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CCR4与肿瘤的关系及其临床意义

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摘要：

CCR4是CC趋化因子受体（CC chemokine receptor, CCR）家族中的一员，主要表达于多种淋巴细胞。其高亲和力配体为胸腺和活化调节的趋化因子（thymus and activation regulated chemokine，TARC/CCL17)及巨噬细胞衍生的趋化因子(macrophage derived chemokine，MDC/CCL22/STCP 1)。CCR4主要通过CCR4 + Treg细胞及CCR4 + Th2细胞发挥免疫效应。CCR4的高表达与多种血液系统肿瘤以及恶性实体瘤的浸润和预后相关，其机制为Treg细胞表面的CCR4通过与其配体TARC、MDC 的结合趋化Treg细胞，引起免疫逃逸，从而导致不良临床后果。多种恶性肿瘤转移模型的研究进一步揭示了CCR4与恶性肿瘤转移之间的关系。抗CCR4嵌合型单克隆抗体KM2760的研究已进入Ⅱ期临床试验阶段，阻断TARC/MDC CCR4信号通路，有可能成为恶性肿瘤分子靶向治疗的新策略。

关键词：CC趋化因子受体 4(CCR4) 胸腺和活化调节的趋化因子(TARC) 巨噬细胞衍生的趋化因子(MDC) 肿瘤

Involvement of CCR4 in tumor and its clinical significance

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Abstract:

CCR4, a member of CCR (CC chemokine receptor) family, is expressed in many kinds of lymphocytes. Its high affinity ligands include thymus, activation regulated chemokine (TARC/CCL17) and macrophage derived chemokine (MDC/CCL22/STCP 1). CCR4 exerts its immune activities by CCR4 +Treg cells and CCR4 +Th2 cells. High expression of CCR4 is associated with infiltration and prognosis of many hematological and solid malignancies; the binding of CCR4 with its ligands TARC and MDC in Treg cells may be responsible for the chemotaxis of Treg cells, the resulting immune tolerance and worse clinical outcomes. The researches of malignant tumor metastatic models further revealed the relationship between CCR4 expression and metastasis of malignant solid tumors. The study of KW 0761, a defucosylated humanized anti CCR4 antibody,has already been in the phase Ⅱ clinical trial. Therefore, blockage TARC/MDC CCR4 signal pathway might be a novel therapy strategy for malignant tumors.

Keywords:CC chemokine receptor 4 (CCR4) thymus and activation regulated chemokine (TARC) macrophage derived chemokine (MDC) neoplasms

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