

FOR FURTHER INFORMATION CONTACT: To request more information on this project or to obtain a copy of the data collection plans and instrument, write to Dr. Margaret Tucker, Chief, Genetic Epidemiology Branch, National Cancer Institute, NIH, Executive Plaza South, Room 7122, 6120 Executive Blvd., Bethesda, MD 20892, or call non-toll-free number (301) 496-4375, or E-mail your request, including your address to: tuckerp@mail.nih.gov.

Comments Due Date

Comments regarding this information collection are best assured of having their full effect if received on or before 60 days from the date of this publication.

Dated: January 12, 2000.

Reesa Nichols,

OMB Project Clearance Liaison.

[FR Doc. 00-1422 Filed 1-20-00; 8:45 am]

BILLING CODE 4140-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Invention; Availability for Licensing: "Therapeutic Methods to Treat Tumor Cells—Mutated Anthrax Toxin Protective Antigen Proteins That Specifically Target Cells Containing High Amounts of Cell-Surface Metalloproteinases or Plasminogen Activators"

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

ACTION: Notice.

SUMMARY: The invention listed below is owned by an agency of the U.S. Government and is 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 application referenced below may be obtained by contacting J.R. Dixon, Ph.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 206; fax 301/402-0220; E-Mail: jd212g@NIH.GOV). A signed Confidential Disclosure Agreement is required to receive a copy of any patent application.

SUPPLEMENTARY INFORMATION:

Invention Title: "Mutated Anthrax Toxin Protective Antigen Proteins that Specifically Target Cells Containing High Amounts of Cell-Surface

Metalloproteinases or Plasminogen Activators."

Inventors: Drs. Stephen H. Leppla (NIDCR), Shi-Hui Liu (NIDCR), Sarah Netzel-Arnett (NIDCR), Henning Birkedal-Hansen (NIDCR), and Thomas H. Bugge (NIDCR).

USPA SN: 60/155,061 [=DHHS Ref. No. E-293-99/0]—Filed with the U.S.P.T.O. on Friday, September 24, 1999.

Abstract

Anthrax toxin is a three-part toxin secreted by *Bacillus anthracis* consisting of Protective Antigen ("PA", 83kDa), Lethal Factor ("LF", 90 kDa) and Edema Factor ("EF", 89kDa), which are individually non-toxic. PA, recognized as central, receptor-binding component, binds to an unidentified receptor and is cleaved at the sequence RKKR₁₆₇ by cell-surface furin or furin-like proteases into two fragments: PA63, a 63 kDa C-terminal fragment, which remains receptor-bound and PA20, a 20 kDa N-terminal fragment, which is released into the medium. The resulting hetero-oligomeric complex is internalized by endocytosis and acidification of the vesicle causes insertion of the PA63 heptamer into the endosomal membrane to produce a channel through which LF or EF translocate to the cytosol, where LF or EF induce cytotoxic events. Thus, the combination of PA+LF, named anthrax lethal toxin, kills animals and certain cultured cells, due to intracellular delivery and action of LF, recently proven to be a zinc-dependent metalloprotease that is known to cleave at least two targets, mitogen-activated protein kinase 1 and 2. The combination of PA+EF, named edema toxin, disables phagocyte and probably other cells, due to the intracellular adenylate cyclase activity of EF.

Technology

The technology disclosed in the 60/155,961 patent application relates to anthrax toxin protective antigen (PA) mutants in which the furin site is replaced by sequences specifically cleaved by matrix metalloproteinases (MMPs) or plasminogen activators. These MMP or plasminogen activator targeted PA mutants are only activated by plasminogen activator or MMP-expressing tumor cells so as to specifically deliver a toxin or a therapeutic agent. This is important because a wide variety of tumor cell lines and tissues overexpress MMPs or plasminogen activators, and this overexpression is highly correlated to tumor invasion and metastasis. Activation of these mutants occurs mainly on the cell surface and the

targeted agent is then translocated to the interior of the cell. Current treatment models include the use of MMP inhibitors. The disclosed technology provides a viable alternative to this model and has the advantage of being highly targetable and specific to tumor cells expressing MMPs or plasminogen activators.

The above mentioned Invention is available, including any available foreign intellectual property rights, for licensing.

Dated: January 12, 2000.

Jack Spiegel,

Division of Technology Development & Transfer, Office of Technology Transfer.

[FR Doc. 00-1423 Filed 1-20-00; 8:45 am]

BILLING CODE 4140-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Invention; Availability for Licensing: "Compositions and Methods for Specifically Targeting Tumors—Using a Blocker Reagent"

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

ACTION: Notice.

SUMMARY: The invention listed below is owned by an agency of the U.S. Government and is 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.

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SUPPLEMENTARY INFORMATION: *Invention Title:* "Compositions and Methods for Specifically Targeting Tumors"

Inventors: Drs. Waldemar Debinski (EM) and Raj K. Puri (U.S.F.D.A.).

USPA SN: 08/706,207 [=DHHS Ref. No. E-042-00/0]—Filed with the U.S.P.T.O. on August 30, 1996.

Abstract

In a chimeric molecule, two or more molecules that exist separately in their native state are joined together to form