[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 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. 209 and 37 CFR Part 404 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: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301-496-7057; fax: 301-402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

SUPPLEMENTARY INFORMATION: Technology descriptions follow.

The Use of Chimeric Antigen Receptor to Control HIV Infection

Description of Technology: Chimeric Antigen Receptors (CARs) are engineered proteins expressed by transduction on autologous CD8 T cells; after adoptive transfer, they promote targeted killing of specific cell types. CARs are showing great promise for treating cancer. The present invention (CD4-CRD CAR) is a novel bifunctional targeting motif for an anti-HIV CAR, consisting of a region of human CD4 linked to a carbohydrate recognition domain (CRD) from one of several human C-type lectins known to interact with high-mannose glycans on HIV gp120. Compared to a "standard" CD4 CAR, the CD4-CRD CAR displays two major enhancements: 1) increased potency for suppression of HIV-1 infection by selective killing of productively infected cells, and 2) complete absence of CD4-mediated entry receptor activity that would otherwise render the transduced CD8 T cells susceptible to HIV infection. Compared to antibody-based anti-HIV CARs, the CD4-CRD CAR of the present invention is predicted to have two major advantages: 1) Lower escape potential, due to the universality of HIV CD4-dependence and high-mannose glycan display on gp120, and 2) reduced immunogenicity, since the all-human CD4-CRD CAR sequences are devoid of variable regions that would likely elicit anti-idiotypic antibody responses against scFv-based targeting motifs.

Potential Commercial Applications:

- Therapy for HIV infection
- Research on antiretroviral infection

Competitive Advantages: Enhanced potency for HIV inhibition and does not render transduced CD8T cells susceptible to HIV infection.

Development Stage:

• In vitro data available

• In vivo data available (animal)

Inventors: Mustafa H. Ghanem, Bama Dey, Edward Berger (all of NIAID)

Publications:

1. Scholler J, et al. Decade-long safety and function of retroviral-modified chimeric antigen receptor T cells. Sci Transl Med. 2012 May 2;4(132):132ra53. [PMID 22553251]

2. Du T, et al. Bifunctional CD4-DC-SIGN fusion proteins demonstrate enhanced avidity to gp120 and inhibit HIV-1 infection and dissemination. Antimicrob Agents Chemother. 2012 Sep;56(9):4640-9. [PMID 22687513]

3. Lamers CH, et al. Immune responses to transgene and retroviral vector in patients treated with ex vivo-engineered T cells. Blood. 2011 Jan 6;117(1):72-82. [PMID 20889925]

Intellectual Property: HHS Reference No. E-212-2014/0 - US Provisional Application No. 62/040,398 filed 21 August 2014

Licensing Contact: John Stansberry, Ph.D.; 301-435-5236; stansbej@mail.nih.gov

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 this technology. For collaboration opportunities, please contact Chris Kornak at chris.kornak@nih.gov.

Photo-Controlled Removal of Targets In Vitro and In Vivo

Description of Technology: The invention relates to a novel technology for separation, isolation and removal of target molecules or cells from a complex mixture. The technology can be used for both in vitro and in vivo applications. It comprises a conjugate of a biomolecule with specific binding activity (e.g. antibody, hapten, protein, nucleic acid) and the fluorescence dye IR700. When the conjugate is allowed to contact with a sample, it binds to the target molecule in the sample to form a biological complex. Upon exposure to near infrared light (NIR) of approximately 700 nm the biological complex becomes hydrophobic due to cleavage of a part of the fluorescent dye. Such hydrophobic complex can aggregate and readily be separated and removed from the biological mixture. The technology can be used in a broad range of applications, such as environmental or food (removal of contaminants from samples), or in vivo removal of toxins, pathogens or drugs from a subject, where the latter may provide a photo-controlled way to control the pharmacokinetics of a drug in vivo. The technology can also be applied in the therapeutic field, for example in cancer therapy, by killing and removal of tumor cells in a subject with the aid of wearable NIR device. In such treatment, the aggregated target cells may be removed from the subject via the liver and/or spleen.

Potential Commercial Applications:

• Environmental or food (removal of contaminants from samples)

• In vivo removal of toxins, pathogens or drugs from a subject

• Cancer therapy

Competitive Advantages: Simple and versatile way to separate and remove molecules or cells from a complex mixture.

Development Stage: Early-stage

Inventors: Hisataka Kobayashi, et al. (NCI)

Intellectual Property: HHS Reference No. E-209-2014/0 - US Provisional Application No. 62/034,990 filed 08 August 2014

Licensing Contact: Uri Reichman, Ph.D., MBA; 301-435-4616; ur7a@nih.gov

Collaborative Research Opportunity: The National Cancer Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize this technology. For collaboration opportunities, please contact John D. Hewes, Ph.D. at hewesj@mail.nih.gov.

Human Monoclonal Antibodies Against 5T4 as Therapeutic Agents

Description of Technology: 5T4 is an antigen expressed in a number of carcinomas. Its expression is limited in normal tissue, but is prevalent in malignant tumors throughout their development. This confined expression makes it an attractive target for cancer immunotherapy. 5T4 is often found in colorectal, ovarian, and gastric tumors and thus has been used as a prognostic aid for these cancers. In addition, its role in antibody-directed immunotherapy for delivering response modifiers to tumors has been studied using murine monoclonal antibodies (mAbs) and the cancer vaccine TroVax (currently in clinical trials for multiple solid tumors) targets 5T4.

The present invention describes the identification and characterization of two fully human mAbs (m1001 and m1002) that bind to 5T4. Since the mAbs are fully human, they could have less immunogenicity and better safety profiles than the existing mouse and humanized antibodies. These mAbs have the potential to be cancer therapeutics as naked mAbs, Chimerica Antigen Receptors (CARs) and/or Antibody-Drug Conjugates (ADCs).

Potential Commercial Applications: A mAb, CAR, or ADC therapeutic for the treatment of various human cancers expressing 5T4.

Competitive Advantages:

• The fully human antibodies may have better drugability, especially less immunogenicity and better safety.

• This antibodies could be used as naked mAbs, CARs and/or as ADCs.

• The confined expression of 5T4 makes it an attractive target for cancer immunotherapy.

• 5T4 mAbs could be used to treat several solid tumor cancers.

Development Stage: In vitro data available

Inventors: Dimiter Dimitrov, Tianlei Ying, Yang Feng (all of NCI)

Intellectual Property: HHS Reference No. E-158-2014/0 - U.S. Provisional Application No. 62/034,995 filed 08 August 2014

Licensing Contact: Whitney Hastings; 301-451-7337; hastingw@mail.nih.gov

Quantitative Multiplex Methods for Rapid Detection and Identification of Viral Nucleic Acids

Description of Technology: The subject technologies are quantitative multiplex loop mediated isothermal amplification assays that can detect and distinguish different viral pathogens, including HIV, Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Hepatitis E Virus (HEV), Dengue Virus (DENV), Chikungunya virus (CHIKV) and West Nile Virus (WNV). The assay has the advantage of distinguishing between different genotypes of HCV. It has the potential to detect other pathogens. A quantitative multiplex variation of the assay can detect and identify all seven viruses using one reaction mixture. The detection-reaction is performed on a simple heat-source and viral quantitation can be measured using a simple fluorospectrophotometer. The entire detection process using these assays can be accomplished within 30 to 60 minutes in a doctor's office, laboratory setting, or in the field. Detection limits of as little as 1-10 International Units (viral copies) are possible with the use of fluorogenic oligonucleotides. The assays demonstrate very high specificity when tested with human clinical samples.

Potential Commercial Applications: Detection assays for viral pathogens such as HIV, HBV, HCV, HEV, Dengue Virus, Chikungunya, and West Nile Virus.

Competitive Advantages:

• Assays can be completed within 30 to 60 minutes and in a doctor's office, laboratory setting, or in the field.

• Assays can be performed without expensive instrumentation or specialized technical operators.

• Assays are highly specific and can distinguish between different viruses and between different genotypes of viruses.

Development Stage:

• Early-stage

• In vitro data available

• In vivo data available (human)

Inventors: Dougbeh-Chris Nyan (FDA), Deborah R. Taylor (FDA), Maria Rios (FDA), Kevin L. Swinson (Morgan State University), Laura E. Ulitzky (FDA)

Publication: Nyan DC, et al. Rapid Detection of Hepatitis B Virus in Blood Plasma by a Specific and Sensitive Loop-Mediated Isothermal Amplification Assay. Clin Infect Dis. 2014 July 1;59(1):16-23. [PMID 24704724]

Intellectual Property: HHS Reference No. E-135-2014/0 - US Provisional Patent Application No. 61/979,446 filed 14 April 2014

Licensing Contact: Kevin W. Chang, Ph.D.; 301-435-5018; changke@mail.nih.gov

Collaborative Research Opportunity: The Food and Drug Administration, Center for Biologics Evaluation and Research, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize blood screening test and/or diagnostic test for infectious diseases. For collaboration opportunities, please contact Nisha Narayan at Nisha.Narayan@fda.hhs.gov or 240-402-9770.

Dated: October 8, 2014

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Richard U. Rodriguez, M.B.A.
Director
Division of Technology Development and Transfer

Office of Technology Transfer
National Institutes of Health

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