[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: Chris Kornak at 240-627-3705 or *Chris.Kornak@nih.gov*. Licensing information may be obtained by communicating with 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 A signed Confidential Disclosure Agreement will be required to receive copies of unpublished information related to the invention.

SUPPLEMENTARY INFORMATION: Technology description follows:

Use of the Intracellular Signaling Domain of Receptor CD28H as a Component of Chimeric Antigen Receptors to Overcome Inhibition of Cytotoxic Lymphocytes by Checkpoint Receptors

Description of Technology:

Engineered chimeric antigen receptors (CARs) that are expressed in cytotoxic T cells and natural killer (NK) cells have been used to specifically target tumor cells. However, CAR-T and CAR-NK cells are still subject to downregulation by their inhibitory receptors after injection into patients.

Scientists at NIAID have developed CAR constructs that overcome inhibition of NK cells by receptors for human major histocompatibility complex molecules HLA-E and HLA-C, based on *in vitro* studies. The CAR contains an antigen binding domain of receptor CD28 homolog (CD28H), a CD28H transmembrane domain (TM), a CD28H signaling domain, and other intracellular signaling domains, such as 2B4 (CD244) and CD3 zeta chain (CD3zeta). A variant of this CAR, in which the antigen binding domain of CD28H is replaced by a single-chain antibody variable region (scFv) that binds to CD19, rendered NK cells resistant to inhibition by HLA-E and HLA-C on $CD19^{+}$ tumor cells.

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:

- Method of adoptive therapy where CAR-NK cell or CAR-T cell is the effector cell.

Competitive Advantages:

- Resistant to inhibition of NK cells or T cells by HLA-E and HLA-C.
- Manufacturing efficiency
- CAR-NK can be developed without the need to genetic silencing of TCR.

Development Stage:

- Pre-clinical

Inventors: Eric O. Long (NIAID), Xiaoxuan Zhuang (NIAID)

Publications: Zhuang X and Long EO, "CD28 homolog is a strong activator of natural killer cells for lysis of B7H7-positive tumor cells." Cancer Immunol Res 7(6):939-951. https://cancerimmunolres.aacrjournals.org/content/7/6/939.long. April 24, 2019.

Trends Immunol: "Inhibition-resistant CARs for NK cell cancer immunotherapy" Trends Immunol 40:1078-1081, December 2019.

Intellectual Property: HHS Reference No. E-097-2020-0-PCT-01, PCT Patent Application No. PCT/US2020/024985.

Licensing Contact: To license this technology, please contact Chris Kornak at 240-627-3705 or *Chris.Kornak@nih.gov*, and reference E-097-2020-0.

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 240-627-3705 or Chris.Kornak@nih.gov.

Date: April 12, 2020.

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Wade W. Green,

Acting Deputy Director,

Technology Transfer and Intellectual Property Office,

National Institute of Allergy and Infectious Diseases.

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