



(51) International Patent Classification:

C07K 19/00 (2006.01) C07K 14/715 (2006.01)
C12N 5/078 (2010.01)

(21) International Application Number:

PCT/CN2024/113452

(22) International Filing Date:

20 August 2024 (20.08.2024)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

PCT/CN2023/114033

21 August 2023 (21.08.2023) CN

(71) Applicants: **HANGZHOU HERVOR THERAPEUTICS CO., LTD** [CN/CN]; RM111, 319 Shenjia Rd., Gongshu District, Hangzhou, Zhejiang 310022 (CN). **TCRCURE BIOPHARMA CORP.** [US/US]; P.O. Box 110087, Research Triangle Park, Durham, North Carolina 27709 (US). **GUANGDONG TCRCURE BIOPHARMA TECHNOLOGY CO., LTD.** [CN/CN]; Building 12, No. 6 Nanjiang Second Road, Zhujiang Avenue, Nansha District,

Guangzhou, Guangdong 511400 (CN). **TCRCURE HONG KONG LTD.** [CN/CN]; Unit 2508a 25/F Bank of America Tower, 12 Harcourt Road, Central, Hong Kong (CN).

(72) Inventors: **CHEN, Rui**; 666 Longyang Avenue, Pudong New Area, Shanghai 200125 (CN). **YU, Jianshuai**; Room 3202, Unit 2, Building 7, Qingtianbandao Community, Xingqiao Street, Linping District, Hangzhou, Zhejiang 311199 (CN). **HUA, ChaoJu**; Room 401, Unit 2, Building 23, Dingshan Homeland, Zhuantang Street, Xihu District, Hangzhou, Zhejiang 310024 (CN). **LI, Si**; 28 E Linda Vista Ave, Alhambra, CA 91801 (US). **DU, Weiting**; 807 W. Camino Real Ave, Unit N, Arcadia, CA 91007 (US).

(74) Agent: **BEIJING QIKUN INTELLECTUAL PROPERTY AGENCY LTD.**; 4F Wangfu International Center, 219 Wangfujing Street, Dongcheng District, Beijing 100006 (CN).

(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,

(54) Title: SYNTHETIC CYTOKINE SIGNALING SYSTEM, PREPARATION METHOD, AND USES THEREOF

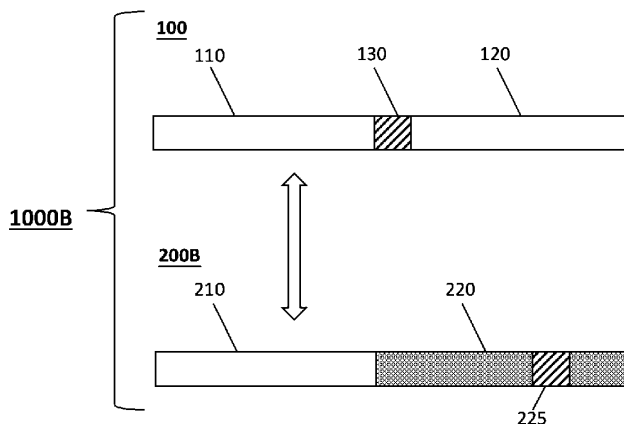


FIG. 2B

(57) Abstract: A synthetic cytokine signaling system includes an engineered cytokine signaling chain encoding a transmembrane polypeptide that contains a particular variant intracellular domain of IL9R and an extracellular domain of a cytokine receptor such as IL2R β , IL4R α , IL7R α , IL9R, and IL21R. Depending on whether a functionally compatible cytokine ligand domain is fused on the N-terminus, the engineered cytokine signaling chain may be in a self-activating form, or optionally may be in a non-self-activating form. In the latter case, the synthetic cytokine signaling system may further include an engineered cytokine ligand chain encoding a corresponding cytokine ligand that can be membrane-bound or secreted. Immune cells modified with the synthetic cytokine signaling system displays improved characteristics compared with unmodified immune cells, such as the zero or reduced dependency on IL-2 when cultured in vitro, enhanced activation upon antigen stimulation, increased cytotoxicity against target cells, and improved tumor control capacity when transferred in vivo.

[Continued on next page]

KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY,
MA, MD, MG, MK, MN, MU, 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, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, 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, ME, 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))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))