US005512294A

United States Patent [19]

Li et al.

[11] Patent Number: 5,512,294

[45] Date of Patent: Apr. 30, 1996

[54] **TARGETED POLYMERIZED LIPOSOME CONTRAST AGENTS**

[76] Inventors: **King C. Li**, 21 Ryan Ct., Stanford, Calif. 94305; **Mark D. Bednarski**, 816 Amber La., Los Altos, Calif. 94024; **Richard W. Storrs**, 2755 Rose Bud Ct., Union City, Calif. 94587; **Henry Y. Li**, 3350 W. Sunnyside Ave., Visalia, Calif. 93277; **Francois D. Trooper**, 1851 Magellan Dr., Oakland, Calif. 94611; **Curtis K. H. Song**, 548 E. Maude Ave., Sunnyvale, Calif. 94086; **Dorothy A. Sipkins**, 933 Addison St., Palo Alto, Calif. 94301; **Jeremy K. Kuniyoshi**, 22344 Carta Blanca St., Cupertino, Calif. 95014

[21] Appl. No.: **286,555**

[22] Filed: **Aug. 5, 1994**

[51] **Int. Cl.**[6] **A61K 9/127**

[52] **U.S. Cl.** **424/450**; 424/1.21; 436/829

[58] **Field of Search** 424/450, 1.21; 436/829

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,544,545	10/1985	Ryan et al.	424/1.1
4,938,947	7/1990	Nicolau et al.	424/1.1
5,017,359	5/1991	Nicolau et al.	423/1.1
5,077,057	12/1991	Szoka, Jr.	424/450
5,078,986	1/1992	Bosworth et al.	424/9
5,135,737	8/1992	Keana	424/9
5,158,760	10/1992	Phillips et al.	424/1.1
5,213,804	5/1993	Martin et al.	424/450
5,246,707	9/1993	Haynes	424/450
5,277,914	1/1994	Szoka, Jr.	424/450
5,366,881	11/1994	Singth	435/177
5,387,410	2/1995	Bosworth	424/9
5,395,619	3/1995	Zalipsky	424/450

FOREIGN PATENT DOCUMENTS

0054384	3/1988	Japan .
9221017	11/1992	WIPO .

OTHER PUBLICATIONS

Purnima Pinnaduwage and Leaf Haung, "Stable Target–Sensitive Immunoliposomes", *Biochemistry* (1992), 31, 2850–2855.

Marja–Leena Laukkanen, Kaija Alfthan, and Kari Keinanen, "Functional Immunoliposomes Harboring a Biosynthetically Lipid–Tagged Single–Chain Antibody", *Biochemistry* (1994), 33, 11664–11670.

Unger, E. C., Shen, D. K., and Fritz, T. A., Status of Liposomes as MR Contrast Agents, JMRI, 3, 195–198, (1993).

Gore, J. C. and Smith, F. W., Special Issue: Contrast Agents, Magn. Reson. Img., 3, 1–97, (1985).

Hasso, A. N. and Stark, D. D., Special Issue: Contrast Agents, JMRI, 3, 137–310, (1993).

Wehrli, F. W., SMRM Workshop: Contrast Enhanced Magnetic Resonance, Magn. Reson. Med., 22, 177–378, (1991).

Reimer, P., Weissleder, R. Brady, T. J., Baldwin, B. H., Tennant, B. C., and Wittenberg, J., Experimental Hepatocellular Carcinoma: MR Receptor Imaging, Radiology, 180, 641–645 (1991).

Reimer, P., Weisslender, R., Lee, A. S., and Brady, T. J., Receptor Imaging: Application to MR Imaging of Liver Cancer, Radiology, 177, 729–734 (1990).

Reimer, P., Weissleder, R., Wittenberg, J., and Brady, T. J., Receptor–Directed Contrast Agents for MR Imaging: Preclinical Evaluation With Affinity Assays, Radiology, 182, 565–569 (1992).

Weissleder, R., Reimer, P., Lee, A. S., Wittenberg, J. and Brady T. J., MR Receptor Imaging: Ultrasmall Iron Oxide Particles Targeted to Asialoglycoprotein Receptors, AJR, 155, 1161–67, (1990).

Unger, E. C., Totty, W. G., Neufeld, D. M., Otsuka, F. L., Murphy, W. A., Welch, M. S., Connett, J. M., and Philpott, G. W., Magnetic Resonance Imaging Using Gadolinium labeled Monoclonal Antibody, Invest. Radiol., 20, 693–700. (1985).

Weissleder, R., Lee, A. S., Fischman, A. J., Reimer, P., Shen, T., Wilkinson, R., Callahan, R. J., and Brady, T. J., Polyclonal Human Immunoglobulin G Labeled with polymeric Iron Oxide: Antibody MR Imaging, Radiology, 181, 245–249, (1991).

Primary Examiner—Gollamudi S. Kishore

Attorney, Agent, or Firm—Speckman, Pauley & Fejer