Inhibitors of Human Apurinic/Apyrimidinic Endonuclease 1 (APE1), an Anticancer Drug Target

Description of Technology: APE1 is the primary mammalian enzyme responsible for the removal of abasic (AP sites) in DNA and functions as part of the base excision DNA repair pathway (BER). BER is instrumental in the repair of DNA damage caused by DNA alkylating agents (e.g., many cancer chemotherapeutics). APE1 has been shown to be overexpressed in cancer cells. It has been postulated that APE1 would be an attractive target in anticancer treatment paradigms; preclinical and clinical data confirm that APE1 is a viable anticancer drug target.

To date, only one APE1 small molecule inhibitor has progressed to clinical trials (methoxyamine hydrochloride), and this compound inhibits a wide range of repair processes, which could result in undesired side-effects. The NIH inventors now report the discovery of a novel APE1 small molecule inhibitor, which exhibits potent in vitro activity, potentiates the cytotoxicity of DNA damaging agents (alkylators methylmethane sulfonate and Temozolomide), results in the accumulation of AP sites, and has favorable pharmacokinetic properties. The inventors plan to carry out further studies in mouse tumor xenograft models.

Applications: Cancer therapeutics as single agent as well as in combination therapy.

Development Status: In vivo pharmacokinetics data on lead compounds available.


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

Collaborative Research Opportunity: The NIEHS Laboratory of Signal Transduction is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize these mice or other strains derived from them, or cells or other reagents derived from them. Please contact Dr. Elizabeth Denholm (denholm@niehs.nih.gov) in the NIEHS Office of Technology Transfer, or the Inventor Dr. Perry Blackshear (black009@niehs.nih.gov) for more information.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

National Center on Minority Health and Health Disparities; 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 materials, 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 on Minority Health and Health Disparities Special Emphasis Panel, R13 Review.

Date: July 11, 2011.

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

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, 6707 Democracy Boulevard, Suite 800, Bethesda, MD 20892. (Virtual Meeting.)

Contact Person: Robert Nettey, M.D., Chief, Scientific Review Officer, National Institute on Minority Health and Health Disparities, 6707 Democracy Boulevard, Suite 800, Bethesda, MD 20892. (301) 496–3996. nettey@mail.nih.gov.

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.

Dated: July 1, 2011.

Jennifer S. Spaeth, Director, Office of Federal Advisory Committee Policy.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

National Center for Research Resources; 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 Center for Research Resources Special Emphasis Panel, NCRR Animal Resource.

Date: July 28, 2011.

Time: 1 to 2 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health/NCRR/OR, Democracy 1, 6701 Democracy Blvd., 1078, Bethesda, MD 20892.

Contact Person: Lee Warren Slice, PhD, Scientific Review Officer, Office of Review, National Center for Research Resources, 6701...