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IL-27促进人单个核细胞来源树突状细胞的分化成熟及其作用机制 点此下载全文

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摘要:

目的: 探讨IL-27对人外周血单个核细胞来源的树突状细胞(dendritic cell, DC)形态和功能的影响及其作用机制。 方法: 从正常健康人外周血中分离出单个核细胞,将其用GM-CSF、IL-4体外培养7 d,并于培养的第5天加入不同刺激因子,并将细胞分为4组: 阴性对照组、阳性对照组(20 ng/ml TNF-a)、IL-27(20 ng/ml)组、IL-27+TNF-a组(即双细胞因子组,10 ng/ml TNF-a+10 ng/ml IL-27)。用倒置显微镜观察培养7 d的DC形态,用流式细胞术检测DC表面共刺激分子CD1a/CD83和CD80/CD86的水平,RT-PCR检测DC表面趋化因子受体 CCR5、CCR7 mRNA的表达,混合淋巴细胞实验检测DC刺激同种异体T淋巴细胞增殖的能力,Western blotting检测DC信号通路蛋白P-STAT1/STAT3的含量。 结果: IL-27组和双细胞因子组诱导7 d 时 DC呈现典型的成熟形态学特征: DC表面CD1a和CD83双阳性表达\[(35.75±4.10)%、(52.49±2 65)% vs(23.29±4.49)%, P<0 05\]、CD80和CD86双阳性表达\[(39.06±1.61)%、(54.10±6.46)% vs(22.66±3 20)%, P<0 05\]、趋化因子受体 CCR7 mRNA\[3 98±0.09、4.75±0.11 vs 3.09±0.18,P<0.05\]和转录因子蛋白P-STAT1/STAT3水平均较阴性对照组明显上调,而 CCR5 mRNA\[0.99±0.03、0.61±0.02 vs 1.23±0.26,P<0.05\]表达含量则明显下降: IL-27组和双细胞因子组DC均可明显刺激T细胞增殖,且随DC与T细胞比例增加而增强,以双细胞因子组的刺激作用更为明显。 结论: 细胞因子IL-27可以直接或者协同TNF-a诱导人DC分化成熟,并增强DCs的抗原提呈功能,其机制可能与活化P-STAT1/STAT3信号通路有关。

关键词: 白介素-27 树突状细胞 共刺激分子 趋化因子受体 P-STAT1/STAT3

Promotability and mechanism of IL-27 on differentiation and maturation of dendritic cells derived from human periperal blood mononuclear cells

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Abstract:

Objective: To observe the effect and mechanism of IL-27 on the morphology and function of human peripheral blood mononuclear cell (PBMC)-derived dendritic cells (DCs). Methods: PBMCs were purified from peripheral blood of healthy adults and incubated with granulocyte/macrophage colony stimulating factor (GM-CSF) and interleukin-4 (IL-4) for 7 days. The DCs were divided into four groups by different stimulatory factors at the fifth day: a negative group, a positive group (TNF-a: 20 ng/ml), IL-27 group (20 ng/ml) and TNF-a+IL-27 group (co-cytokines group, 10 ng/ml TNF-a+ IL-27 10 ng/ml). The morphology of DCs was observed under an inverted microscope at the 7th day. The expressions of CD1a and CD83, CD80 and CD86 on DCs were analyzed by flow cytometry. The mRNA levels of chemokine receptors of CCR5 and CCR7 on DCs were analyzed by RT-PCR. The stimulatory ability of DCs on proliferation of allogeneic T cells was detected by MLR. The proteins of P-STAT1 and P-STAT3 were detected by Western blotting. Results: DCs from the IL-27 group and TNF-a + IL-27 group had a typical morphological characteristic of mature DCs after 7 days. The expressions of co-stimulatory molecules of CD1a and CD83 (\[$[35.75\pm 4 \ 10\]$)%, \[$[52.49\pm 2.65\]$ % vs \[$[23 \ 29\pm 4 \ 49\]$)%, P<0.05), CD80 and CD86 (\[$[39.06\pm 1.61\]$)%, \[$[54.10\pm 0.46\]$ % vs \[$[35.75\pm 4 \ 10\]$ %, \[$[54.10\pm 0.46\]$ % vs \[$[36.10\pm 0.46\]$ % vs \[$[36.10\pm$ \[22.66±3.20\]%, P<0.05), chemokine receptor of CCR7 (3.98±0.09, 4.75±0.11 vs 3.09±0.18, P<0.05) and the proteins of P-STAT1/STAT3 on DCs were up-regulated both in the IL-27 group and co-cytokines group compared with the negative group, while chemokine receptor of CCR5 (0.99±0.03, 0.61±0.02 vs 1.23±0.26, P<0.05) was down-regulated. The proliferation of T cells was improved by DCs from the IL-27 group and TNF-a + IL-27 group. The tendency was especially obvious in the co-cytokines group. Conclusion: IL-27 can directly or synergically enhance the differentiation, maturation and antigen presentation ability of DCs with TNF-a. The mechanism might relate to the activation of P-STAT1/STAT3 signal transduction pathway.

Keywords: interleukin-27 dendritic cell; co-stimulatory molecule; chemokine receptor; P-STAT1/STAT3

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