Subject, city, state	Effective date
WOONSOCKET, RI	
UNDERWOOD, GWENDOLYN HAMBRIGHT TUSCALOOSA, AL	12/20/1999
UNDERWOOD, MARY C KEZZIAH COLUMBUS, GA	12/20/1999
WALKER, PATRICK O'NEAL SELMA, AL	12/20/1999
WALLACE, LOIS J HARDY HANCEVILLE, AL	12/20/1999
WATKINS, JUDITH MAEBELL TUSCUMBIA, AL	12/20/1999
WESTWOOD, RENEE M WARREN, MI	12/20/1999
WILLIAMS, DEBORAH K OCEAN SPRINGS, MS	12/20/1999
WILLIAMS, MARK STEVEN MENLO PARK, CA	12/20/1999
WITTMAYER, JODY GRAND FORKS, ND	12/20/1999
WOOTEN, DUSTY CANDEANIA ATMORE, AL	12/20/1999
YOOD, STEVEN H NASHVILLE, TN	12/20/1999
FRAUD/KICKBACKS	
GILL, CHRISTOPHER F LEXINGTON, SC	06/24/1999
MIDLAND MEDICALS, INC LEXINGTON, SC	06/24/1999
SOUTHWEST HOME HEALTH PHOENIX, AZ	08/30/1999
OWNED/CONTROLLED BY CONVICTED/EXCLUDED	
ADVANCED CHIROPRACTIC CENTER SANTA CLARA, CA	12/20/1999
ADVANCED CHIROPRACTIC CLINIC JAMAICA, NY	12/20/1999
AFFORDABLE CHIROPRACTIC WHEAT RIDGE, CO	12/20/1999
ANN L LAGONEGRO, D M D, P C GLOUCESTER, VA	12/20/1999
B & G DIAGNOSTIC SYSTEMS, INC BOCA RATON, FL	12/20/1999
CALLENDER & CALLENDER LOS ANGELES, CA	12/20/1999
CANOGA CHIROPRACTIC LOS ANGELES, CA	12/20/1999
COASTAL INDUSTRIAL HEALTH CARE LOS ANGELES, CA	12/20/1999
COTHRAN CHIROPRACTIC CLINIC POTEAU, OK	12/20/1999
FAMILY DENTISTRY PATERSON, NJ	12/20/1999
GREGORY A WALSH, D C, P A DAYTONA BEACH, FL	12/20/1999
HAWKINS CHIROPRACTIC CLINIC SANDY, UT	12/20/1999
IXE, INC SAN FRANCISCO, CA	12/20/1999
PAN AMERICAN DRUGS, INC MIAMI, FL	12/20/1999
PHOENIX TREATMENT CTR, P C PHOENIX, AZ	12/20/1999
R & A DIAGNOSTIC SERVICES, INC MIAMI, FL	12/20/1999
RAINBOW CHIROPRACTIC HOUSTON, TX	12/20/1999
RIVERLAND MEDICAL CENTER BALDWIN, LA	12/20/1999
SANDERS CHIROPRACTIC INDIAN HARBOUR BCH, FL	12/20/1999
DEFAULT ON HEAL LOAN	
ALLEN, SAM J BROWNSVILLE, TX	12/20/1999
ARTEAGA, WALTER J PASO ROBLES, CA	12/20/1999
BENAVIDEZ, CHARLES A ELK GROVE, CA	12/20/1999
BROWN, JON DAVID PHOENIX, AZ	12/20/1999
CALDWELL, ANDRIA P BIRMINGHAM, AL	12/20/1999
CAMILING, ADOR Z ALTADENA, CA	12/20/1999
CARSON, BRAD W OMAHA, NE	12/20/1999
CONTRERAS, LAWRENCE OCEANSIDE, CA	12/20/1999
ENCARNACION, DANNY R BRONX, NY	12/20/1999
ENGEL, ROB L GARDEN GROVE, CA	12/20/1999
EPSTEIN, JUDY J SAN DIEGO, CA	12/20/1999
FAIR, BENNY JR FORT WAYNE, IN	11/08/1999
GRATIA, ALLAN R BANDERA, TX	12/20/1999
GUTIERREZ, OSCAR V LAREDO, TX	12/20/1999
HARMAN, HAROLD C PHILADELPHIA, PA	12/20/1999
HARNESS, DONITA M HAMLET, IN	12/20/1999
HARPER, JOHN L OCEANSIDE, CA	12/20/1999
IGBOKWE, NDUBUISI A HOUSTON, TX	12/20/1999
INMAN, THOMAS C JR HOUSTON, TX	12/20/1999
JOHNSON, CRAIG B GLENDALE, CA	12/20/1999
LOCK, JANE M ROYERSFORD, PA	12/20/1999
LONGO, TONY D GRESHAM, OR	12/20/1999
LOVELACE, GEORGE E RUSSELL, KY	12/20/1999
LUTA, PATRICIA L SANTA ROSA, CA	12/20/1999
MAGER, DENNIS J DEPEW, NY	12/20/1999
MILES, JAMIE A MOORPARK, CA	12/20/1999
MOAREFI, MAHMOUD R LOS ANGELES, CA	12/20/1999
MOORE, KEITH S KANSAS CITY, MO	12/20/1999
NEWELL, CHARLES F SANTEE, CA	12/20/1999
NGUYEN, TUAN ANN PORTLAND, OR	12/20/1999
ORNER, RETA G CHICO, CA	12/20/1999
PORTILLO, CARLOS J SAN JOSE, CA	12/20/1999
SABAL, MARY M ORANGE BEACH, AL	12/20/1999
SCHARTMAN, ALLYSON C SAN DIEGO, CA	12/20/1999
SCHIFF, BARBARA S WOODLAND HILLS, CA	12/20/1999
STEVENSON, ROBERT C ALEXANDRIA, VA	12/20/1999
STRONG-FIELDS, MICHELLE A PHILADELPHIA, PA	12/20/1999
TAYLOR, LINDA C JONESBORO, AR	12/20/1999
TAYLOR, JAMES W HAMPTON, VA	12/20/1999
TRIPP, ROBERT A LAKEWOOD, CA	12/20/1999
WILSON, RICHARD E OPELOUSAS, LA	12/20/1999

Dated: December 2, 1999.

Joanne Lanahan,

Director, Health Care Administrative Sanctions, Office of Inspector General.

[FR Doc. 99–32216 Filed 12–10–99; 8:45 am]

BILLING CODE 4150–04–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute: Opportunity for a Cooperative Research and Development Agreement (CRADA) for the Further Development and Commercialization of Methods Designed To Screen and Use Modulators of Nitric Oxide Synthase 2 (NOS2) Activity for the Diagnosis and Treatment of Cancer

The National Cancer Institute's Laboratory of Human Carcinogenesis (LHC) has identified and characterized *in vitro* and *in vivo* methods designed to screen modulators of NOS2 activity using cell lines that are deficient in the expression of the tumor suppressor gene, p53. Furthermore, LHC has created methods to predict the chemotherapeutic benefit of administering NOS2 inhibitors to cancer patients as a method for treating cancer.

AGENCY: National Institutes of Health, PHS, DHHS.

ACTION: Notice.

SUMMARY: The National Cancer Institute (NCI) seeks a Cooperative Research and

Development Agreement (CRADA) Collaborator to aid NCI in the identification and characterization of modulators of nitric oxide synthase 2 (NOS2) activity and in the development, evaluation and commercialization of methods for treating cancer that involve the clinical use of novel NOS2 modulators. NOS2 is an inducible enzyme that produces nitric oxide (NO), a mutagenic and angiogenic molecule (1,2). To define a role of NO in tumor progression, NCI has generated human carcinoma cell lines that produce NO constitutively. NCI has determined that tumor-associated NO production may promote cancer progression by providing a selective growth advantage to tumor cells bearing a mutant form of the tumor suppressor and transcription factor, p53. Furthermore, NCI has determined that accelerated tumor growth in these cells is associated with an increased expression of the vascular endothelial growth factor (''VEGF''), leading to tumor neovascularization. NCI has generated methods for screening modulators of NOS2 activity using cells lines that contain a mutant p53 gene. In addition, NCI has generated methods for using these cell lines in screening assays that test the use of potential NOS2 inhibitors in the treatment of patients with tumors lacking p53 function.

Several applications for this technology have been identified. They include the use of these methods as (1) diagnostic assays to determine the genetic and functional status of the p53 gene; (2) assays to predict the chemotherapeutic benefit of administering current NOS2 inhibitors to cancer patients; and (3) assays to screen for novel modulators of NOS2 activity for use in the treatment of cancers. NCI is looking for a CRADA Collaborator with a demonstrated record of success in cancer diagnostics and therapeutics. The proposed term of the CRADA can be up to five (5) years.

DATES: Interested parties should notify the Technology Development and Commercialization Branch of the NCI in writing of their interest in filing a formal proposal no later than (February 11, 2000. Potential CRADA Collaborators will then have an additional thirty (30) days to submit a formal proposal.

ADDRESSES: Inquiries and proposals regarding this opportunity should be addressed to Holly S. Symonds, Technology Development Specialist (Tel. # 301–496–0477, FAX # 301–402–2117), Technology Development and Commercialization Branch, National Cancer Institute, 6120 Executive Blvd., Suite 450, Rockville, MD 20852. Inquiries directed to obtaining patent license(s) needed for participation in the CRADA opportunity should be addressed to Richard Rodriguez, Technology Licensing Specialist, Office of Technology Transfer, National Institutes of Health, 6011 Executive Blvd., Suite 325, Rockville, MD 20852, (Tel. 301–496–7056, ext. 287; FAX 301–402–0220).

SUPPLEMENTARY INFORMATION: A Cooperative Research and Development Agreement (CRADA) is the anticipated joint agreement to be entered into with NCI pursuant to the Federal Technology Transfer Act of 1986 and Executive Order 12591 of April 10, 1987 as amended by the National Technology Transfer Advancement Act of 1995. NCI is looking for a CRADA partner to collaborate with NCI in the further development and commercialization of screening assays and methods relating to the analysis of NOS2 activity in cancers exhibiting a nonfunctional p53 and to the use of NOS2 inhibitors in the treatment of such cancers. The expected duration of the CRADA would be from one (1) to five (5) years.

Increased expression of inducible nitric oxide synthase (NOS2) has been found in a variety of human cancers (3–6). NOS2 is an inducible enzyme that produces nitric oxide (NO), a mutagenic and angiogenic molecule (1,2). NO is an activator of the p53 tumor suppressor gene function (7–9), however, p53 will repress the expression of NOS2, both *in vitro* and *in vivo* (8,10,11). To investigate the role of NO in tumor progression, NCI created genetically engineered human carcinoma cell lines that constitutively produce endogenous NO. Using these cell lines, NCI has found that the effect of NO on tumor growth is p53-dependent due to its ability to repress the expression of NOS2, and that endogenously produced NO accelerates tumor growth by inducing expression of the vascular endothelial growth factor (VEGF) and neovascularization.

The NCI's data indicates that, in the presence of wild-type p53, constitutive expression of NOS2 in tumors could lead to a p53-mediated growth arrest in the epithelial cells closely surrounding the source of NO production. The growth inhibition of such cells would provide a strong selective pressure for a mutation to occur in the p53 gene. Indeed, tumors of the breast, brain, head and neck and colon that overexpress NOS2 have a high frequency of p53 mutations (3, 4, 6, 11, 12). Tumor growth would then be further supported by the NO-mediated induction of VEGF and angiogenesis. Since p53 has been shown to regulate the production of NO by altering the activity of NOS2, NO production would remain unchecked, supporting the growth of the tumor (8, 10, 11). The loss of p53 function in p53 deficient or mutant cells would permit both the growth of tumor cells in the presence of moderate NO concentrations and the release of angiogenic factors such as VEGF. However, NCI suggests that such tumors with mutant p53 function could be therapeutically and prophylactically treated with NOS2 inhibitors.

To address this possibility, NCI has developed a series of methods aimed at screening modulators of NOS2 activity using p53 mutant cells that express NOS2. In one method, modulators of NOS2 activity are screened *in vitro,* using p53 mutant cells that constitutively or endogenously express NOS2. The cells are exposed to potential NOS2 inhibitors, and the level of VEGF expression is determined by various methods. In addition, the level of nitrate versus nitrite produced is measured to determine the level of NOS2 activity in the presence of the potential inhibitor compounds.

To further assess the therapeutic benefit of a potential NOS2 inhibitor, NCI has developed an *in vivo* method of screening modulators of NOS2 activity. In such method, p53 mutant cells that constitutively or endogenously express NOS2 are implanted into an immune deficient athymic nude mouse model and then are treated with potential NOS2 inhibitor compounds. Modulation of NOS2 activity can be determined as above and also by measuring tumor growth in the treated animals as compared to untreated control animals.

NCI suggests that the benefit of administering potential NOS2 inhibitors to cancer patients may be assessed by determining the p53 status and NOS2 expression pattern of the tumors. If a patient has a cancer that expresses NOS2 and is deficient in normal p53 activity, then the patient may be a candidate for treatment with NOS2 inhibitors. NCI has developed methods to both assess the benefit of such treatment and to administer potential NOS2 inhibitors to cancer patients in a clinical setting.

NCI is seeking one or more CRADA Collaborators to further develop the above methods for preclinical, diagnostic and clinical uses. Specifically, NCI believes the methods could be applied to a drug screening protocol in which potential modulators of NOS2 could be identified and characterized. Furthermore, NCI predicts that the methods could be applied to a diagnostic kit for use in a

clinical setting to determine whether or not a particular cancer patient is a candidate for such treatment with regards to the p53 status of the tumor. Once identified and characterized, novel NOS2 inhibitors may be administered to candidate cancer patients and evaluated in their ability to treat various tumors.

The described methods are the subject of U.S. provisional patent application, USSN 60/109,563, filed on November 23, 1998 by the Public Health Service on behalf of the Federal Government. Furthermore, the initial report and characterization of the invention is described in: Ambs *et al,* Nature Medicine (1998) vol. 4, no.12:1371–1376.

References

1. Nguyen *et al* (1992) PNAS 89:3030–3034.
2. Jenkins *et al* (1995) PNAS 92:4392–4396.
3. Thomsen *et al* (1995) Br. J. Cancer 72:41–44.
4. Ellie *et al* (1995) Neuroreport 7:294–296.
5. Ambs *et al* (1998) Cancer Res. 58:334–341.
6. Gallo *et al* (1998) J. Natl. Cancer Inst. 90:587–596.
7. Messmer *et al* (1996) Biochem J. 319:299–305.
8. Forrester, K. *et al* (1996) PNAS 93:2442–2447.
9. Calmels *et al* (1997) Cancer Res. 57:3365–3369.
10. Ambs *et al* (1997) Faseb J. 11:443–448.
11. Ambs *et al* (1998) PNAS 95:8823–8828.
12. Thomsen *et al* (1997) Cancer Res. 57:3300–3304.

Under the present proposal, the overall goal of the CRADA collaboration will involve the following:

1. Use of the genetically engineered cells lines and assays in preclinical screening assays of potential NOS2 inhibitors; and

2. Use of the cell lines and candidate NOS2 inhibitors in diagnostic, preclinical and clinical settings.

Party Contributiions:

The role of the NCI in the CRADA may include, but not be limited to:

1. Providing intellectual, scientific, and technical expertise and experience to the research project.

2. Providing the CRADA Collaborator with information and data relating to the methods developed to assess the activity of p53 and NOS2 and to screen for potential modulators of NOS2 activity.

3. Planning research studies and interpreting research results.

4. Carrying out research to validate the use of the NOS2-related methods and candidate NOS2 inhibitors in preclinical, diagnostic and clinical settings.

5. Publishing research results.

6. Developing additional potential applications of the methods.

The role of the CRADA Collaborator may include, but not be limited to:

1. Providing significant intellectual, scientific, and technical expertise or experience to the research project.

2. Planning research studies and interpreting research results.

3. Producing candidate NOS2 inhibitors under cGMP conditions in sufficient quantities to support the CRADA studies.

4. Carrying out research to validate the use of the NOS2-related methods and candidate NOS2 inhibitors in preclinical, diagnositc and clinical settings, including toxicologic and pharmacologic assays, as appropriate.

5. Providing technical and/or financial support to facilitate scientific goals and for futher design of applications of the technology outlined in the agreement.

6. Publishing research results.

Selection criteria for choosing the CRADA Collaborator may include, but not be limited to:

1. A demonstrated record of success in the screening of chemotherapeutic agents.

2. A demonstrated background and expertise in cancer research and treatment.

3. The ability to collaborate with NCI on further research and development of this technology. This ability will be demonstrated through experience and expertise in this or related areas of technology indicating the ability to contribute intellectually to ongoing research and development.

4. The demonstration of adequate resources to perform the research and development of this technology (*e.g.* facilities, personnel and expertise) and to accomplish objectives according to an appropriate timetable to be outlined in the CRADA Collaborator's proposal.

5. The willingness to commit best effort and demonstrated resources to the research and development of this technology, as outlined in the CRADA Collaborator's proposal.

6. The demonstration of expertise in the commercial development and production of products related to this area of technology.

7. The level of financial support the CRADA Collaborator will provide for CRADA-related Government activities.

8. The willingness to cooperate with the National Cancer Institute in the timely publication of research results.

9. The agreement to be bound by the appropriate DHHS regulations relating to human subjects and to all PHS policies relating to the use and care of laboratory animals.

10. The willingness to accept the legal provisions and language of the CRADA with only minor modifications, if any. These provisions govern the distribution of future patent rights to CRADA inventions. Generally, the rights of ownership are retained by the organization that is the employer of the inventor with (1) the grant of a license for research and other Government purposes to the Government when the CRADA Collaborator's employee is the sole inventor, or (2) the grant of an option to elect an exclusive or nonexclusive license to the CRADA Collaborator when the Government employee is the sole inventor.

Dated: October 8, 1999.

Kathleen Sybert,

Chief, Technology Development and Commercialization Branch, National Cancer Institute, National Institutes of Health.

[FR Doc. 99–32138 Filed 12–10–99; 8:45 am]

BILLING CODE 4140–01–P

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 if 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: Center for Scientific Review Special Emphasis Panel ZRG1 BM–1 01.

Date: December 7, 1999.

Time: 2:00 p.m. to 3:30 p.m.

Agenda: To review and evaluate grant applications.

Place: NIH, Rockledge 2, Bethesda, MD 20892 (Telephone Conference Call).