[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The invention listed below is owned by an agency of the U.S. Government and is available for licensing to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION CONTACT: Dr. Natalie Greco, 301-761-7898; Natalie.Greco@nih.gov. Licensing information and copies of the patent applications listed below may be obtained by communicating with the indicated licensing contact at the Technology Transfer and Intellectual Property Office, National Institute of Allergy and Infectious Diseases, 5601 Fishers Lane, Rockville, MD, 20852; tel. 301-496-2644. A signed Confidential Disclosure Agreement will be required to receive copies of unpublished patent applications.

SUPPLEMENTARY INFORMATION: Technology description follows.

Human and Veterinary Cancer Therapeutic Agent Utilizing Anthrax Toxin-Based Technology

Description of Technology:

Due to the disorganized nature of blood vessels that run through tumors, chemotherapeutic agents often fail to penetrate tumors and kill cancer cells at the tumor's center. This can lead to ineffective chemotherapeutic treatments, because tumors can quickly grow back if the entire tumor is not destroyed. NIH researchers have developed a therapeutic agent that solves this problem facing current chemotherapy treatments. By elegantly exploiting cell surface proteases present at high levels in tumors, they have developed a tumor-targeted anthrax based toxin that inactivates the blood vessels within tumors. While in some cases cancer cells are also killed by the tumor-targeted toxin, the primary mechanism of action is thought to be a decrease in blood flow to the center of tumors, causing cancer cell death and tumor necrosis. Preliminary and on-going studies have demonstrated that the targeted toxins have antitumor effects on melanomas, lung cancers and colon cancer in mouse models, and on feline and canine oral tumors. Interestingly, this therapy does not target a specific type of cancer cell, rather it targets the vasculature in and around tumors. Therefore, it has great potential to treat a wide range of solid tumors. Additionally, because few non-surgical treatments are available to treat many human and veterinary solid tumors, this technology would fill an unmet need in cancer therapy.

This technology is available for licensing for commercial development in accordance with 35 U.S.C. 209 and 37 CFR Part 404, as well as for further development and evaluation under a research collaboration.

Potential Commercial Applications:

Therapeutic agent for a wide range of human and veterinary solid tumors, including:

- Melanomas
- Lung and colon cancers
- Oral squamous carcinomas

Competitive Advantages:

- Proven effective in a variety of models, including models of important veterinary cancers
- Agent is only active in tumor micro-environments, resulting in low toxicity to healthy tissue
- Cancer cells are not directly targeted, so this agent can be used to treat a broad spectrum of solid tumors and resistance is unlikely to arise
- Fills an unmet need in cancer therapy, because few non-surgical treatments exist

Development Stage:

- *in vitro* data available
- *in vivo* data available (animal)
- prototype

Inventors:

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Publications:

Chen KH, et al., Selection of anthrax toxin protective antigen variants that discriminate between the cellular receptors tem8 and cmg2 and achieve targeting of tumor cells. J Biol Chem. 2007 Mar 30; 282(13): 9834–9845 [PMID: 17251181 PMCID: PMC2530824]

Liu S, et al., Solid tumor therapy by selectively targeting stromal endothelial cells. Proc Natl Acad Sci U S A. 2016 Jul 12; 113(28): E4079–E4087 [PMID: 27357689 PMCID: PMC4948345]

Wein AN, et al., An anthrax toxin variant with an improved activity in tumor targeting. Sci Rep. 2015; 5: 16267 [PMID: 26584669 PMCID: PMC4653645]

Peters DE, et al., Comparative toxicity and efficacy of engineered anthrax lethal toxin variants with broad anti-tumor activities. Toxicol Appl Pharmacol. 2014 Sep 1; 279(2): 220–229 [PMID: 24971906 PMCID: PMC4137396]

Bachran C, et al., Cytolethal distending toxin B as a cell-killing component of tumor-targeted anthrax toxin fusion proteins. Cell Death Dis. 2014 Jan; 5(1): e1003 [PMID: 24434511 PMCID: PMC4040664]

Wein AN, et al., Tumor therapy with a urokinase plasminogen activator-activated anthrax lethal toxin alone and in combination with paclitaxel. Invest New Drugs. 2013 Feb; 31(1): 206–212 [PMID: 22843210 PMCID: PMC3757568]

Phillips DD, et al., Engineering Anthrax Toxin Variants That Exclusively Form Octamers and Their Application to Targeting Tumors. J Biol Chem. 2013 Mar 29; 288(13): 9058–9065 [PMID: 23393143 PMCID: PMC3610978]

Liu S, et al., Intermolecular complementation achieves high specificity tumor targeting by anthrax toxin. Nat Biotechnol. 2005 Jun; 23(6): 725–730 [PMID: 15895075 PMCID: PMC2405912]

Intellectual Property:

HHS E-256-2015 - US Application Nos. 62/210,771, filed 27 Aug 2015; 62/323,218, filed 15 Apr 2016; PCT App. No. PCT/US16/48706, filed 25 Aug 2016.

HHS E-120-2013 - US App. No. 14/898,248, filed 14 Dec 2015; PCT App. No. PCT/US2014/043131, filed 19 Jun 2014.

HHS E-246-2012 - US App. No. 14/423,408, filed 23 Feb 2015; PCT App. No. PCT/US13/56205

HHS E-059-2004 - US Patent No. 7,947,289, filed 09 Feb 2005.

HHS E-293-1999 - US Patent Nos. 7,468,352, filed 22 Mar 2002; 8,791,074, filed 20 Oct 2008, and 9,403,872 filed 24 Jun 2014.

Licensing Contact:

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Collaborative Research Opportunity: The National Institute of Allergy and Infectious Diseases is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize anthrax toxin-based

cancer therapeutics. For collaboration opportunities, please contact Dr. Natalie Greco, 301-761-7898; Natalie.Greco@nih.gov.

Dated: June 1, 2017.

Suzanne Frisbie,

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Technology Transfer and Intellectual Property Office,

National Institute of Allergy and Infectious Diseases.

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