

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**National Institutes of Health**

**Licensing Opportunity and/or Cooperative Research and Development Agreement (CRADA) Opportunity for Novel Treatment of Tumors With Anticancer Drugs Activated by Thymidylate Synthase**

**AGENCY:** National Institutes of Health, Public Health Service, DHHS.

**ACTION:** Notice.

**SUMMARY:** The National Institutes of Health and the Laboratory of Clinical Pharmacology, Center for Drug Evaluation and Research, of the Food and Drug Administration are seeking licensees and/or CRADA partners for the further development, evaluation, and commercialization of materials and methods for a novel class of chemotherapeutic agents and a novel treatment strategy. The invention claimed in DHHS Reference No. E-058-97/0, "Novel Treatment of Tumors With Anticancer Drugs Activated by Thymidylate Synthase" (J Collins, R Klecker, A Katki), filed 29 Oct 97, is available for licensing (in accordance with 35 U.S.C. 207 and 37 CFR Part 404) and/or further development under one or more CRADAs in the clinically important applications described below in the Supplementary Information section.

**DATES:** There is no deadline by which license applications must be received. CRADA proposals should be received on or before May 12, 1998 for priority consideration. However, CRADA proposals submitted thereafter will be considered until a suitable CRADA Collaborator is selected.

**ADDRESSES:** Questions about the licensing opportunity should be addressed to Joseph Contrera, M.S., J.D., Technology Licensing Specialist, Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; Telephone: 301/496-7056 ext. 244; Fax: 301/402-0220; E-mail: ContrerJ@od.nih.gov.

CRADA proposals and questions should be addressed to Ms. Beatrice A. Droke, Food and Drug Administration, 5600 Fishers Lane, Park 3-30 HFA 500, Rockville, MD 20853; Telephone: 301/443-6890; Fax: 301/443-3690; E-mail: bdroke@bangate.fda.gov.

**SUPPLEMENTARY INFORMATION:** Thymidylate Synthase (TS) is an enzyme of metabolism which is part of the DNA synthesis pathway in both normal and tumor cells. It has been

known for decades that TS is expressed in tumor cells in quantities that are significantly higher than most non cancerous tissues. There has been much research into developing chemotherapeutic drugs which attempt to block or inhibit TS in tumor cells in an effort to shrink or slow their growth in vivo. Drugs such as fluorouracil and floxuridine are examples of this class of TS inhibitors.

The problem with enzyme inhibiting drugs is that over a short period of time, if the tumor cells are not killed, they become tremendously resistant to the inhibitors by various mechanisms. Usually the tumors boost expression of TS to overcome the inhibitor, but many other avenues are available to the tumor, such as pumping the drug out of the cell and mutating the enzyme to minimize the drug effect. At present, once the treated tumors start producing high levels of TS there is no effective therapy available.

Instead of inhibiting TS, this new strategy involves using TS to turn a uracil analog with low toxicity into highly toxic thymidine analog. The treatment would benefit patients with resistant tumors who were previously treated with TS inhibitors. The benefits of this type of prodrug are obvious. Patients could be treated with relatively high doses of the low toxicity prodrug thus ensuring high enough concentrations to penetrate the patients tissues and only the tumor cells will be actively converting the prodrug to its toxic metabolite thus dramatically lowering the severity of chemotherapeutic side effects. Moreover, there is less chance of the cells becoming resistant because they cannot down-regulate TS synthesis without slowing their own growth while making more and more toxic metabolites which in turn will kill the cancer cells.

Information about the patent application and pertinent information not yet publicly described can be obtained under a Confidential Disclosure Agreement. Respondees interested in licensing the invention(s) will be required to submit an Application for License to Public Health Service Inventions. Respondees interested in submitting a CRADA proposal should be aware that it may be necessary to secure a license to the above patent rights in order to commercialize products arising from a CRADA.

Dated: February 3, 1998.

**Barbara M. McGarey,**  
*Deputy Director, Office of Technology Transfer.*

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**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 the following meeting of the National Cancer Institute Initial Review Group:

*Agenda/Purpose:* To review, discuss and evaluate grant applications

*Committee Name:* Subcommittee A—Cancer Centers.

*Date:* April 6-7, 1998.

*Time:* April 6-8:00 a.m. to Recess; April 7-8:00 a.m. to Adjournment.

*Place:* Double Tree Hotel, 1750 Rockville Pike, Rockville, MD 20852.

*Contact Person:* David E. Maslow, Ph.D., Scientific Review Administrator, National Cancer Institute, NIH, 6130 Executive Blvd., EPN, Room 643A, Bethesda, Md 20892, Telephone: 301-496-2330.

The meeting will be closed in accordance with the provisions set forth in secs. 552b(c)(4) and 552b(c)(6), Title 5, U.S.C. Applications and the discussions could reveal confidential trade secrets or commercial property such as patentable material and personal information concerning individuals associated with the applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

(Catalog of Federal Domestic Assistance Program Numbers: 93.393, Cancer Cause and Prevention Research; 93.394, Cancer Detection and Diagnosis Research; 93.395, Cancer Treatment Research; 93.396, Cancer Biology Research; 93.397, Cancer Centers Support; 93.398, Cancer Research Manpower; 93.399, Cancer Control)

Dated February 6, 1998.

**LaVerne Y. Stringfield,**  
*Committee Management Officer, NIH.*

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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**National Institute 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