

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 moiety 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 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. The primary molecular target of these very potent compounds is the inhibition of both topoisomerase I and II, although other targets may be important as well. 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.

Dated: June 16, 2003.

Steven M. Ferguson,

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

[FR Doc. 03-15972 Filed 6-24-03; 8:45 am]

BILLING CODE 4140-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, HHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by agencies of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

ADDRESSES: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301/496-7057; fax: 301/402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Zap70 Protein Expression as a Marker for Chronic Lymphocytic Leukemia (CLL)

Louis M. Staudt *et al.* (NCI)
Serial No. 60/375,966 filed 25 Apr 2002
and Serial No. 10/309,548 filed 03 Dec 2002

Licensing Contact: Catherine Joyce; 301/435-5031; joycec@mail.nih.gov.

The presence or absence of somatic mutations in the expressed immunoglobulin heavy chain variable regions (IgVH) of chronic lymphocytic leukemia (CLL) cells provides prognostic information. Patients whose leukemic cells express unmutated IgVH regions (Ig-unmutated CLL) often have progressive disease whereas patients whose leukemic cells express mutated IgVH regions (Ig-mutated CLL) more often have an indolent disease. Given the difficulty in performing IgVH sequencing in a routine diagnostic

laboratory, this prognostic distinction is currently unavailable to most patients.

The present invention relates to the discovery that ZAP-70 expression also distinguishes the two CLL subtypes. Ig-unmutated CLL expressed ZAP-70 5.54-fold more highly than Ig-mutated CLL. ZAP-70 expression correctly predicted IgVH mutation status in 93% of patients, and ZAP-70 expression and IgVH mutation status were comparable in their ability to predict time to treatment requirement following diagnosis. Clinically applicable RNA and protein-based assays for ZAP-70 expression have been developed. These assays would yield important prognostic information for CLL patients.

The above-mentioned invention is available for licensing on an exclusive or non-exclusive basis.

ABCA13 Nucleic Acids and Proteins, and Uses Thereof

Michael Dean *et al.* (NCI)

DHHS Reference No. E-304-2000/0
filed August 20, 2003

Licensing Contact: Catherine Joyce; 301/435-5031; e-mail: joycec@mail.nih.gov.

This technology relates to the identification of a novel gene in the ABC (ATP-binding cassette transporter) gene superfamily, the ABCA13 gene. The ABC proteins are involved in extra- and intracellular membrane transport of various substrates such as ions, amino acids, peptides, sugars, vitamins, or steroid hormones and at least 14 members of the ABC gene superfamily have been described as associated with human disease. ABCA13 has high similarity with other ABCA subfamily genes that are associated with human inherited diseases. This includes ABCA1, the gene responsible for the cholesterol transport disorders Tangier disease and familial hypoalphalipoproteinemia, and ABCA4, the gene responsible for several retinal degeneration disorders. The ABCA13 gene is expressed in trachea, testes, and bone marrow. The ABCA13 gene maps to chromosome 7p12.3, a region that contains an inherited disorder affecting the pancreas and bone marrow (Shwachman-Diamond syndrome) as well as a locus involved in T-cell tumor invasion and metastasis (INM7), and therefore is a positional candidate for these disorders.

The above-mentioned invention is available for licensing on an exclusive or non-exclusive basis.

Dated: June 16, 2003.

Steven M. Ferguson,

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

[FR Doc. 03-15973 Filed 6-24-03; 8:45 am]

BILLING CODE 4140-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute on Alcohol Abuse and Alcoholism; Notice of Closed Meetings

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 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 on Alcohol Abuse and Alcoholism Special Emphasis Panel.

Date: July 14, 2003.

Time: 1 p.m. to 3 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, Wilco Building, 6000 Executive Boulevard, Bethesda, MD 20892 (Telephone Conference Call).

Contact Person: Eugene G. Hayunga, PhD, Chief, Extramural Project Review Branch, OSA, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Wilco Building, Suite 409, 6000 Executive Boulevard, MSC 7003, Bethesda, MD 20892-7003, (301) 443-2860, ehayunga@mail.nih.gov.

Name of Committee: National Institute on Alcohol Abuse and Alcoholism Special Emphasis Panel, RFA-AA03-008—College Drinking.

Date: July 17, 2003.

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

Agenda: To provide concept review of proposed grant applications.

Place: Bethesda Marriott Suites, 6711 Democracy Boulevard, Bethesda, MD 20817.

Contact Person: Jeffrey I. Toward, PhD, Scientific Review Administrator, National Institutes of Health, National Institute on Alcohol Abuse and Alcoholism, Extramural Project Review Branch, 6000 Executive Blvd., Suite 409, Bethesda, MD 20892-7003. (301) 435-5337.

(Catalogue of Federal Domestic Assistance Program Nos. 93.271, Alcohol Research Career Development Awards for Scientists and Clinicians; 93.272, Alcohol National Research Service Awards for Research Training; 93.273, Alcohol Research Programs; 93.891, Alcohol Research Center Grants, National Institutes of Health, HHS)

Dated: June 18, 2003.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 03-15967 Filed 6-24-03; 8:45 am]

BILLING CODE 4140-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Allergy and Infectious Disease; 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 Institute of Allergy and Infectious Diseases Special Emphasis Panel, Immunology Training Grant Applications.

Date: July 10, 2003.

Time: 11 a.m. to 12:30 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, 6700B Rockledge Drive, Bethesda, MD 20892 (Telephone Conference Call).

Contact Person: Geetha P. Bansal, PhD, Scientific Review Administrator, National Institute of Allergy and Infectious Diseases, National Institutes of Health, 6700-B Rockledge Drive, Bethesda, MD 20892-7616. (301) 402-5658, gbansal@niaid.nih.gov.

(Catalogue of Federal Domestic Assistance Program Nos. 93.855, Allergy, Immunology, and Transplantation Research; 93.856, Microbiology and Infectious Diseases Research, National Institutes of Health, HHS)

Dated: June 18, 2003.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 03-15968 Filed 6-24-03; 8:45 am]

BILLING CODE 4140-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Allergy and Infectious Diseases; 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 Institute of Allergy and Infectious Diseases Special Emphasis Panel, Biodefense and Emerging Infectious Diseases Research Opportunities.

Date: July 21, 2003.

Time: 12 p.m. to 4 p.m.

Agenda: To review and evaluate grant applications.

Place: 6700B Rockledge Drive, Bethesda, MD 20892 (Telephone Conference Call).

Contact Person: Priti Mehrotra, PhD, Scientific Review Administrator, Division of Extramural Activities, National Institute of Allergy and Infectious Diseases, National Institutes of Health, 6700-B Rockledge Drive, Room 2100, Bethesda, MD 20892-7616, (301) 496-2550, pm158b@nih.gov.

(Catalogue of Federal Domestic Assistance Program Nos. 93.855, Allergy, Immunology, and Transplantation Research; 93.856, Microbiology and Infectious Diseases Research, National Institutes of Health, HHS)

Dated: June 18, 2003.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 03-15969 Filed 6-24-03; 8:45 am]

BILLING CODE 4140-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Center for Scientific Review; Notice of Closed Meetings

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 meetings.

The meetings will be closed to the public in accordance with the