(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
15 October 2015 (15.10.2015)

WIPO | PCT

(10) International Publication Number
WO 2015/157384 A1

(51) International Patent Classification:
A61K 39/395 (2006.01) *C12N 5/10* (2006.01)

(21) International Application Number:
PCT/US2015/024866

(22) International Filing Date:
8 April 2015 (08.04.2015)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

61/977,751	10 April 2014 (10.04.2014)	US
61/986,479	30 April 2014 (30.04.2014)	US
62/058,973	2 October 2014 (02.10.2014)	US
62/088,363	5 December 2014 (05.12.2014)	US
62/089,730	9 December 2014 (09.12.2014)	US
62/090,845	11 December 2014 (11.12.2014)	US

(71) Applicant: **SEATTLE CHILDREN'S HOSPITAL (DBA SEATTLE CHILDREN'S RESEARCH INSTITUTE)** [US/US]; 1900 Ninth Avenue, Seattle, WA 98101 (US).

(72) Inventor: **JENSEN, Michael, C.**; 1900 Ninth Avenue, Seattle, WA 98101 (US).

(74) Agent: **FURMAN, Eric, S.**; Knobbe Martens Olson & Bear LLP, 2040 Main Street, 14th Floor, Irvine, CA 92614 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

— *with international search report (Art. 21(3))*

[Continued on next page]

(54) Title: DEFINED COMPOSITION GENE MODIFIED T-CELL PRODUCTS

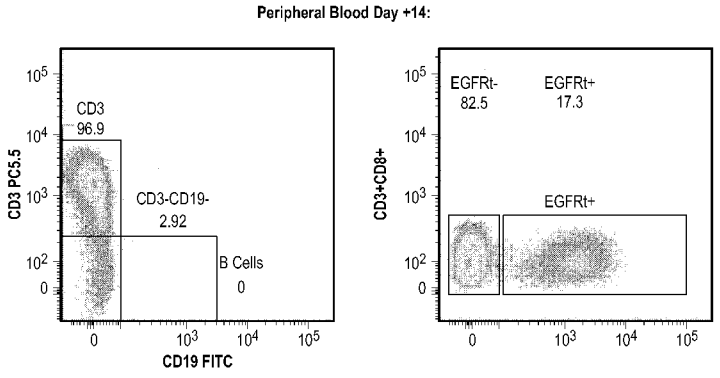


FIG. 11A FIG. 11B

(57) Abstract: Aspects of the invention described herein, concern approaches to make genetically modified T-cells comprising a chimeric antigen receptor for human therapy. In some alternatives, the methods utilize a selection and/or isolation of CD4+ and/or CD8+ T-cells from a mixed T-cell population, such as, peripheral blood or apheresis derived mononuclear cells. Once selected/isolated, the CD4+ and/or CD8+ T-cells are then activated, genetically modified, and propagated, preferably, in separate or isolated cultures in the presence of one or more cytokines, which support survival, engraftment and/or proliferation of the cells, as well as, preferably promoting or inducing the retention of cell surface receptors, such as CD62L, CD28, and/or CD27. Included herein are also methods of treatment, inhibition, amelioration, or elimination of a cancer by administering to a subject in need thereof, one or more types of the genetically engineered T-cells or compositions that comprise the genetically engineered T-cell prepared as described herein.

WO 2015/157384 A1

— *with sequence listing part of description (Rule 5.2(a))*