within 30 days of this notice directly to the HCFA Paperwork Clearance Officer designated at the following address: OMB Human Resources and Housing Branch, Attention: Allison Eydt, New Executive Office Building, Room 10235, Washington, D.C. 20503.

Dated: November 15, 1996.

Edwin J. Glatzel,

Director, Management Analysis and Planning Staff, Office of Financial and Human Resources, Health Care Financing Administration.

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BILLING CODE 4120–03–P

National Institutes of Health

National Cancer Institute and the Food and Drug Administration

Opportunity for a Cooperative Research and Development Agreement (CRADA) for the Scientific and Commercial Development of Soluble Tat Peptide Analogs for the Inhibition of HIV Transcription and Viral Replication.

AGENCY: National Institutes of Health and the Food and Drug Administration, PHS, DHHS.

ACTION: Notice.

SUMMARY: The National Cancer Institute (NCI) and the Food and Drug Administration (FDA), wherein the participation of the FDA is contingent on resolution of any apparent conflict of interest issues, seek a company that can collaboratively pursue the pre-clinical and clinical development of Soluble Tat Peptide Analogs for the Inhibition of HIV Transcription and Viral Replication. The National Cancer Institute, Laboratory of Molecular Virology (LMV) and the Food and Drug Administration, Center for Biologics, Laboratory of Immunochemistry, have established that particular Soluble Tat Peptide Analogs can inhibit the transcription and replication of the Human Immunodeficiency Virus *in vitro.* The selected sponsor will be selected as a CRADA partner for the co-development of this agent with the National Cancer Institute and the Food and Drug Administration for the co-development of this agent with the NCI and with the FDA, wherein the participation of the FDA is contingent on resolution of any apparent conflict of interest issues.

ADDRESSES: Questions about this opportunity may be addressed to Jeremy A. Cubert, M.S., J.D., Office of Technology Development, NCI, 6120 Executive Blvd. MSC 7182, Bethesda, MD 20892–7182, Phone: (301) 496–0477, Facsimile: (301) 402–2117, from whom further information may be obtained. The Government has filed a patent application related to this CRADA opportunity. For further information on licensing this patent application (DHHS ref. no. E–059–96/0) contact Cindy Fuchs, J.D., NIH Office of Technology Transfer, 6011 Executive Blvd., Suite 325, Rockville, MD 20852, Phone: (301) 496–7735 (ext. 232); Facsimile: (301) 40002–0220.

DATES: In view of the important priority of developing new agents for the treatment of infectious disease and related malignancies, interested parties should notify this office in writing no later than January 21, 1997. Respondents will then be provided an additional 30 days for the filing of formal proposals.

SUPPLEMENTARY INFORMATION: ''Cooperative Research and Development Agreement'' or ''CRADA'' means the anticipated joint agreement to be entered into by NCI pursuant to the Federal Technology Transfer Act of 1986 and amendments (including 104 Pub. L. 133) and Executive Order 12591 of October 10, 1987 to collaborate on the specific research project described below.

The Government is seeking a pharmaceutical company which, in accordance with the requirements of the regulations governing the transfer of agents in which the Government has taken an active role in developing (37 CFR 404.8), can further develop the subject compounds through Federal Food and Drug Administration approval and to a commercially available status to meet the needs of the public and with the best terms for the Government. The government has applied for a patent application directed to Inhibition of HIV Transcription and Viral Replication Using Soluble Tat Peptide Analogs. Licenses to intellectual property rights related to this opportunity are available from the National Institutes of Health, Office of Technology Transfer and may be necessary to continue development of the technology.

The *tat* gene encodes an 86 amino acid protein with a number of identified domains including an N-terminus, a cysteine rich, a core domain and a basic domain. Tat, through the core region, has been shown to interact with and stabilize the TFIID basal transcription factor and TFIIA preinitiation complex. Mutations within the core domain of Tat significantly decrease both gene expression and viral replication. National Cancer Institute (''NCI'') and Food and Drug Administration (''FDA'') studies have been directed at synthesis of Tat peptide analogs to compete with wild-type Tat *in vivo.* The NCI and FDA synthesized soluble peptide analogs of the HIV–1 Tat protein. These peptide analogs inhibit transactivation of HIV, viral replication and formation of viral particles. The peptide analogs compete with Tat in down-regulating Tat transactivation and induce a ninety percent reduction of viral particles from infected cells *in vitro.* The inhibitory peptide analogs are not toxic *in vitro.*

The Laboratory of Molecular Virology, Division of Basic Sciences, NCI and the Laboratory of Immunochemistry, Division of Transfusion and Transmitted Diseases, FDA are interested in establishing a CRADA with a company to assist in the continuing development of these peptide analogs, wherein the participation of the FDA is contingent on resolution of any apparent conflict of interest issues. The Government will provide all available expertise and information to date and will jointly pursue pre-clinical and clinical studies as required, giving the company full access to existing data and data developed pursuant to the CRADA. The successful company will provide the necessary scientific, financial and organizational support to establish clinical efficacy and possible commercial status of the subject compounds.

The expected duration of the CRADA will be two (2) to five (5) years.

The role of the National Cancer Institute and Food and Drug Administration, wherein the participation of the FDA is contingent on resolution of any apparent conflict of interest issues, includes the following:

1. Determine the stability, half-life, and distribution of the Tat peptides upon delivery into cells.
2. Determine the mechanism of the Tat peptide inhibition.
3. Determine the inhibitory effect of peptides on human ''primary'' T-lymphocytic and monocytic cells infected with various HIV–1 clades (subtypes A, G, O, M).
4. Determine the inhibitory effect of peptide derivatives on Kaposi's sarcoma primary cells.
5. Determine the effective dose of Tat Peptide analogs in combination with other anti-retroviral drugs.
6. Conduct *in vivo* testing of appropriate compounds and/or peptide analogs.
7. Evaluate *in vivo* test results.
8. Prepare manuscripts for publication.

The role of the collaborator, includes the following:

1. Synthesize soluble organic compounds using peptide mimetics to

mimic the inhibitory activity of the soluble peptide analogs.

2. Determine the mechanism of the Tat peptide inhibition.

3. Establish a suitable non-invasive peptide delivery system for the preclinical and animal model studies.

4. Determine the effective dose of Tat peptide analogs in combination with other anti-retroviral drugs.

5. Determine the stability, half-life, and distribution of the Tat peptides upon delivery into cells.

6. Conduct *in vivo* testing of appropriate compounds and/or peptide analogs.

7. Evaluate *in vivo* test results.

8. Develop vehicle for delivery of compounds to patients.

9. Conduct pre-clinical and clinical trials of appropriate candidate compounds and/or peptide analogs.

10. Prepare manuscripts for publication.

Criteria for choosing the collaborator include its demonstrated experience and commitment to the following:

1. The aggressiveness of the development plan, including the appropriateness of milestones and deadlines for preclinical and clinical development.

2. Scientific expertise in and demonstrated commitment to the development of drug delivery systems.

3. Experience in preclinical and clinical drug development.

4. Experience and ability to produce, package, market and distribute pharmaceutical products.

5. Experience in the monitoring, evaluation and interpretation of the data from investigational agent clinical studies under an IND.

6. A willingness to cooperate with the NCI and FDA in the collection, evaluation, publication and maintaining of data from pre-clinical studies and clinical trials regarding the subject compounds.

7. Provision of defined financial and personnel support for the CRADA to be mutually agreed upon.

8. An agreement to be bound by the DHHS rules involving human and animal subjects.

9. Scientific expertise in and demonstrated commitment to the treatment of HIV infection and related disorders.

10. Provisions for equitable distribution of patent rights to any CRADA inventions. Generally the rights of ownership are retained by the organization which is the employer of the inventor, with (1) an irrevocable, nonexclusive, royalty-free license to the Government and (2) an option for the collaborator to elect an exclusive or nonexclusive license to Government owned rights under terms that comply with the appropriate licensing statutes and regulations.

Dated: November 12, 1996.

Kathleen Sybert,

Deputy Director, Office of Technology Development, OD, NCI.

[FR Doc. 96–29892 Filed 11–21–96; 8:45 am]

BILLING CODE 4140–01–M

Government-Owned Inventions; Availability for Licensing

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

ACTION: Notice.

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development.

ADDRESSES: Licensing information and a copy of the U.S. patent applications referenced below may be obtained by contacting Joseph Contrera, M.S., J.D., at the 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). A signed Confidential Disclosure Agreement will be required to receive a copy of the patent applications.

A Novel Vector for Polynucleotide Vaccines

EL Nelson, PJ Nelson (NCI)
Serial No. 60/023,931 filed 14 Aug 96

This invention is directed to a ''humanized'' polynucleotide vector vaccine which uses covalent closed circular (CCC) plasmid DNA, ''naked DNA,'' to express target antigens. The vector contains the necessary elements to express mRNA for a target antigen. The plasmids are non-replicating but are capable of extended stable expression of the target sequences in skeletal muscle and professional antigen presenting cells generating an immune response to the target antigen in immunized individuals. The polynucleotide vector is particularly useful in accommodating monomorphic and polymorphic tumor antigens via PCR technology. This invention could be useful in constructing polynucleotide vector cancer vaccines or ''naked DNA'' vaccines containing one or more tumor antigens.

Heterologous Boosting Immunizations for the Generation of CTL and Anti-Tumor Responses

RS Chamberlain, KR Irvine, SA Rosenberg, NP Restifo (NCI)
Serial No. 60/015,893 filed 22 Apr 96

A number of recombinant and synthetic vectors expressing tumor associated antigens have been developed which each induce powerful cellular and humoral immune responses that correlated with anti-tumor immunity in murine tumor model systems. Examples of these vectors include (1) recombinant viruses, such as vaccinia, fowlpox and adenovirus, (2) recombinant plasmid DNA, and (3) minimal determinant peptides. This invention involves the use of more than one of these vectors expressing a particular antigen for priming and boosting immunization regimens with the goal of enhancing anti-tumor immunity. Boosting with heterologous vectors induced more powerful primary antigen-specific cytotoxic T lymphocyte responses than boosting with the same vector. These more powerful immune responses induced by subsequent immunization with a different vector than the priming agent also resulted in a significant prolongation in survival of tumor-bearing mice as compared to mice that received two vaccinations with the same vector. Specifically, the combinations that were most efficacious were recombinant vaccinia virus followed by recombinant fowlpox and vice versa and recombinant DNA immunization followed by either recombinant fowlpox or vaccinia virus and vice versa.

The invention is significant because these heterologous boosting strategies may provide for increased therapeutic potential in the design and development of immunotherapies for cancer treatment. This approach may also be useful in the development of treatments for infectious bacterial and viral disease.

Point Mutated ras Peptides for the Generation of CD8+ Cytotoxic T Lymphocytes

J. Schlom, S Abrams (NCI)
Serial No. 08/635,344 filed 19 Apr 96

This invention is directed to a method of inducing a cytotoxic T cell response where the cytotoxic T cells are $CD8^+$ T cells. The $CD8^+$ cytotoxic T cell response is induced by peptides which contain a mutation in the K-*ras* oncogene at codon 12. The invention discloses 13 mer K-*ras* peptides spanning position 5–17 of the K-*ras* gene and which contain a mutation at codon 12. In addition, 9 mer and 10 mer K-*ras* peptides are also described in