抗人卵巢癌/抗人CD3单链双特异性抗体介导的αβT细胞CDR3谱系漂移(点击查看pdf全文)

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Title: An anti-human ovarian carcinoma and CD3 bispecific single-chain antibody mediates CDR3 spectratype drift of T cell receptor alpha and beta chains

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关键词: 双特异性抗体; 抗人卵巢癌/抗人CD3单链双特异性抗体; T细胞受体; 互补决定区3; 基因扫描

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摘要: 目的探讨抗人卵巢癌/抗人CD3单链双特异性抗体(BHL-1)介导的αβT细胞CDR3 谱系漂移，为双特异性抗体介导的T细胞免疫应答机制提供理论基础。方法采用免疫扫描谱型分析技术，分析6例正常献血员T细胞在人卵巢癌SKOV3细胞联合BHL-1刺激前后的TCR库多样性变化（CDR3谱型分布特征）及刺激后T细胞TCR α、β链CDR3优势利用情况，对克隆性增生T细胞的CDR3区进行序列分析。结果刺激前6例正常献血员TCR CDR3谱型均呈高斯分布，刺激后发生CDR3谱系漂移，部分TCR Vα、Vβ家族出现优势增生，明确了BHL-1介导下单克隆增生T细胞的α、β链CDR3序列。结论SKOV3联合BHL-1诱导的T细胞CDR3谱系出现明显漂移，提示CDR3的选择性表达可能与BHL-1介导的特异性T细胞免疫反应有关，特异应答T细胞TCR CDR3序列的确定，将为卵巢癌的T细胞免疫治疗提供基础。

Abstract: Objective To analyze the drift of T cell receptor (TCR) Vα and Vβ gene family CDR3 spectratype in response to ovarian carcinoma cells mediated by an anti-human ovarian carcinoma/CD3 bispecific single-chain antibody (BHL-1), and explore the mechanism of the bispecific single-chain antibody-mediated T cell immune response. Methods Immunoscopic spectratyping technique was used to analyze the TCR repertoire diversity (CDR3 spectratype distribution) of the T cells from 6 healthy donors before and after stimulation of the cells with human ovarian carcinoma in the presence of BHL-1. The predominant usage of TCR α and β chain CDR3 was analyzed after the stimulation,

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and sequence analysis was performed for
the CDR3 region of the monoclonal T cells. Results The spectratypes of Vα and
Vß gene family TCR CDR3 region showed a
Gaussian distribution before stimulation of the T cells from the 6 donors. After
stimulation of the T cells, CDR3 spectratype
drift occurred in the T cells, and some TCR Vα and Vß families showed an
anomalous and oligoclonal expansion. Different
CDR3 sequences of the Vα and Vß gene family TCR were found in the monoclonal
T cells stimulated with BHL-1. Conclusion
CDR3 spectratype drift occurs in TCR α and ß chains of T cells after stimulation
with human ovarian carcinoma cells and
BHL-1, indicating that the predominant usage of TCR Vα and Vß families is
associated with the specific T cell immune
response mediated by BHL-1.

参考文献/REFERENCES

［1］ Fang M, Zhao R, Yang Z, et al. Characterization of an anti-humanovarian carcinomaxanti-human CD3 bispecific single-chainantibody with an albumin-original interlinker［J］. Gynecol Oncol,2004, 92(1): 135-46.
［2］ 杨介钻，张众，马骊，等. 抗人卵巢癌/抗人CD3单链双特异性抗体的生物学活性研究［J］. 癌症，2005, 24(7): 787-91.
［3］ 常红，罗微，马骊，等. IL-2体外诱导健康人外周血T细胞TCR ß链CDR3谱系漂移的研究［J］. 南方医科大学学报，2007, 27(4): 433-5.
［4］ 邹红云，马骊，姚新生，等. Jurkat细胞TCR基因重排对BV CDR3的影响［J］. 南方医科大学学报，2006, 26(7): 939-43.
［5］ 罗微，马骊，姚新生，等. 系统性红斑狼疮患者外周血T细胞TCRß链CDR3 谱系漂移和序列鉴定［J］. 南方医科大学学报，2006, 26(8):1128-31.
［6］ Luo W, Ma L, Wen Q, et al. Analysis of the interindividualconservation of T cell receptor alpha- and beta-chain variableregions gene in the peripheral blood of patients with systemic lupuserythematosus［J］. Clin Exp Immunol, 2008, 154(3): 316-24.
［7］ Luo W, Ma L, Wen Q, et al. Analysis of the conservation of T cellreceptor alpha and beta chain variable regions gene in pp65peptide-specific HLA-A*0201-restricted CD8+ T cells［J］. Cell MolImmunol, 2009, 6(2): 105-10.
［8］ Luo W, Liao WJ, Huang YT, et al. Cancer of the gastrointestinaltract results in a restricted T-cell repertoire dependent upon tumordifferentiation［J］. Cell Immunol, 2011, 270(1): 47-52.
［9］ Luo W, Liao WJ, Ma L, et al. Dynamic monitoring the TCR CDR3spectratypes in patients with metastatic CRC treated with acombination of bevacizumab, irinotecan, fluorouracil, andleucovorin［J］. Cancer Immunol Immunother, 2010, 59(2): 247-56.
［10］Luo W, Liao WJ, Huang YT, et al. Normalization of T cell receptorrepertoire diversity in patients with advanced colorectal cancer whoresponded to chemotherapy［J］. Cancer Sci, 2011, 102(4): 706-12.
［11］Schneider MA, Brühl H, Wechselberger A, et al. In vitro and in vivoproperties of a dimeric bispecific single-chain antibody IgG-fusionprotein for depletion of CCR2 + target cells in mice［J］. Eur JImmunol, 2005, 35(3): 987-95.
［12］Zocher M, Baeuerle PA. A bispecific single-chain antibody fusionprotein for targeted depletion of autoreactive B cells via unstimulatedhuman T lymphocytes［J］. Mol Immunol, 2004, 41(5): 511-8.
［13］Hönemann D, Kufer P, Rimpler MM, et al. A novel recombinantbispecific single-chain antibody, bscWue-1 x CD3, inducesT-cell-mediated cytotoxicity towards human multiple myeloma cells［J］. Leukemia, 2004, 18(3): 636-44.
［14］Hudson PJ, Souriau C. Engineered antibodies［J］. Nat Med, 2003, 9(1): 129-34.
［15］Morecki S, Lindhofer H, Yacovlev E, et al. Induction of longlastingantitumor immunity by concomitant cell therapy withallogeneic lymphocytes and trifunctional bispecific antibody［J］.Exp Hematol, 2008, 36(8): 997-1003.
［16］Mølhøj M, Crommer S, Brischwein K, et al. CD19-/CD3-bispecificantibody of the BiTE class is far superior to tandem diabody withrespect to redirected tumor cell lysis［J］. Mol Immunol, 2007, 44(8):1935-43.
［17］Kornacker M, Verneris M, Kornacker B, et al. The apoptotic andproliferative fate of cytokine-induced killer cells after redirection totumor cells with bispecific Ab［J］. Cytotherapy, 2006, 8(1): 13-23.
［18］Viatte S, Alves PM, Romero P. Reverse immunology approach forthe identification of CD8 T-cell-defined antigens: advantages andhurdles［J］. Immunol Cell Biol, 2006, 84(3): 318-30.
［19］杨介钻，马骊，姚新生，等. 单链双特异性抗体(BHL-1)介导的细胞毒作用及其可能机制研究［J］. 中国免疫学杂志，2007, 23(5): 402-6.
［20］Luo W, Zhang XB, Huang YT, et al. Development of geneticallyengineered CD4+ and CD8+ T cells expressing TCRs

specific for aM. tuberculosis 38-kDa antigen [J] . J Mol Med, 2011, 89(9): 903-13.

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