

41. Kyle Youngberg Ames, Iowa, Court of Federal Claims Number 00-0345V
42. Wanda E. Dennis on behalf of Brian Keith Wingate, Manning, South Carolina, Court of Federal Claims Number 00-0346V
43. Tracy and Scott Weeks on behalf of Jenica Weeks, Deceased, Boston, Massachusetts, Court of Federal Claims Number 00-0348V
44. Chue Xiong, Sacramento, California, Court of Federal Claims Number 00-350V
45. Marion Underwood on behalf of Cesar Zachary Moreno, Deceased, Boston, Massachusetts, Court of Federal Claims Number 00-0357V
46. Ann Haynes on behalf of Elizabeth Haynes, Boston, Massachusetts, Court of Federal Claims Number 00-0358V
47. Cynthia Wells on behalf of Ezra James McCorkle, Boone, North Carolina, Court of Federal Claims Number 00-0359V
48. Sandra and William Spoon on behalf of William Spoon, Phoenix, Arizona, Court of Federal Claims Number 00-0360V
49. Kimberly Willingham on behalf of Courtney Willingham, Rockford, Illinois, Court of Federal Claims Number 00-0363V
50. Kristin and Mark Rogers on behalf of Colin Rogers, Chapel Hill, North Carolina, Court of Federal Claims Number 00-0368V
51. Stephanie and Cory Geho on behalf of Griffin Cole Geho, Portsmouth, Ohio, Court of Federal Claims Number 00-0370V
52. Sherri Lynn Boothby, Vienna, Virginia, Court of Federal Claims Number 00-0371V
53. Kristin Rogers on behalf of Colin Rogers, Chapel Hill, North Carolina, Court of Federal Claims Number 00-0372V
54. Anthony Joseph Tedesco, Clinton Township, Michigan, Court of Federal Claims Number 00-0373V

Dated: October 26, 2000.

**Claude Earl Fox,**

*Administrator.*

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**BILLING CODE 4160-15-U**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

#### **National Cancer Institute: Opportunity for a Cooperative Research and Development Agreement (CRADA) for the Identification and Development of Chemical Compounds That Interact With the Polo-Box of Polo Kinases, as Potential Therapeutic Targets for the Inhibition of Cellular Proliferation**

**AGENCY:** National Institutes of Health, PHS, DHHS

**ACTION:** Notice.

**SUMMARY:** Members of the polo subfamily of protein kinases play important roles in cell proliferation, and regulation of polo kinases may be crucial in the control of cell division. The polo kinases contain a distinct region of homology in the C-terminal non-catalytic domain, termed the polo-box. Scientists from the National Cancer Institute (NCI) have demonstrated that over-expression of this non-catalytic C-terminal domain in budding yeast results in a dominant-negative inhibition of cell division. NCI seeks a Cooperative Research and Development Agreement (CRADA) Collaborator to aid in the identification and development of chemical compounds that interact with the polo-box of polo kinases, as potential therapeutic targets for the inhibition of cellular proliferation.

**DATES:** Interested parties should notify this office in writing of their interest in filing a formal proposal no later than January 2, 2000. Potential CRADA Collaborators will then have an additional thirty (30) days to submit a formal proposal. CRADA proposals submitted thereafter may be considered if a suitable CRADA Collaborator has not been selected.

**ADDRESSES:** Inquires and proposals regarding this opportunity should be addressed to Laurie W. Whitney, Ph.D., 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 Vasant Gandhi, J.D., Ph.D., Technology Licensing Specialist, Office of Technology Transfer, National Institutes of Health, 6011 Executive Blvd., Suite 325, Rockville, MD 20852, (Tel: 301-496-7056, ext. 224, 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 aide NCI in the identification and development of chemical compounds which act as polo-box inhibitors. The expected duration of the CRADA would be from one (1) to five (5) years.

Members of the polo subfamily of protein kinases appear to play pivotal roles in cell division and proliferation. These include mammalian Plk, Snk, and Fnk/Prk, *Xenopus laevis* Plx1, *Drosophila melanogaster* polo, *Schizosaccharomyces pombe* Plo1, and *Saccharomyces cerevisiae* Cdc5. The polo subfamily members are characterized by the presence of a distinct region of homology in the C-terminal non-catalytic domain, termed the polo-box, which is essential for subcellular localization and mitotic functions of the polo kinases. Regulation of polo kinases may be crucial in the control of cell division. In mammalian cells, Plk is expressed at high levels in mitotically active cells and in tumors of various origins. Constitutive expression of Plk in NIH3T3 cells induces oncogenic focus formation, and these Plk-transformed cells can form tumors in nude mice. These data suggest that Plk expression is closely related to cellular proliferation, and that uncontrolled Plk expression may lead to the development of cancers in humans. Genetic and biochemical analyses indicate that polo kinases regulate diverse cellular events at various stages of the M phase. In addition to their roles in spindle formation and centrosome maturation, polo kinases appear to regulate important biochemical steps at the G2/M transition, such as activation of Cdc2 through Cdc25C phosphatase, DNA damage checkpoint adaptation, and activation of the anaphase-promoting complex (APC) in various eukaryotic systems. In addition, recent data suggest that polo kinases play important roles in cytokinesis.

In budding yeast, overexpression of the non-catalytic C-terminal domain of either Plk or Cdc5 (plkΔN or cdc5ΔN), but not the corresponding polo-box mutant, results in severe connected cell morphology. Provision of functional Cdc5 remedies this phenotype, indicating that over-expression of cdc5ΔN or plkΔN results in a dominant-negative inhibition of cell division and

that an intact polo-box is required for this event. These data raise an intriguing possibility that conditional expression of the polo-box domain may selectively inhibit the mitotic functions of polo kinases. Furthermore, our observation suggests that the polo-box peptide may act as a potential anti-cancer therapeutic agent. Alternatively, isolation of small chemical compounds that bind to the polo-box and interfere with its function may yield a strategy to regulate highly proliferative malignant cells. We have developed two yeast strains that conditionally express the polo-box domains of Plk (KLY1212) or Cdc5 (KLY1083). Isolation of chemical compounds alleviating the dominant-negative cell division defect of these strains may lead to identification of polo-box inhibitors. Since the polo-box is an essential and unique domain for polo kinases, these inhibitors may likely provide selective tools to control the cell proliferation without interfering with other protein kinases.

The described methods are the subject of a U.S. provisional patent application filed May 23, 2000 by the Public Health Service on behalf of the Federal Government. Furthermore, the initial report and characterization of the invention is described in: Song S, and Lee KS. A novel function of *Saccharomyces cerevisiae* CDC5 in cytokinesis (submitted for publication). Further reference to the invention can be found in: (1) Song S, Grenfell TX, Garfield S, Erikson RL, and Lee KS. (2000). Essential function of the polo-box of Cdc5 in subcellular localization and induction of cytokinetic structures. *Mol. Cell. Biol.* 20, 286–298, and (2) Lee KS, Grenfell TZ Yarm, FR, and Erikson RL (1998). Mutation of the polo-box disrupts localization and mitotic functions of the mammalian polo kinase Plk. *Proc. Natl. Acad. Sci. USA* 95:9301–9306.

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

(1) Identification and isolation of chemical compounds that alleviate the dominant-negative cell division defect of yeast strains that conditionally express the polo-box domains of Plk or Cdc5.

(2) Development of these chemical compounds as tools to control cellular proliferation without interfering with other protein kinases.

#### Party Contributions

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 polo kinases.

3. Planning research studies and interpreting research results.

4. Carrying out research with validates and expands on the role of the dominant-negative inhibition of cell proliferation found using the intact polo-box.

5. Publishing research results.

6. Developing additional potential applications related to inhibition of cell proliferation using polo-box inhibitors.

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

4. 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 areas of isolation, purification, characterization, and therapeutic development of chemical compounds.

2. A demonstrated background and expertise in cancer-related sciences.

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 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 17, 2000.

**Kathleen Sybert,**

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

[FR Doc. 00–28120 Filed 11–1–00; 8:45 am]

**BILLING CODE 4140–01–M**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

#### National Cancer Institute, 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 a meeting of the President's Cancer Panel.

The meeting will be closed to the public in accordance with the provisions set forth in section 552b(c)(9)(B), Title 5 U.S.C., as amended because the premature disclosure of other and the discussions would likely to significantly frustrate implementation of recommendations.

*Name of Committee:* President's Cancer Panel.

*Date:* October 26, 2000.

*Time:* 4 pm to 6 pm.

*Agenda:* To review and evaluate other.

*Place:* National Institutes of Health, 31 Center Drive, Building 31, Room 4A48, Bethesda, MD 20892–2473 (Telephone Conference Call).

*Contact Person:* Maureen O. Wilson, Phd, Executive Secretary, National Cancer Institute, National Institutes of Health, 31 Center Drive, Building 31, Room 4A48, Bethesda, MD 20892, 301/496–1148.

This notice is being published less than 15 days to the meeting due to scheduling conflicts.

(Catalogue of Federal Domestic Assistance Program Nos. 93.392, Cancer Construction; 93.393, Cancer Cause and Prevention Research; 93.394, Cancer Detection and Diagnosis Research; 93.395, Cancer