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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 October 2004 (21.10.2004)

PCT

(10) International Publication Number
WO 2004/089291 A3

(51) International Patent Classification[7]: A61K 31/335

(21) International Application Number:
PCT/US2004/010230

(22) International Filing Date: 2 April 2004 (02.04.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/460,827 3 April 2003 (03.04.2003) US

(71) Applicants and
(72) Inventors *(for all designated States except US)*: **AU, Jessie, L.-S.** [US/US]; 2287 Palmleaf Court, Columbus, OH 43235 (US). **WIENTJES, M., Guillaume** [NL/US]; 2287 Palmleaf Court, Columbus, OH 43235 (US).

(74) Agents: **MUELLER, Jerry, K., Jr.** et al.; Mueller and Smith, LPA, 7700 Rivers Edge Drive, Columbus, OH 43235 (US).

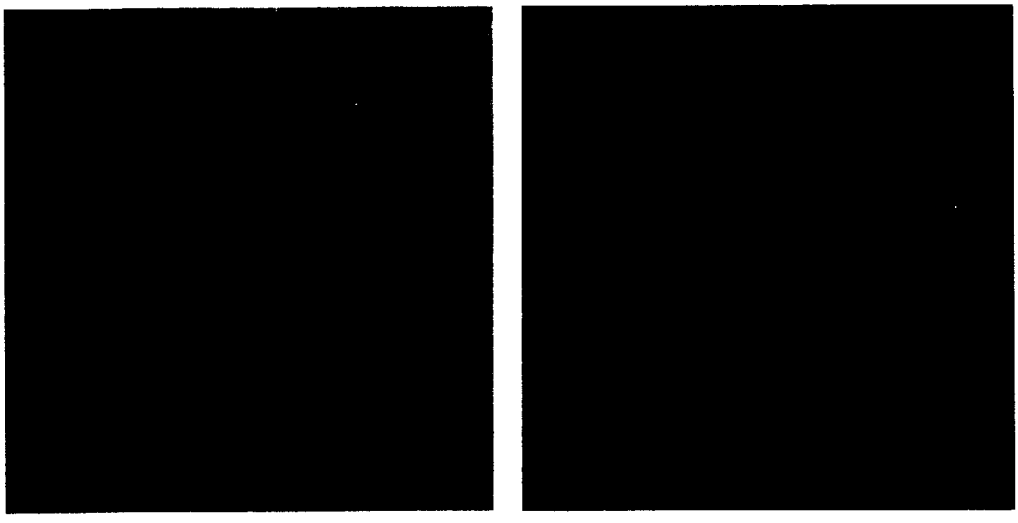
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,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

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

[Continued on next page]

(54) Title: TUMOR-TARGETING DRUG-LOADED PARTICLES



(57) Abstract: A composition for delivering a tumor therapeutic agent to a patient includes a fast-release formulation of a tumor apoptosis inducing agent, a slow-release formulation of a tumor therapeutic agent, and a pharmaceutically acceptable carrier. An apoptosis-inducing agent in a pharmaceutically acceptable carrier may be administered before or concomitantly therewith. Nanoparticles or microparticles (*e.g.*, cross-linked gelatin) of the therapeutic agent (*e.g.*, paclitaxel) also may be used. The nanoparticles or microparticles may be coated with a bioadhesive coating. Microspheres that agglomerate to block the entrance of the lymphatic ducts of the bladder to retard clearance of the microparticles through the lymphatic system also may be employed. This invention also uses drug-loaded gelatin and poly(lactide-co-glycolide) (PLGA) nanoparticles and microparticles to target drug delivery to tumors in the peritoneal cavity, bladder tissues, and kidneys. Fig. 1 (left) shows multiple tumors disseminated through the peritoneal cavity of a mouse implanted with intraperitoneal human Hs766T pancreatic xenograft tumors under room light and (right) under UV light.

WO 2004/089291 A3

(88) Date of publication of the international search report:
21 April 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.