

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

(19) World Intellectual Property  
Organization  
International Bureau

(43) International Publication Date  
17 November 2022 (17.11.2022)



(10) International Publication Number  
**WO 2022/240917 A3**

(51) International Patent Classification:  
C07K 14/74 (2006.01)

TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,  
KM, ML, MR, NE, SN, TD, TG).

(21) International Application Number:  
PCT/US2022/028645

**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))

(22) International Filing Date:  
10 May 2022 (10.05.2022)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
63/186,770 10 May 2021 (10.05.2021) US

(88) Date of publication of the international search report:  
05 January 2023 (05.01.2023)

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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, 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,

(54) Title: POCKET ENGINEERING OF HLA ALLELES FOR TREATING AUTOIMMUNITY

(57) Abstract: Methods of preventing or treating autoimmune disease are disclosed. In some cases, subjects with having or at risk of developing autoimmune disease are identified as possessing one or more autoimmunity-susceptibility HLA alleles at one or more HLA loci. In many cases, the HLA loci are selected from Class I and Class II loci, for example Class I A, B, and C, and Class II DQ, DR, and DP. In many cases, subjects suffering from or at risk of developing an autoimmune disease may be administered a plurality engineered autologous HSCs modified to carry and express a variant susceptibility allele having at least one mutation in the antigen binding cleft that alters antigen binding and/or specificity of that variant HLA molecule. In many embodiments, the engineered HSCs are CD34+ immune cells that express one or more modified HLA proteins.



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