



(51) International Patent Classification:

A61K 9/16 (2006.01) *A61K 38/17* (2006.01)
A61K 47/48 (2006.01) *A61K 31/7105* (2006.01)
A61K 49/08 (2006.01) *A61K 31/7088* (2006.01)
A61K 48/00 (2006.01)

(21) International Application Number:

PCT/US2012/060072

(22) International Filing Date:

12 October 2012 (12.10.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/547,402 14 October 2011 (14.10.2011) US
 61/577,410 19 December 2011 (19.12.2011) US
 61/578,463 21 December 2011 (21.12.2011) US

(71) Applicants: **STC.UNM** [US/US]; 801 University Blvd. DE, Suite 101, Albuquerque, NM 87106 (US). **SANDIA CORPORATION** [US/US]; 1515 Burbank SE, Albuquerque, NM 87123 (US).

(72) Inventors: **ASHLEY, Carlee Erin**; 3708 Tewa Dr. NE, Albuquerque, NM 87111 (US). **BRINKER, C., Jeffrey**; 14 Eagle Nest Drive NE, Albuquerque, NM 87122 (US). **CARNES, Eric C.**; 13309 Chaco Cliff Trail SE, Albuquerque, NM 87123 (US). **FEKRAZAD, Mohammad Houman**; 4261 Altura Mesa Lane NE, Albuquerque, NM 87110 (US). **FELTON, Linda A.**; 11500 Arroyo De Vista NE, Albuquerque, NM 87111 (US). **NEGRETE, Oscar**; 2341 Willet Way, Pleasanton, CA 94566 (US). **PADILLA, David Patrick**; 11012 Escensia NW, Albuquerque, NM 87114 (US). **WILKINSON, Brian S.**; 6308 Zimmerman Ave. NE, Albuquerque, NM 87110 (US). **WILKINSON, Dan C.**; 6308 Zimmerman Ave, NE, Albuquerque, NM

87110 (US). **WILLMAN, Cheryl L.**; 4633 Los Poblanos Circle NW, Albuquerque, NM 87107 (US).

(74) Agent: **COLEMAN, Henry, D.**; 714 Colorado Avenue, Bridgeport, CT 06605-1601 (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, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, 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, 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, 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, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— of inventorship (Rule 4.17(iv))

Published:

— without international search report and to be republished upon receipt of that report (Rule 48.2(g))

(54) Title: POROUS NANOPARTICLE-SUPPORTED LIPID BILAYERS (PROTOCELLS) FOR TARGETED DELIVERY INCLUDING TRANSDERMAL DELIVERY OF CARGO AND METHODS THEREOF

(57) Abstract: The present invention is directed to protocells for specific targeting of hepatocellular and other cancer cells which comprise a nanoporous silica core with a supported lipid bilayer; at least one agent which facilitates cancer cell death (such as a traditional small molecule, a macromolecular cargo (e.g. siRNA or a protein toxin such as ricin toxin A-chain or diphtheria toxin A-chain) and/or a histone-packaged plasmid DNA disposed within the nanoporous silica core (preferably supercoiled in order to more efficiently package the DNA into protocells) which is optionally modified with a nuclear localization sequence to assist in localizing protocells within the nucleus of the cancer cell and the ability to express peptides involved in therapy (apoptosis/cell death) of the cancer cell or as a reporter, a targeting peptide which targets cancer cells in tissue to be treated such that binding of the protocell to the targeted cells is specific and enhanced and a fusogenic peptide that promotes endosomal escape of protocells and encapsulated DNA. Protocells according to the present invention may be used to treat cancer, especially including hepatocellular (liver) cancer using novel binding peptides (c-MET peptides) which selectively bind to hepatocellular tissue or to function in diagnosis of cancer, including cancer treatment and drug discovery.

