A Novel Approach to Genome-Wide Identification of Gene Regulatory Sequences

Gregory E. Crawford (NHGRI).
U.S. Provisional Application 60/511,905 filed 15 Oct 2003 (DHHS Reference No. E–286–2003/0–US–01)
Licensing Contact: Fatima Sayyid; (301) 435–4521; *sayyidf@mail.nih.gov*

Sequence analysis of the human genome has identified approximately 30,000 protein-coding genes, but little is known about how most of these genes are regulated. A major goal of current genome research is to identify the location of all cis-acting gene regulatory elements for all genes. This will be necessary if we are to understand global gene regulation in different tissues as well as identify regulatory variants that make individuals more susceptible to common diseases.

The present invention relates to methods of studying gene regulatory elements on a genome-wide scale. Particularly, it relates to methods of generating libraries of DNAse hypersensitive genomic sequences, which are believed to correlate well with the locations of gene regulatory elements. These methods involve obtaining nuclei from the cell sample, subjecting the nuclei to DNAse I digestion, and embedding the DNAsed sample in low melt agarose to substantially prevent non-specific shearing of the genomic DNA. The DNAsed fragments are then blunted and further processed, to permit isolation and analysis of the putative regulatory elements.

Retrovirus-Like Particles and Retroviral Vaccines

David E. Ott (NCI)
PCT Application filed 27 Oct 2003 (DHHS Reference No. E–236–2003/0–PCT–01)
Licensing Contact: Susan Ano; (301) 435–5515; *anos@mail.nih.gov*

This technology describes retrovirus-like particles and their production from retroviral constructs in which the gene encoding all but seven amino acids of the nucleocapsid (NC) protein was deleted. This deletion functionally eliminates packaging of the genomic RNA, thus resulting in non-infectious retrovirus-like particles. These particles can be used in vaccines or immunogenic compositions. Specific examples using HIV–1 constructs are given. Furthermore, efficient formation of these particles requires inhibition of the protease enzymatic activity, either by mutation to the protease gene in the construct or by protease inhibitor thereby ensuring the production of non-infectious retrovirus-like particles. This technology is further described in Ott *et al.*, Journal of Virology, 2003, 77(5), 5547.

Aerosolized Capreomycin for Inhibition of Pulmonary Tuberculosis

Carl N. Kraus, Clifton E. Barry III, Bernard Doan (NIAID)
U.S. Provisional Application No. 60/500,001 filed 11 Sep 2002 (DHHS Reference No. E–286–2002/0–US–01).
Licensing Contact: Michael Ambrose; (301) 594–6565; *ambrosem@mail.nih.gov*.

This technology involves the methods of reformulation of Capreomycin for the aerosol treatment of pulmonary tuberculosis.

Tuberculosis is a devastating lung disease that is highly infectious and easily transmitted, especially in areas of overcrowding such as prisons. Furthermore, underdeveloped countries with large populations living in close quarters maintain an endemic disease reservoir limiting the health and economic viability of the population. The WHO estimates that as many as ⅓ of the population may be infected. Current treatment requires the patient to take medication over an extended period of time, up to 12 months or more in some cases. This leads to clinical failure and the potential development of multi-drug resistant strains. Resistant strains of tuberculosis further tax the health care delivery as second line anti-tubercular therapies are more likely to have side effects yet still require long-term adherence to therapy regimens.

The disclosed technology provides for the delivery of Capreomycin in an aerosol formulation. This provides for ease of delivery in both first and second line tuberculosis regimens. Furthermore, the aerosol formulation does not require extensive training of health-care workers to administer the therapy, minimizing the need for added personnel in underdeveloped countries. This, along with the increased product stability will enhance patient adherence to therapy and the potential reduction of disease burden, both for the patient and the population.

Dated: February 13, 2004.

Steven M. Ferguson,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. 04–3710 Filed 2–19–04; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Prospective Grant of Exclusive License: Combined Growth Factor-Deleted and Thymidine Kinase-Deleted Vaccinia Virus Vector

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

ACTION: Notice.

SUMMARY: This is notice, in accordance with 35 U.S.C. 209(c)(1) and 37 CFR part 404.7(a)(1)(i), that the National Institutes of Health, Department of Health and Human Services is contemplating the grant of an exclusive patent license to practice the inventions embodied in the PCT Patent Application No. PCT/US00/14679, filed May 26, 2000 [DHHS ref. E–181–1999/0–PCT–02], entitled ''Combined Growth Factor-Deleted and Thymidine Kinase-Deleted Vaccinia Virus Vector,'' and all related foreign patents/patent applications, to PNP Therapeutics, Inc., which is located in Birmingham, Alabama. The patent rights in these inventions have been assigned to the United States of America.

The prospective exclusive license territory will be worldwide and the field of use may be limited to human therapeutics for the treatment of cancer via use of vaccinia virus vector in combination with the company's proprietary technology. This notice should be considered a modification of an earlier **Federal Register** notice (68 FR 6930–6931; February 11, 2003).

DATES: Only written comments and/or applications for a license which are received by the NIH Office of Technology Transfer on or before April 20, 2004, will be considered.

ADDRESSES: Requests for copies of the patent application, inquiries, comments and other materials relating to the contemplated exclusive license should be directed to: George G. Pipia, Ph.D., Technology Licensing Specialist, Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, MD 20852–3804; Telephone: (301) 435–5560; Facsimile: (301) 402–0220; E-mail: *pipiag@mail.nih.gov.*

SUPPLEMENTARY INFORMATION: The prospective exclusive license will be royalty bearing and will comply with the terms and conditions of 35 U.S.C. 209 and 37 CFR part 404.7. The prospective exclusive license may be granted unless within sixty (60) days from the date of this published notice, the NIH receives written evidence and

argument that establish that the grant of the license would not be consistent with the requirements of 35 U.S.C. 209 and 37 CFR part 404.7.

The present technology describes the use of ''Growth Factor-Deleted and Thymidine Kinase-Deleted Vaccinia Virus Vector'' for cancer therapy. Tumor-selective, replicating viruses may infect and kill cancer cells and efficiently express therapeutic genes in cancer cells. The current invention embodies mutant vaccinia virus expression vectors. These vectors, which are vaccinia virus growth factor-deleted and thymidine-kinase deleted, are substantially incapable of replicating in non-dividing cells, while maintaining specificity for cancer cells. It is therefore believed that the vectors will be of value for cancer therapy either by directly killing cancer cells or by expressing therapeutic agents in cancer cells while sparing normal, non-dividing cells.

Applications for a license in the field of use filed in response to this notice will be treated as objections to the grant of the contemplated exclusive license. Comments and objections submitted to this notice will not be made available for public inspection and, to the extent permitted by law, will not be released under the Freedom of Information Act, 5 U.S.C. 552.

Dated: February 13, 2004.

Steven M. Ferguson,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. 04–3709 Filed 2–19–04; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) Announcement of Availability of the Draft Expert Panel Report on Acrylamide; Announcement of Expert Panel Meeting on Acrylamide; Request for Public Comments

SUMMARY: The NTP CERHR announces:

(1) availability of sections 1–4 of the draft expert panel report on acrylamide on March 15, 2004, and solicits written public comments on the report by April 29, 2004.

(2) the acrylamide expert panel meeting May 17–19, 2004, at the Holiday Inn Old Town Select, Alexandria, Virginia and invites the public to present oral comments at this meeting.

Questions ublic comments should be directed to Dr. Michael Shelby, CERHR Director (contact information below).

Draft Expert Panel Report on Acrylamide Available

The CERHR announces the availability of the draft expert panel report on acrylamide (CAS RN 79–06–1). Acrylamide is used in the production of polyacrylamide, which is used in water treatment, pulp and paper production, mineral processing, and scientific research. Polyacrylamide is used in the synthesis of dyes, adhesives, contact lenses, soil conditioners, cosmetics and skin creams, food packaging materials, and permanent press fabrics. In scientific research, it is used in molecular biology procedures such as electrophoresis. Acrylamide is a neurotoxicant and in animal studies has been shown to be a carcinogen, germ cell mutagen, and reproductive toxicant. The CERHR selected acrylamide for expert panel evaluation because of recent public concern for human exposures through its presence in some starchy foods cooked at high temperatures. In addition, recent data are available on human exposure, bioavailability, and reproductive toxicity.

Each draft expert panel report has the following sections:

1.0 Chemistry, Use, and Human Exposure
2.0 General Toxicological and Biological Effects
3.0 Developmental Toxicity Data
4.0 Reproductive Toxicity Data
5.0 Summary, Conclusions, and Critical Data Needs (to be prepared at expert panel meeting)

Sections 1–4 will be available to the public on March 15, 2004, and can be obtained electronically on the CERHR Web site (*http://cerhr.niehs.nih.gov*) or in hard copy or compact disk by contacting Dr. Michael Shelby, Director CERHR [NIEHS, 79 T.W. Alexander Drive, Building 4401, Room 103, P.O. Box 12233, MD EC–32, Research Triangle Park, NC 27709, telephone: (919) 541–3455; facsimile: (919) 316–4511; *shelby@niehs.nih.gov*].

Request for Written Comments on Draft Expert Panel Report

The CERHR invites written public comments on sections 1–4 of the draft expert panel report on acrylamide. Comments can be submitted in hard copy or electronic format and must be received by the CERHR by April 29, 2004. These comments will be distributed to the expert panel and CERHR staff for consideration in revising the draft report and in preparing for the expert panel meeting. They will be posted on the CERHR web site prior to the expert panel meeting. These comments should be sent to Dr. Michael Shelby at the address provided above. Persons submitting written comments are asked to include their name and contact information (affiliation, mailing address, telephone and facsimile numbers, e-mail, and sponsoring organization, if any).

Expert Panel Meeting Planned

The CERHR will hold an expert panel meeting May 17–19, 2004, at the Holiday Inn Old Town Select 480 King Street Alexandria, VA 22314 (telephone: 703–549–6080, facsimile: 703–684–6508). The CERHR has asked the expert panel to review the scientific evidence regarding the potential reproductive and/or developmental toxicity associated with exposure to acrylamide. The expert panel will review and revise the draft expert panel report and reach conclusions regarding whether exposure to acrylamide is a hazard to human development or reproduction. The expert panel will also identify data gaps and research needs.

This meeting is open to the public and attendance is limited only by the available meeting room space. The meeting will begin at 8:30 a.m. each day. On May 17 and 18, it is anticipated that a lunch break will occur from noon–1 p.m. and that the meeting will adjourn 5–6 p.m. The meeting is expected to adjourn by noon on May 19; however, adjournment may occur earlier or later depending upon the time needed by the expert panel to complete its work. Anticipated agenda topics for each day are listed below. Following the expert panel meeting and completion of the expert panel report, the CERHR will post the report on its web site and solicit public comment through a **Federal Register** notice.

Preliminary Meeting Agenda

Meeting begins at 8:30 a.m. each day. Lunch break anticipated from noon–1 p.m.

May 17, 2004

Opening remarks
Oral public comments (7 minutes per speaker; one representative per group, see below)
Review of sections 1–4 of the draft expert panel report on acrylamide
Discussion of Section 5.0 Summary, Conclusions, and Critical Data Needs

May 18, 2004

Discussion of Section 5.0 Summary, Conclusions, and Critical Data Needs