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(72) Inventors; and
(71) Applicants : **BETTER, Marc** [US/US]; 2225 Colorado Avenue, Santa Monica, California 90404 (US). **FELDMAN, Steven, A.** [US/US]; National Cancer Institute, 10 Center Dr., Bethesda, Maryland 20892-1201 (US). **ROSENBERG, Steven, A.** [—/US]; National Cancer Institute, 10 Center Dr., Bethesda, Maryland 20892-1201 (US).

(74) Agents: **WISE, Michael, J.** et al; Perkins Coie LLP, P.O. Box 1247, Seattle, WA 981 11-1247 (US).

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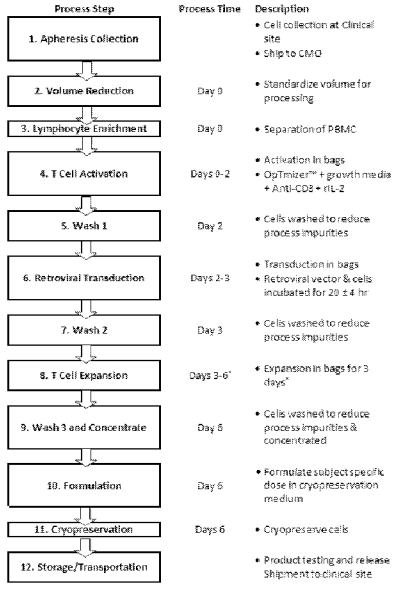
(54) **Title:** METHODS FOR PRODUCING AUTOLOGOUS T CELLS USEFUL TO TREAT B CELL MALIGNANCIES AND OTHER CANCERS AND COMPOSITIONS THEREOF

FIG. 1




**(57) Abstract:** Provided herein are methods for manufacturing T cells. In certain embodiments, methods for manufacturing T cells which express a cell surface receptor that recognizes a specific antigenic moiety on the surface of a target cell are provided. Such methods may include, but are not limited to, steps of (1) enriching a population of lymphocytes obtained from a donor subject; (2) stimulating the population of lymphocytes with one or more T-cell stimulating agents to produce a population of activated T cells, wherein the stimulation is performed in a closed system using serum-free culture medium; (3) transducing the population of activated T cells with a viral vector comprising a nucleic acid molecule which encodes the cell surface receptor, using a single cycle transduction to produce a population of transduced T cells, wherein the transduction is performed in a closed system using serum-free culture medium; and (4) expanding the population of transduced T cells for a predetermined time to produce a population of engineered T cells, wherein the expansion is performed in a closed system using serum-free culture medium. Also provided herein are populations of engineered T cells produced by the methods described herein and pharmaceutical compositions thereof.

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# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 15/14520

A. CLASSIFICATION OF SUBJECT MATTER
**IPC(8)** - C07K 16/30, 14/705; A61K 35/14 (2015.01)
**CPC** - C12N 2799/027; A61K 35/17
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8): A61K 48/00, 35/14; C07K 16/28, 16/30, 14/705; A61P 35/00 (2015.01)
CPC: C07K 2319/72, 2319/03, 14/82; C12N 2799/027, 15/11; A61K 48/00, 35/17, 45/06

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatSeer (US, EP, WO, JP, DE, GB, CN. FR, KR, ES, AU, IN, CA, INPADOC Data); Google; Google Scholan NCBI/PubMed; Dialog ProQuest; T cell,' engineer, activate, naive, population, cells, 'CAR,' TCR,' tumor, cancer, vector, 'MSGV,' 'B cell,' system, bag

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | WO 2013/040557 A2 (THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA); March 21, 2013; page 3, lines 3-14; page 5, lines 7-18; page 20, lines 29-34; page 21, lines 15-20; page 29, lines 1-3; page 31, lines 25-30; page 35, lines 20-30; page 48, lines 25-30; page 49, lines 1-11; page 50, lines 25-35; page 54, lines 5-15; page 55, lines 30-35; page 56, lines 1-10; page 57, lines 9-15; page 63, lines 10-20; page 91, lines 5-15 | 1-7, 9-13, 18-24, 26-30, 35/18-35/24, 35/26, 35/28-35/30, 36/35/18-36/35/24, 36/35/26-36/35/30, 37/36/35/18-37/36/35/24, 37/36/35/26-37/36/35/30, 41, 42 |
| Y | | 8, 14-17, 25, 31-34, 35/25, 35/31-35/34, 36/25, 36/35/31-36/35/34, 37/36/35/31-37/36/35/34, 38-40 |

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| Date of the actual completion of the international search | Date of mailing of the international search report |
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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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|---|---|---|
| Y | WO 2012/138475 A1 (THE UNITED STATES OF AMERICA, AS REPRESENTED BY THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES); October 11, 2012; paragraph [01 11] | 8, 25, 35/25, 36/35/25, 38/37/36/35/1 8-38/37/36/35/26, 38/37/36/35/28-38/37/36/35/34, 39/38/37/36/35/1 8-39/38/37/36/35/26, 38/37/36/35/28-38/37/36/35/28-38/37/36/35/34, 39/38/37/36/35/1 8-39/38/37/36/35/26, 39/38/37/36/35/28-39/38/37/36/35/34, 40/39/38/37/36/35/18-40/39/38/37/36/35/26, 40/39/38/37/36/35/28-40/39/38/37/36/35/34 |
| Y | BEYER, M et al. CD4+CD25highFOXP3+ Regulatory T Cells In Peripheral Blood Are Primarily Of Effector Memory Phenotype. JCO. 20 June 2007, Vol. 25, No. 18; pages 2628-263. DOI: 10.1200/JCO.2006.08.0192; page 2628, column 1, paragraph 2; page 2628, column 2, paragraph 1; page 2629, column 2, paragraph 2. | 14-17, 31-34, 35/31-35/34, 36/35/31-36/35/34, 37/36/35/31 -37/36/35/34 |
| Y | KOCHENDERFER, J N et al. Construction And Pre-Clinical Evaluation Of An Anti-CD19 Chimeric Antigen Receptor. J Immunother. September 2009, Vol. 32, No. 7; pages 689-702. DOI: 10.1097/CJI.0b013e3181ac6138; page 3 paragraph 1. | 38-40 |