



[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Invention; 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.

FOR FURTHER INFORMATION CONTACT: Licensing information may be obtained by emailing the indicated licensing contact at the National Heart, Lung, and Blood, Office of Technology Transfer and Development Office of Technology Transfer, 31 Center Drive Room 4A29, MSC 2479, Bethesda, MD 20892-2479; telephone: 301-402-5579. A signed Confidential Disclosure Agreement may be required to receive any unpublished information.

SUPPLEMENTARY INFORMATION: The following inventions are available for licensing 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. Technology description follows.

Efficient mRNA-Based Genetic Engineering of Human NK Cells with High-Affinity CD16 and CCR7

Description of Technology: A highly efficient method to genetically modify natural killer (NK) cells to induce expression of high affinity CD16 (HA-CD16) through mRNA electroporation, to potentiate NK cell-mediated antibody-dependent cellular cytotoxicity (ADCC). ADCC is mediated by CD16⁺ NK cells following adoptive NK cell transfer, but most humans express CD16 which has a relatively low affinity for IgG1 antibodies. However, a single nucleotide polymorphism (SNP rs396991) in the CD16 gene, resulting in an amino acid substitution at position 158 (F158V), is associated with substantially higher affinity and superior NK cell-mediated ADCC than those with the 158F genotype. This HA-CD16-158V polymorphism has also been linked to enhanced ADCC capacity in vivo. The nearly 100% efficiency of our method resulted in: a) sustained surface expression of transgenes at high levels for up to 4 days without compromising NK cell cytotoxicity and viability; and b) augmented ADCC against Daratumumab coated multiple myeloma cells by ex vivo expanded NK cells electroporated with mRNA coding for HA-CD16. This system is GMP compliant and has been used previously in FDA approved clinical trials.

Potential Commercial Applications: Infusion of a large number of highly cytotoxic autologous ex vivo expanded NK cells expressing high-affinity CD16 into patients, to induce a more profound anti-malignancy response to specific monoclonal antibodies, including: multiple myeloma (Daratumumab); lymphoma (Rituximab); breast cancer (Trastuzumab); and colon cancer (Cetuximab).

Development Stage: Early-stage; In vitro data available.

Inventors: Richard W. Childs and Mattias Carlsten (NHLBI)

Publications:

- 1) Carlsten M, Levy E, Karambelkar A, Li L, Reger R, Berg M, Peshwa MV and Childs RW (2016) Efficient mRNA-Based Genetic Engineering of Human NK Cells with High-Affinity CD16 and CCR7 Augments Rituximab-Induced ADCC against Lymphoma and Targets NK Cell Migration toward the Lymph Node-Associated Chemokine CCL19. *Front. Immunol.* 7:105. doi: 10.3389/fimmu.2016.00105.
- 2) Carlsten M and Childs RW (2015) Genetic manipulation of NK cells for cancer immunotherapy: techniques and clinical implications. *Front. Immunol.* 6:266. doi: 10.3389/fimmu.2015.00266.

Intellectual Property: NIH Reference No. E-036-2015/0,1 - US Application No. 62/079,975, filed 14 Nov 2014; and PCT Application No. PCT/US2015/060646, filed 13 Nov 2015.

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