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IFN-α联合GM-CSF诱导胃癌患者外周血单个核细胞分化为树突状细胞

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摘要：

目的： 探索干扰素-α（interferon-α，IFN-α）联合粒细胞-巨噬细胞集落刺激因子（granulocyte-macrophage colony-stimulating factor, GM-CSF）体外诱导胃癌患者外周血单个核细胞（peripheral blood mononuclear cell，PBMC）向树突状细胞（dendritic cell，DC）分化的可能性。 方法： 10 例胃癌患者PBMC分别用GM-CSF 100 ng/ml联合IFN-α 500 IU/ml（命名为IFN-α DC） 或GM-CSF 100 ng/ml联合50 ng/ml IL-4（命名为IL-4 DC）体外培养，然后用CD40L、LPS诱导DC成熟。Giemsa染色法观察 IFN-α DC和IL-4 DC的形态，流式细胞术分析IFN-α DC和IL-4 DC表面CD1a、CD80、CD83、CD86和HLA-DR的表达情况，同种异体混合淋巴细胞反应（mixed lymphocyte reaction，MLR）检测不同的成熟DC刺激同种异体T淋巴细胞增殖的能力。 结果： IFN-α DC和IL-4 DC均呈现典型DC形态。IFN-α DC和IL-4 DC分别在诱导第3天和第5天时，细胞表面CD1a、CD80、CD83、CD86和HLA-DR表达达到较高水平，成熟IFN-α DC表面CD83\[（78.25±15.36）% vs （50.14±10.24）%， P <0.05\]和CD86\[（84.84±10.12）% vs （62.93±15.12）%， P <0.05\]的表达均高于成熟IL-4 DC。成熟IFN-α DC刺激异体T淋巴细胞增殖能力强于未成熟IFN-α DC（ P <0 05）。在DC与T细胞数量比为1：40和1：20时，成熟IFN-α DC刺激同种异体T淋巴细胞增殖的能力明显强于成熟IL-4 DC\[（39.43±9.21）% vs （27.34±10.63）%，（60.31±7.86）% vs （48.63±6.25）%；均 P <0.05\]。 结论： 相比常用的IL-4联合GM-CSF诱导方法，IFN-α联合GM-CSF可以在更短时间内将胃癌患者PBMC诱导成具有更强刺激同种异体T淋巴细胞增殖能力的DC细胞，这可能与其表面CD83和CD86表达增高有关。

关键词：树突状细胞 干扰素-α 粒细胞-巨噬细胞集落激因子 IL-4 胃癌

Dendritic cells induced by IFN-α combined with GM-CSF from peripheral blood mononuclear cells of gastric cancer patients

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Abstract:

Objective: To investigate the possibility of inducing dendritic cells (DCs) by interferon-α (IFN-α) combined with granulocyte-macrophage colony-stimulating factor (GM-CSF) from peripheral blood mononuclear cells (PBMCs) in gastric cancer patients. Methods: PBMCs from 10 gastric cancer patients were cultivated using granulocyte macrophage colony stimulating factor (GM-CSF) 100 ng/ml combined with IFN-α 500 IU/ml (named IFN-α DC) or IL-4 50 ng/ml (named IL-4 DCs) and then CD40L and LPS were added to induce DC maturation. The morphologic features of IFN-α DCs and IL-4 DCs were observed by Giemsa staining. The expressions of CD1a, CD80, CD83, CD86 and HLA-DR on the surface of IFN-α DCs and IL-4 DCs were assayed by flow cytometry. The abilities of IFN-α DCs and IL-4 DCs to induce the proliferation of allogenic T cells were determined by mixed lymphocyte reaction (MLR). Results: Both IFN-α DCs and IL-4 DCs displayed typical DC features in morphology. The expressions of CD1a, CD80, CD83, CD86 and HLA-DR in IFN-α DCs and IL-4 DCs were achieved at high levels at 3 d and 5 d after induced. Mature IFN-α DCs expressed a higher value of CD83 (\[78.25±15.36\]% vs \[50.14±10.24\]%, P <0.05) and CD86 (\[84.84± 10 12\]% vs \[62.93±15.12\]%, P <0.05) than mature IL-4 DCs. Mature IFN-α DCs was stronger than immature IFN-α DCs on the ability to induce proliferation of allogenic T cells (P <0.05). At the ratios of DCs〖DK〗：T cell being 1：40 and 1：20, mature IFN-α DCs had a stronger ability to induce proliferation of allogeneic T cells than did mature IL-4 DCs (\[39.43±9.21\]% vs \[27.34±10.63\]%, P <0.05; \[60.31±7.86\]% vs \[48.63±6 25\]%, P <0.05). Conclusion: IFN-α combined with GM-CSF can induce the differentiation of DCs from PBMCs of gastric cancer patients, which have a shorter culture period and stronger ability to induce the proliferation of allogenic T cells than traditional DCs induced by IL-4 and GM-CSF. It may result from the up-regulation of CD83 and CD86 expressions on IFN-α DCs.

Keywords:dendritic cell interferon-α granulocyte-macrophage colony-stimulating factor IL-4 gastric cancer

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