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 valid 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.

Inventors: David J. Maloney, et al. (NHGRI).

Publication: Manuscript submitted.


Licensing Contact: Betty B. Tong, PhD; 301–594–6565; tongb@mail.nih.gov.
DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Arthritis and Musculoskeletal and Skin Diseases

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 Institute of Arthritis and Musculoskeletal and Skin Diseases, Special Emphasis Panel, Ancillary Studies to Large Ongoing Clinical Projects

Date: July 20, 2011.

Time: 10 a.m. to 11 a.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, One Democracy Plaza, 6701 Democracy Boulevard, Suite 800, Bethesda, MD 20892.

Contact Person: Charles H Washabaugh, PhD, Scientific Review Officer, Scientific Review Branch, National Institute of Arthritis, Musculoskeletal and Skin Diseases, National Institutes of Health, 6701 Democracy Blvd, Suite 800, Bethesda, MD 20817. 301–594–4952. washbabc@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.

(Catalogue of Federal Domestic Assistance Program Nos. 93.846, Arthritis, Musculoskeletal and Skin Diseases Research, National Institutes of Health, HHS)

Dated: July 1, 2011.

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

DEPARTMENT OF HOMELAND SECURITY

U.S. Citizenship and Immigration Services

Agency Information Collection Activities: Form I–907, Extension of a Currently Approved Information Collection; Comment Request

ACTION: 30-Day notice of information collection under review: form I–907, request for premium processing service.

The Department of Homeland Security, U.S. Citizenship and Immigration Services (USCIS) will be submitting the following information collection request to the Office of Management and Budget (OMB) for review and clearance in accordance with the Paperwork Reduction Act of 1995. The information collection was previously published in the Federal Register on April 12, 2011, at 76 FR 20361, allowing for a 60-day public comment period. USCIS did not receive any comments.

The purpose of this notice is to allow an additional 30 days for public comments. Comments are encouraged and will be accepted until August 8, 2011. This process is conducted in accordance with 5 CFR 1320.10.

Written comments and/or suggestions regarding the item(s) contained in this notice, especially regarding the estimated public burden and associated response time, should be directed to the Department of Homeland Security (DHS), and to the Office of Management and Budget (OMB), USCIS Desk Officer. Comments may be submitted to: USCIS, Chief, Regulatory Products Division, Clearance Office, 20 Massachusetts Avenue, Washington, DC 20529–2020. Comments may also be submitted by DHS via facsimile to 202–272–0997 or via e-mail at uscisfrcomment@dhs.gov, and to the OMB USCIS Desk Officer via facsimile at 202–395–8506 or via e-mail at oira_submission@omb.eop.gov.

When submitting comments by e-mail please make sure to add OMB Control Number 1615–0048 in the subject box. Written comments and suggestions from the public and affected agencies should address one or more of the following four points:

1. Evaluate whether the collection of information is necessary for the proper performance of the functions of the agency, including whether the information will have practical utility;
2. Evaluate the accuracy of the agency’s estimate of the burden of the collection of information, including the validity of the methodology and assumptions used;
3. Enhance the quality, utility, and clarity of the information to be collected; and
4. Minimize the burden of the collection of information on those who are to respond, including through the use of appropriate automated, electronic, mechanical, or other technological collection techniques, or other forms of information technology, e.g., permitting electronic submission of responses.

Overview of This Information Collection

1. Type of Information Collection: Extension of an existing information collection.
2. Title of the Form/Collection: Request for Premium Processing Service.
4. Affected public who will be asked or required to respond, as well as a brief abstract: Primary: Businesses. Through this form, USCIS provides employers with the opportunity to request expedite processing of certain employment-based requests.
5. An estimate of the total number of respondents and the amount of time estimated for an average respondent to respond:
   - Filing by Mail 96,000 responses at .50 hours (30 minutes) per response.
   - Electronically 4,000 responses at .333 hours (20 minutes) per response.
6. An estimate of the total public burden (in hours) associated with the collection: 49,332 annual burden hours.

If you need a copy of the information collection instrument, please visit the Web site at: http://www.regulations.gov. We may also be contacted at: USCIS, Regulatory Products Division, 20 Massachusetts Avenue, NW., Washington, DC 20529–2020, telephone number 202–272–8377.

Dated: July 1, 2011.

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

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