



- (51) **International Patent Classification:**
A61K 39/395 (2006.01) *A61P 35/00* (2006.01)
- (21) **International Application Number:**
PCT/US2015/060331
- (22) **International Filing Date:**
12 November 2015 (12.11.2015)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
62/079,357 13 November 2014 (13.11.2014) US
62/190,977 10 July 2015 (10.07.2015) US
- (71) **Applicant:** THE JOHNS HOPKINS UNIVERSITY [US/US]; 3400 N Charles Street, Baltimore, Maryland 21218 (US).
- (72) **Inventors:** DIAZ, Luis; 5135 Crystal Springs Drive, Ellicott City, Maryland 21043 (US). VOGELSTEIN, Bert; 3700 Breton Way, Baltimore, Maryland 21208 (US). KINZLER, Kenneth W.; 616 Ponte Villas North, Baltimore, Maryland 21208 (US). PAPADOPOULOS, Nickolas; 606 Homcrest Road, Towson, Maryland 21204 (US). LE, Dung; 12 Laurel Circle, Lutherville, Maryland 21093 (US).
- (74) **Agent:** KAGAN, Sarah A.; 1100 13th Street NW, Suite 1200, Washington, District of Columbia 20005 (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, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, 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, SA, 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, ST, 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, KM, ML, MR, NE, SN, TD, TG).
- Published:**
— with international search report (Art. 21(3))

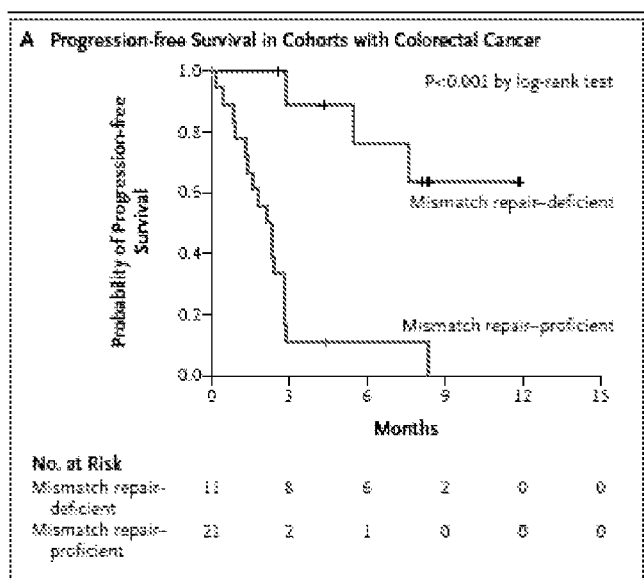
(54) **Title:** CHECKPOINT BLOCKADE AND MICROSATELLITE INSTABILITY

Fig. 2A

(57) **Abstract:** Blockade of immune checkpoints such as cytotoxic T-lymphocyte antigen-4 (CTLA-4) and programmed death-1 (PD-1) shows promise in patients with cancer. Inhibitory antibodies directed at these receptors have been shown to break immune tolerance and promote anti-tumor immunity. These agents work particularly well in patients with a certain category of tumor. Such tumors may be particularly susceptible to treatment because of the multitude of neoantigens which they produce.