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 SERVICE

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 contacing 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 $RKKR_{167}$ 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 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.

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:* ''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

a single entity (i.e., molecule) having the desired functionality of all of its constituent molecules. Frequently, one of the constituent molecules of a chimeric molecule is a ''targeting molecule''. The targeting molecule is a molecule such as a ligand or an antibody that specifically binds to its corresponding target, for example a receptor on a cell surface. Thus, for example, where the targeting molecule is an antibody, the chimeric molecule will specifically bind (target) cells and tissues bearing the epitope to which the antibody is directed.

Another constituent of the chimeric molecule may be an ''effector molecule''. The effector molecule refers to a molecule that is to be specifically transported to the target to which the chimeric molecule is specifically directed. The effector molecule typically has a characteristic activity that is desired to be delivered to the target cell. Effector molecules include cytotoxins, labels, radionuclides, other ligands, drugs, prodrugs, liposome, etc. In particular, where the effector component is a cytotoxin, the chimeric molecule may act as a potent cell-killing agent specifically targeting the cytotoxin to cells bearing a particular target molecule. For example, chimeric fusion protein which include interleukin–4 (''IL–4'') or transforming growth factor (RGFα'') fused to *Pseudomonas exotoxin* (''PE'') or interleukin–2 (''IL–2'') fused to Diphtheria toxin (''DT'') have been shown to specifically target and kill cancer cells.

Generally, it is desirable to increase specificity and affinity and decrease cross-reactivity of chimeric cytotoxins with targets to be spared in order to increase their efficacy. To the extent a chimeric modecule preferentially selects and binds to its target (*e.g.,* a tumor cell) and not to a non-target (e.g., a healthy cell), side effects of the chimeric molecule will be minimized. Unfortunately, many targets to which chimeric cytotoxins have been directed (e.g., the IL–2 receptor), while showing elevated expression on tumor cells, are also expressed to some extent, and often at significant levels, on healthy cells. Thus, chimeric cytotoxins directed to these targets frequently show adverse side-effects as they bind non-target (e.g., healthy) cells that also express the targeted receptor.

Technology

The technology disclosed in the 08/706,207 patent application is directed to a method and compositions to deliver an effector molecule to tumor cell. Specifically the technology relates to a chimeric molecule that specifically binds to IL–13 receptors which when combined with a blocker reagent (e.g., interleukin–4, an interleukin–4 antagonist, an interleukin–4 receptor binding antibody etc.) specifically delivers receptor directed cytotoxins to tumors over expressing IL–13 receptors without causing undesired cytotoxicity to normal cells. This is because a variety of human cancer cells including brain tumors, kidney tumors, and AIDS-associated Kaposi's tumors etc. over express private IL–13 receptors and normal cells express low levels of shared IL–13 receptors with IL–4 receptors. IL–13 cytotoxin remains very cytotoxic to cancel cells in the presence of IL–4 receptor blocker agents while cytotoxicity and undesired side effects of cytotoxin administration are prevented in normal cells. This approach provides unique specificity of delivering IL–13 receptor directed cytotoxic agents to cancer cells.

The above mentioned Invention is available for licensing.

Dated: January 12, 2000.

Jack Spiegel, Ph.D.,

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

[FR Doc. 00–1424 Filed 1–20–00; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

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.E. Fahner-Vihtelic at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; Telephone: 301/496–7735 ext. 270; Fax: 301/402–0220; E-mail; jf36z@nih.gov. A signed Confidential Disclosure Agreement is required to receive a copy of any patent application.

Artificial Salivary Gland

Bruce J. Baum et al. (NIDCR)

Serial No. 60/121,335
Filed 24 Feb 1999

The present application describes an artificial fluid secreting prosthetic device for non-invasive insertion and methods of using this device. Specifically, compositions and methods based on the discovery of an artificial fluid secreting prosthesis are disclosed in this application. Currently, there is no conventional effective treatment for salivary gland hypofunction. And although the transplantation of mammalian salivary glands has also been tried, this option has not proven desirable due to lack of sufficient donor supplies. To date, the inventors have performed experiments that have demonstrated: (1) Subjects having irradiated salivary gland cells can be induced to secrete fluid subsequent to transfer of a gene; (2) heterologous genes can be transferred to salivary gland cells; and (3) an artificial gland has been designed having a support, an attachment surface joined to the support, and a monolayer of allogenic cells, engineered to secrete ions and water unidirectionally, joined to the attachment surface.

Dated: January 11, 2000.

Jack Spiegel, Ph.D.,

Director, Division of Technology Development and Transfer, Office of Technology Transfer.

[FR Doc. 00–1425 Filed 1–20–00;8:45am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Heart, Lung, and Blood Institute; Notice of Closed Meetings

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 meetings.

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

Name of Committee: National Heart, Lung, and Blood Institute Special Emphasis Panel Mentored Clinical Scientist Development Award.

Date: February 7–8, 2000.