

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
02 March 2023 (02.03.2023)



(10) International Publication Number
WO 2023/028494 A2

(51) International Patent Classification:
C07K 14/705 (2006.01) A61K 39/00 (2006.01)

(21) International Application Number:
PCT/US2022/075362

(22) International Filing Date:
23 August 2022 (23.08.2022)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
63/236,556 24 August 2021 (24.08.2021) US

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(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, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, 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, 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:

- without international search report and to be republished upon receipt of that report (Rule 48.2(g))
- with sequence listing part of description (Rule 5.2(a))

(54) Title: PEPTIDE-CENTRIC CHIMERIC ANTIGEN RECEPTORS TO CANCER SELF-PEPTIDES

(57) Abstract: The neuroblastoma immunopeptidome is enriched with peptides derived from proteins essential for tumorigenesis including the unmutated peptide QYNPIRTTF (SEQ ID NO: 1) discovered on HLA-A*24:02 which is derived from the neuroblastoma dependency gene and master transcriptional regulator PHOX2B. To target QYNPIRTTF, peptide-centric chimeric antigen receptors (PC-CARs) were developed via a counter panning strategy using predicted potentially cross-reactive peptides. Informed by computational modeling, PHOX2B peptide-centric CARs were demonstrated to also recognize QYNPIRTTF (SEQ ID NO: 1) presented by HLA-A*23:01 and the highly divergent HLA-B*14:02. Potent and specific killing of neuroblastoma cells expressing these HEAs in vitro was shown along with complete tumor regression in mice.



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