US005935568A

United States Patent [19]

Dow et al.

[11] **Patent Number: 5,935,568**

[45] **Date of Patent: Aug. 10, 1999**

[54] **GENE THERAPY FOR EFFECTOR CELL REGULATION**

[75] Inventors: **Steve W. Dow**; **Robyn E. Elmslie**; **Terence A. Potter**, all of Denver, Colo.

[73] Assignee: **National Jewish Medical & Research Center**, Denver, Colo.

[21] Appl. No.: **08/580,806**

[22] Filed: **Dec. 29, 1995**

Related U.S. Application Data

[63] Continuation-in-part of application No. 08/446,918, May 18, 1995, Pat. No. 5,705,151, and a continuation-in-part of application No. 08/484,169, Jun. 7, 1995, abandoned.

[51] **Int. Cl.**[6] **A61K 48/00**; C12N 15/63; C12N 15/09

[52] **U.S. Cl.** **424/93.21**; 514/44; 435/69.1; 435/172.3; 435/375

[58] **Field of Search** 514/44; 435/320.1, 435/69.1, 172.3, 375; 935/62, 56, 57, 71, 65; 424/93.21

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,994,369	2/1991	Krensky et al.	435/6
5,145,676	9/1992	Fahey, III et al.	424/85.1
5,580,859	12/1996	Felgner et al.	514/44
5,589,466	12/1996	Felgner et al.	514/44
5,593,972	1/1997	Weiner et al.	514/44
5,641,662	6/1997	Debs et al.	435/172.1

FOREIGN PATENT DOCUMENTS

WO 91/04053	4/1991	WIPO .
WO 91/04272	4/1991	WIPO .
WO 92/14823	9/1992	WIPO .
WO 93/24136	12/1993	WIPO .
WO 95/00178	1/1995	WIPO .

OTHER PUBLICATIONS

Howard et al., "Chemokines: progress toward identifying molecular targets for therapeutic agents," TIBTECH, vol. 14, p. 7799–7804, Feb. 1996.
Taub et al., "Chemokines, inflammation and the immune system," Therapeutic Immunology, vol. 1, pp. 229–246, 1994.
Blackman et al., *Life Sci.*, 57(19):1717–1735, 1995.
Donnelly et al., *Ann. N.Y. Acad. Sci.*, 772:40–46, 1995.
Liu, *Ann. N.Y. Acad. Sci.*, 772(DNA Vaccines):15–21, 1995.
Miethke et al., *Int. Arch. Allergy Immunol.*, 106:3–7, 1995.
Miethke et al., *Immunobiol.*, 189:270–284, 1993.
"Chemokines", pp. 79–85.
Bhardwaj et al., 1993, *J. Exp. Med.*, 178:633–642.
Borremans et al., 1989, *Infection and Immunity*, 57(10):3123–3130.
Davatelis et al., 1988, *J. Exp. Med.*, 167: 1939–1944.
Dohlsten et al., 1991, *Proc. Natl. Acad. Sci. U.S.A.*, 88:9287–9291.
Hansson et al., 1992, *Immunol. Lett.*, 34(3):229–236.
Hedlund et al., 1993, *Cancer Immunol. Immunother.*, 36:89–93.
Hermann et al., 1993, *Seminars in Immumol.*, 5:33–39.
Kalland et al., 1993, *Med. Oncol. & Tumor Pharmacother.*, 10(1/2):37–47.
Lando et al., 1993, *Cancer Immunol. Immunother.*, 36:223–228.
Lukacs et al., 1993, *J. Exp. Med.*, 178:343–348.
Micusan et al., 1993, *Seminars in Immunol.*, 5:3–11.
Newell et al., 1991, *Proc. Natl. Acad. Sci. U.S.A.*, 88:1074–1078.
Ochi et al., 1993, *J. Immunol.*, 151(6):3180–3186.
Rellahan et al., 1990, *J. Exp. Med.*, 172:1091–1100.
Sherry et al., 1988, *J. Exp. Med.*, 168:2251–2259.
White et al., 1989, *Cell*, 56:27–35.
Wiker et al., 1992, *Microbiological Reviews*, 56:648–661.

Primary Examiner—Brian R. Stanton
Assistant Examiner—Karen M. Hauda
Attorney, Agent, or Firm—Sheridan Ross P.C.

[57] **ABSTRACT**

The present invention provides a nucleic acid-based therapeutic composition to treat an animal with disease by controlling the activity of effector cells, including T cells, macrophages, monocytes and/or natural killer cells, in the animal. Therapeutic compositions of the present invention include superantigen-encoding nucleic acid molecules, either in the presence or absence of a cytokine-encoding nucleic acid molecule and/or chemokine-encoding nucleic acid molecules, depending upon the disease being treated. The present invention also relates to an adjuvant for use with nucleic acid-based vaccines. Adjuvant compositions of the present invention include an immunogen combined with superantigen-encoding nucleic acid molecules, either in the presence or absence of a cytokine-encoding nucleic acid molecule and/or chemokine-encoding nucleic acid molecules.

28 Claims, 14 Drawing Sheets