive Diseases and Nutrition Research; 93.849, Kidney Diseases, Urology and Hematology Research, National Institutes of Health, HHS)

Dated: April 29, 2011.

Jennifer S. Spaeth,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 2011-11037 Filed 5-4-11; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Center for Research Resources; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. App.), 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 Center for Research Resources Initial Review Group, Comparative Medicine Review Committee.

Date: June 7-8, 2011.

Time: 8 a.m. to 12 p.m.

Agenda: To review and evaluate grant applications.

Place: Residence Inn Marriott, 7335 Wisconsin Avenue, Bethesda, MD 20814.

Contact Person: Bonnie B. Dunn, PhD, Scientific Review Officer, National Center For Research Resources, or National Institutes of Health, 6701 Democracy Blvd., 1 Democracy Plaza, Room 1074, MSC 4874, Bethesda, Md 20892-4874, 301-435-0824, dunnbo@mail.nih.gov.

(Catalogue of Federal Domestic Assistance Program Nos. 93.306, Comparative Medicine; 93.333, Clinical Research; 93.371, Biomedical Technology; 93.389, Research Infrastructure, 93.306, 93.333; 93.702, ARRA Related Construction Awards., National Institutes of Health, HHS)

Dated: April 29, 2011.

Jennifer S. Spaeth,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 2011-11040 Filed 5-4-11; 8:45 am]

BILLING CODE 4140-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Allergy and Infectious Diseases; Notice of Meeting

Pursuant to section 10(a) of the Federal Advisory Committee Act, as amended (5 U.S.C. App.), notice is hereby given of a meeting of the AIDS Research Advisory Committee, NIAID.

The meeting will be open to the public, 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.

Name of Committee: AIDS Research Advisory Committee, NIAID, AIDS Vaccine Research Subcommittee.

Date: May 24-25, 2011.

Time: 8:30 a.m. to 5 p.m.

Agenda: Presenting and discussing data on recombinant chimpanzee adenovirus vectors for malaria and AIDS vaccines and discussing future clinical trial plans for AIDS vaccine testing.

Place: National Institutes of Health, Natcher Building, 45 Center Drive, Conference Rooms E1 and E2, Bethesda, MD 20892.

Contact Person: James A. Bradac, PhD, Program Official, Preclinical Research and Development Branch, Division of AIDS, Room 5116, National Institutes of Health/ NIAID, 6700B Rockledge Drive, Bethesda, MD 20892-7628, 301-435-3754, jbradac@mail.nih.gov.

(Catalogue of Federal Domestic Assistance Program Nos. 93.855, Allergy, Immunology, and Transplantation Research; 93.856,