US009511127B2

(12) **United States Patent**
Har-Noy

(10) **Patent No.: US 9,511,127 B2**
(45) **Date of Patent: *Dec. 6, 2016**

(54) **METHOD TO FORMULATE T-CELLS**

(71) Applicant: **Immunovative Therapies, Ltd.**, Jerusalem (IL)

(72) Inventor: **Michael Har-Noy**, Jerusalem (IL)

(73) Assignee: **IMMUNOVATIVE THERAPIES LTD.**, Jerusalem (IL)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 274 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **14/301,700**

(22) Filed: **Jun. 11, 2014**

(65) **Prior Publication Data**

US 2014/0294781 A1 Oct. 2, 2014

Related U.S. Application Data

(60) Continuation of application No. 12/887,039, filed on Sep. 21, 2010, now Pat. No. 8,785,188, which is a continuation of application No. 12/173,330, filed on Jul. 15, 2008, now Pat. No. 8,076,135, which is a division of application No. 11/069,010, filed on Mar. 1, 2005, now Pat. No. 7,402,431, which is a continuation-in-part of application No. 10/838,454, filed on May 4, 2004, now Pat. No. 7,435,592.

(60) Provisional application No. 60/549,032, filed on Mar. 1, 2004, provisional application No. 60/547,966, filed on Feb. 26, 2004, provisional application No. 60/545,450, filed on Feb. 18, 2004, provisional application No. 60/470,171, filed on May 13, 2003.

(51) **Int. Cl.**

C12N 5/00	(2006.01)
C12N 5/02	(2006.01)
A61K 39/00	(2006.01)
C12N 5/0783	(2010.01)
A61K 35/17	(2015.01)

(52) **U.S. Cl.**

CPC ***A61K 39/0005*** (2013.01); ***A61K 35/17*** (2013.01); ***C12N 5/0636*** (2013.01); *A61K 2039/5154* (2013.01); *A61K 2039/57* (2013.01); *C12N 2501/51* (2013.01); *C12N 2501/515* (2013.01); *C12N 2531/00* (2013.01); *C12N 2533/40* (2013.01)

(58) **Field of Classification Search**

None

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,806,529	A	9/1998	Reisner et al.
6,352,694	B1	3/2002	June et al.
6,534,055	B1	3/2003	June et al.
6,905,680	B2	6/2005	June et al.
6,905,874	B2	6/2005	Berenson et al.
2002/0115214	A1	8/2002	June et al.
2002/0127208	A1	9/2002	Waller et al.
2004/0228848	A1	11/2004	Har-Noy

FOREIGN PATENT DOCUMENTS

JP	2001522806	A	11/2001
WO	94/12196	A1	6/1994
WO	01/62895	A2	8/2001
WO	03015705	A2	2/2003
WO	03/024989	A2	3/2003
WO	03/038062	A2	5/2003
WO	03/057171	A2	7/2003
WO	2004/004768	A1	1/2004
WO	2005/001074	A1	1/2005
WO	2005/081982	A2	9/2005

OTHER PUBLICATIONS

Raghupathy, R. et al. (1999). "Maternal Th1- and Th2-Type Reactivity to Placental Antigens in Normal Human Pregnancy and Unexplained Recurrent Spontaneous Abortions." Cellular Immunology, vol. 196, No. 2: pp. 122-130.

Rondon, G., S. Giralt, et al. (1996). "Graft-versus-leukemia effect after allogeneic bone marrow transplantation for chronic lymphocytic leukemia." Bone Marrow Transplant 18(3): 669-72.

Rosenberg, S. A. (2001). "Progress in the development of immunotherapy for the treatment of patients with cancer." Journal of Internal Medicine, vol. 250, No. 6: pp. 462-475.

Roussel, E. et al. (1996). "Predominance of a type 2 intratumoural immune response in fresh tumour-infiltrating lymphocytes from human gliomas." Clinical and Experimental Immunology, vol. 105, No. 2: pp. 344-352.

Rubbi, C.P. et al. (1993). "Evidence of surface antigen detachment during incubation of cells with immunomagnetic beads." Journal of Immunology Methods, vol. 166, No. 2: pp. 233-241.

Santin, A. D. et al. (2000). "Interleukin-10 Increases Th1 Cytokine Production and Cytotoxic Potential in Human Papillomavirus-Specific CD8(+) Cytotoxic T Lymphocytes." Journal of Virology, vol. 74, No. 10: pp. 4729-4737.

Sato, M., S. Goto, et al. (1998). "Impaired production of Th1 cytokines and increased frequency of Th2 subsets in PBMC from advanced cancer patients." Anticancer Res 18(5D): 3951-5.

Saxton, M. L. et al. (1997). "Adoptive Transfer of Anti-CD3-Activated CD4+ T Cells Plus Cyclophosphamide and Liposome-Encapsulated Interleukin-2 Cure Murine MC-38 and 3LL Tumors and Establish Tumor-Specific Immunity." Blood, vol. 89, No. 7: pp. 2529-2536.

Shibuya, T.Y. et al. (2000). "Anti-CD3/Anti-CD28 Bead Stimulation Overcomes CD3 Unresponsiveness in Patients With Head and Neck Squamous Cell Carcinoma." Arch Otolaryngol Head Neck Surg, vol. 126, No. 4: 473-479.

Shinomiya, Y., M. Harada, et al. (1995). "Anti-metastatic activity induced by the in vivo activation of purified protein derivative (PPD)-recognizing Th1 type CD4+ T cells." Immunobiology 193(5): 439-55.

(Continued)

Primary Examiner — Michail Belyavskyi

(74) *Attorney, Agent, or Firm* — Westman, Champlin & Koehler, P.A.; Z. Peter Sawicki; Visala Goswitz

(57) **ABSTRACT**

A method for formulating T-cells for use as a medicant comprises suspending T-cells with cross-linked surface moieties in a media suitable for infusion. The cross-linked T-cells are packaged in a container suitable for administration to a patient.

8 Claims, No Drawings