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论著

乐复能对LPS介导的健康人外周血单核细胞分泌TNF-α的影响及其机制

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摘要:

目的:探讨乐复能在体外对LPS 介导的健康人外周血单核细胞分泌TNF-α 及NF-κB mRNA 表达的影响,以期为乐复能治疗克罗恩病等免疫性疾病提供理论依据。方法:分离30 例健康人外周血单核细胞并进行体外培养, 分别按以下 5 种方法(5 组) 进行体外实验:A 组为空白对照组;B 组为单纯LPS 刺激组;C 组为LPS 与乐复能同时加入组;D 组为先加入LPS 刺激, 后加入乐复能组;E 组为先加入乐复能, 后加入LPS 刺激组。干预后用ELISA 法检测培养液内TNF-α 浓度, 然后采用RT-PCR 方法检测单核细胞内NF-κB mRNA 表达情况。结果:基础状态下, 体外培养的健康人单核细胞分泌少量TNF-α[(470.23±35.24) pg/mL)], 加入LPS 刺激后, TNF-α 的分泌明显增加[(1446.76±72.36) pg/mL)], 在LPS 刺激后再加入乐复能, TNF-α 的分泌明显减少[(1446.76±72.36) pg/mL vs (946.46±46.12)pg/mL, P<0.01], 下降约29.7%。而乐复能在LPS 刺激前或与LPS 同时加入培养细胞内时, 对TNF-α 分泌无影响[(1446.76±72.36) pg/mL vs (1275.62±87.75) pg/mL, P>0.05;(1446.76±72.36) pg/mL vs (1383.62±86.96) pg/mL, P>0.05]。乐复能明显下调经LPS 诱导的单核细胞内NF-κB mRNA 表达(0.2829±0.0365 vs 0.4994±0.0604, P<0.01), 而对于未提前接受LPS 刺激的单核细胞, 乐复能对其NF-κB mRNA 表达无影响(0.4716±0.0616 vs 0.4994±0.0604, P>0.05;0.4767±0.0600vs 0.4994±0.0604, P>0.05)。结论:乐复能在体外能抑制LPS 介导的健康人外周血单核细胞分泌TNF-α, 具有调节单核细胞免疫功能的作用, 其抑制TNF-α 分泌功能可能与其下调单核细胞内NF-κB 表达有关。

关键词: 乐复能 单核细胞 肿瘤坏死因子-α 脂多糖 Toll 样受体4 NF-κB

Mechanism of Novaferon on production of TNF-α by monocytes isolated from normal human peripheral blood

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Abstract:

Objective: To study the role of Novaferon on TNF-α production and expression of NF-κB mRNA in monocytes isolated from normal human peripheral blood and to provide theoretical basis for treatment of immunological diseases with Novaferon.
Methods: Monocytes were isolated from the peripheral blood in 30 healthy volunteers and divided into 5 groups: group A was blank control, group B was stimulated by LPS without Novaferon intervention, group C by LPS together with Novaferon intervention, group D by LPS before Novaferon intervention, which group E by LPS after Novaferon intervention. We detected the concentration of TNF-α after LPS stimulation and Novaferon intervention in the supernatant by ELISA and expression of NF-κB mRNA by RT-PCR.
Results: Novaferon inhibited TNF-α production by monocytes isolated from healthy volunteers induced by LPS in vitro in group D compared with group B [(1446.76±72.36) pg/mL vs (946.46±46.12) pg/mL, P<0.01], and the rate was 29.7%. There was no significant change in TNF-α concentration in group C and E compared with group B [(1446.76±72.36) pg/mL vs (1275.62±87.75) pg/mL, P>0.05; (1446.76±72.36) pg/mL vs (1383.62±86.96) pg/mL, P>0.05]. There was significant change in NF-κB mRNA expression in group D compared with group B (0.2829±0.0365 vs 0.4994±0.0604, P<0.01). There was no significant change in NF-κB mRNA expression in group C and group E compared with group B

(0.4716±0.0616 vs 0.4994±0.0604, *P*>0.05; 0.4767±0.0600 vs 0.4994±0.0604, *P*>0.05). Conclusion: Novaferon can suppress TNF-α secretion by monocytes induced by LPS in vitro, and it can affect the immunity function of monocytes, which may be associated with the downregulation of NF-κB mRNA expression in monocytes.

Keywords: Novaferon monocyte tumor necrosis factor-α lipopolysaccharide Toll-like receptor 4 NF-κB

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参考文献：

1. Bruewer M, Luegering A, Kucharzik T, et al. Proinflammatorycytokines disrupt epithelial barrier function by apoptosisindependentmechanisms［J］. J Immunol, 2003,171(11): 6164-672.

2. Belliard AM, Lacour B, Farinotti R, et al. Effect of tumor necrosisfactor-alpha and interferon gamma on intestinal P-glycoproteinexpression, activity, and localization in Caco-2 cells［J］. J Pharm Sci,2004, 93(6):1524-1536.

3. Ho GT, Moodie FM, Satsangi J. Multidrug resistance 1 gene(P-glycoprotein 170): an important determinant in gastrointestinaldisease［J］? Gut, 2003, 52(5): 759-766.

4. Tak PP, Kalden JR. Advances in rheumatology: new targetedtherapeutics［J］. Arthritis Res Ther, 2011, 13(Suppl 1): S5.

5. Roescher N, Tak PP, Illei GG. Cytokines in Sjogren’s syndrome: potentialtherapeutic targets［J］. Ann Rheum Dis, 2010, 69(6): 945-948.

6. Postal M, Appenzeller S. The role of Tumor Necrosis Factor-alpha(TNF-α) in the pathogenesis of systemic lupus erythematosus［J］.Cytokine, 2011, 56(3): 537-543.

7. Varma RS, Ashok G, Vidyashankar S, et al. Anti-inflammatoryproperties of Septilin in lipopolysaccharide activated monocytes andmacrophage［J］. Immunopharmacol Immunotoxicol, 2011, 33(1): 55-63.

8. Tao JY, Zhao L, Huang ZJ, et al. Anti-inflammatory effects of ethanolextract from Kummerowia striata (Thunb.) Schindl on lps-stimulatedRAW 264.7 cell［J］. Inflammation, 2008, 31(3): 154-166.

9. Cao J, Jiang L, Zhang X, et al. Boric acid inhibits LPS-induced TNFalphaformation through a thiol-dependent mechanism in THP-1cells［J］. J Trace Elem Med Biol, 2008, 22(3): 189-195.

10. Cho JY. Suppressive effect of hydroquinone, a benzene metabolite, onin vitro inflammatory responses mediated by macrophages, monocytes,and lymphocytes［J］. Mediators Inflamm, 2008, 2008: 298010.

11. Ahmad S, Israf DA, Lajis NH, et al. Cardamonin, inhibits proinflammatorymediators in activated RAW 264.7 cells and wholeblood［J］. Eur J Pharmacol, 2006, 538(1-3): 188-194.

12. Takii T, Kawashima S, Chiba T, et al. Multiple mechanisms involved inthe inhibition of proinflammatory cytokine production from humanmonocytes by N-(p-coumaroyl)serotonin and its derivatives［J］. IntImmunopharmacol, 2003, 3(2): 273-237.

13. Ciallella JR, Saporito M, Lund S, et al. CEP-11004, an inhibitorof the SAPK/JNK pathway, reduces TNF-alpha release fromlipopolysaccharide-treated cells and mice［J］. Eur J Pharmacol, 2005,515(1-3): 179-187.

14. Marques LJ, Zheng L, Poulakis N, et al. Pentoxifylline inhibits TNFalphaproduction from human alveolar macrophages［J］.Am J RespirCrit Care Med, 1999, 159(2): 508-511.

15. Bianchi M, Bloom O, Raabe T, et al. Suppression of proinflammatorycytokines in monocytes by a tetravalent guanylhydrazone［J］. J ExpMed, 1996, 183(3): 927-936.

16. Hommes D, van den Blink B, Plasse T, et al. Inhibition of stressactivatedMAP kinases induces clinical improvement in moderate tosevere Crohn’s disease［J］. Gastroenterology, 2002, 122(1): 7-14.

17. Kannaiyan R, Shanmugam MK, Sethi G. Molecular targets of celastrolderived from

Thunder of God Vine: potential role in the treatment ofinflammatory disorders and cancer［J］. Cancer Lett, 2011, 303(1): 9-20.

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