

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
20 January 2022 (20.01.2022)



(10) International Publication Number
WO 2022/015694 A1

- (51) **International Patent Classification:**
C07K 14/725 (2006.01) *A61K 38/00* (2006.01)
- (21) **International Application Number:**
PCT/US2021/041375
- (22) **International Filing Date:**
13 July 2021 (13.07.2021)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
63/050,931 13 July 2020 (13.07.2020) US
- (71) **Applicant: THE UNITED STATES OF AMERICA, AS REPRESENTED BY THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES** [US/US]; Office of Technology Transfer, National Institutes of Health, 6701 Rockledge Drive, Suite 700, MSC 7788, Bethesda, Maryland 20892-7788 (US).
- (72) **Inventors: ROSENBERG, Steven A.;** 10104 Iron Gate Road, Potomac, Maryland 20854 (US). **YOSEPH, Rami;**

14 Landsend Drive, Gaithersburg, Maryland 20878 (US). **LEVIN, Noam;** 357 Congressional Lane, Rockville, Maryland 20852 (US). **CAFRI, Gal;** 305 Congressional Lane, Rockville, Maryland 20852 (US).

(74) **Agent: LAWLEY, Stephanie M. et al.;** Leydig, Voit & Mayer, Two Prudential Plaza, Suite 4900, 180 North Stetson Avenue, Chicago, Illinois 60601 (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, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, 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, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) **Designated States** (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH,

(54) **Title:** HLA CLASS II-RESTRICTED DRB T CELL RECEPTORS AGAINST RAS WITH G12D MUTATION

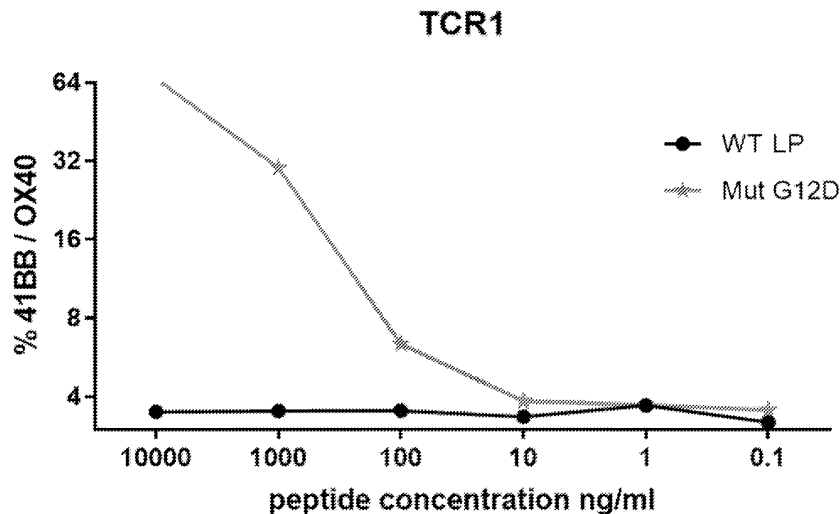


Fig. 2A

(57) **Abstract:** Disclosed is an isolated or purified T cell receptor (TCR), wherein the TCR has antigenic specificity for a mutated human RAS amino acid sequence with a substitution of glycine at position 12 with aspartic acid. The TCRs may recognize G12D RAS presented by an HLA-DR heterodimer. Related polypeptides and proteins, as well as related nucleic acids, recombinant expression vectors, host cells, populations of cells, and pharmaceutical compositions are also provided. Also disclosed are methods of detecting the presence of cancer in a mammal and methods of treating or preventing cancer in a mammal.

[Continued on next page]

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))
- with sequence listing part of description (Rule 5.2(a))