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(81) 指定国(除另有指明，要求每一种可提供的国家保护): 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, 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, UY, UZ, VC, VN, WS, ZA, ZM, ZW。

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(54) **Title:** MODIFIED ENHANCED IMMUNOCYTE TARGETING HPV AND PHARMACEUTICAL USE THEREOF

(54) 发明名称: 经修饰的靶向HPV增强型免疫细胞及其医药用途

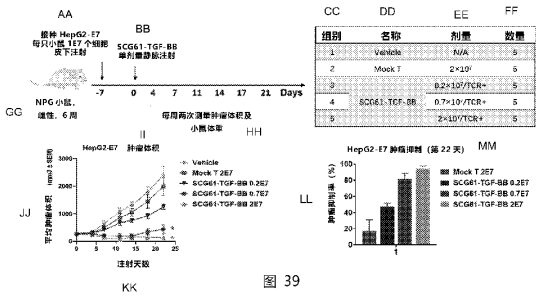


图 39

AA Inoculation of HepG2-E7 via subcutaneous injection of 1E7 cells per mouse
BB Single-dose intravenous injection of SCG61-TGF-BB
CC Group
DD Name
EE Dosage
FF Number
GG NPG mouse, female, 6-weeks old
HH Measurement of tumor volume and body weight of mouse twice a week
II Tumor volume
JJ Average tumor volume
KK Days after injection
LL Tumor inhibitory rate
MM HepG2-E7 tumor inhibition (day 22)

(57) **Abstract:** Disclosed in the present application are a modified enhanced immunocyte targeting HPV and the pharmaceutical use thereof. Provided in the present invention are a T-cell receptor or a fragment thereof targeting the E7 antigen of HPV, and the pharmaceutical use thereof. In addition, further provided are a modified immunocyte simultaneously expressing HPV-targeting TCR and converting a costimulatory molecule, and the pharmaceutical use thereof. In the modified immunocyte of the present application, the intracellular activation signaling domain of a costimulatory molecule is used to replace the intracellular inhibitory signaling domain of an immunosuppressive receptor, so that the inhibitory signal induced by the binding of immunosuppressive factors or ligands is converted into an activation signal, which can effectively block cell depletion induced by immunosuppressive molecules, and thus increase cytokine release, and improve the cell proliferation ability and the tumor cell killing ability. The present invention is expected to overcome a series of problems faced by adoptive T-cell immunotherapy, such as tumor heterogeneity, poor tumor barrier permeability, short duration of action, and local immunosuppressive microenvironment.

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(AM, AZ, BY, KG, KZ, RU, TJ, TM), 欧洲 (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)。

本国际公布:
— 包括国际检索报告(条约第21条(3))。
— 包括说明书序列表部分(细则5.2(a))。

(57) 摘要: 本申请公开了经修饰的靶向HPV增强型免疫细胞及其医药用途。本发明提供了靶向HPV的E7抗原的T细胞受体或其片段及其医药用途。此外，还提供了同时表达靶向HPV的TCR和转换共刺激分子的经修饰的免疫细胞及其医药用途。本申请的经修饰的免疫细胞采用共刺激分子的胞内激活信号域替换免疫抑制受体的胞内抑制信号域，将免疫抑制因子或配体结合诱发的抑制性信号转换为活化信号，能够有效阻断免疫抑制分子诱导的细胞耗竭；并增加细胞因子的释放、提升细胞增殖能力和肿瘤细胞杀伤能力。本发明有望克服过继T细胞免疫治疗所面临的肿瘤异质性、肿瘤屏障难以渗透、作用时间短暂、局部免疫抑制性微环境等一系列难题。