

## 论著

### Th1/Th2细胞炎症因子在大鼠溃疡性结肠炎治疗模型中的表达

1. 中南大学 湘雅三医院消化内科, 长沙 410013;
2. 中南大学 湖南省非可控性炎症与肿瘤重点实验室, 长沙 410013;
3. 中南大学 中南大学肿瘤研究所, 长沙 410078

#### 摘要:

目的: 探讨Th1/Th2细胞因子IL-2,干扰素- $\gamma$ (interferon- $\gamma$ ,IFN- $\gamma$ ),IL-4和IL-10在葡聚糖酸钠 (dextran sulfate sodium,DSS) 诱导的大鼠实验性溃疡性结肠炎治疗模型中的表达。方法: 雄性Sprague Dawley 大鼠40只,随机均分为正常组、模型组、柳氮磺吡啶治疗组(SASP组)、结肠宁治疗组(结肠宁组),每组各10只。对各组大鼠进行疾病活动指数评分 (disease activity index,DAI) 及结直肠组织损伤学评分,运用酶联免疫吸附测定(enzyme-linked immunosorbent assay,ELISA)及real-time PCR检测血清及肠黏膜组织中细胞因子IL-2,IFN- $\gamma$ ,IL-4和IL-10含量水平。结果: 与模型组比较,结肠宁组大鼠的DAI及结直肠组织损伤学评分均明显下降 (均 $P<0.05$ );但与SASP组比较,差异无统计学意义 ( $P>0.05$ )。血清和组织中IL-2表达在治疗前后的各组间比较,差异均无统计学意义 (均 $P>0.05$ )。SASP组和结肠宁组血清及肠黏膜组织IFN- $\gamma$ 水平较模型组下调,血清中差异均有统计学意义 (均 $P<0.05$ ),肠黏膜组织中仅结肠宁组差异均有统计学意义 (均 $P<0.05$ )。SASP组和结肠宁组血清IL-4水平较模型组均上调,但只有结肠宁组差异有统计学意义 ( $P<0.05$ );而肠黏膜组织中差异均无统计学意义(均 $P>0.05$ )。SASP组和结肠宁组血清及肠黏膜组织IL-10水平较模型组上升,差异均有统计学意义(均 $P<0.05$ )。SASP组和结肠宁组血清及肠黏膜组织中细胞因子IL-2,IFN- $\gamma$ ,IL-4和IL-10含量水平比较,差异均无统计学意义 (均 $P>0.05$ )。结论: DSS造模破坏Th1/Th2在结肠中的表达平衡。结肠宁能改善DSS所致的实验性溃疡大鼠模型炎症,通过上调血清和肠黏膜组织IL-10水平、下调IFN- $\gamma$ 水平可保持Th1/Th2细胞间平衡,从而改善免疫功能。

关键词: 溃疡性结肠炎 结肠宁灌肠剂 I类T辅助细胞/II类T辅助细胞 葡聚糖硫酸钠 大鼠模型

### Expression of Th1/Th2 inflammatory cytokines in rat treatment model of ulcerative colitis

PENG Xiaoqing, LI Xiayu, WANG Wei, LI Nan, MA Jian, SHEN Shourong,

1. Department of Gastroenterology, Third Xiangya Hospital, Central South University, Changsha 410013;
2. Hunan Key Laboratory of Nonresolving Inflammation and Cancer, Changsha 410013;
3. Cancer Research Institute, Central South University, Changsha 410078, China

#### Abstract:

Objective: To investigate the expression of Th1/Th2 inflammatory cytokines IL-2, interferon- $\gamma$  (IFN- $\gamma$ ), IL-4, and IL-10 in rat treatment model of dextran sulfate sodium (DSS) -induced ulcerative colitis. Methods: Forty Sprague Dawley (SD) male rats were divided into a normal group, a colitis model group, a sulfasalazine(SASP)-treatment group (SASP group) and a Jiechangning-treatment group (Jiechangning group) (each group n=10). Disease activity index (DAI) and colorectal histological damage scale were assessed. The expression levels of cytokines IL-2, IFN- $\gamma$ , IL-4, and IL-10 in the serum and the colon mucosa tissues were detected by enzyme-linked immuno sorbent assay (ELISA) and real time polymerase chain reaction (RT-PCR). Results: Compared with the colitis model group, the DAI and colorectal histological damage scale were decreased in the Jiechangning group (both  $P<0.05$ ), but there was no obvious difference compared with the SASP group ( $P>0.05$ ). There was no significant difference in IL-2 expression both in the serum and the colon mucosa tissues before or after the treatment in various groups ( $P>0.05$ ). Compared with the colitis model group, IFN- $\gamma$  level both in the serum and the colon mucosa tissues was decreased in the SASP group and the Jiechangning group, with significant difference in the serum (both  $P<0.05$ ), but there was significant difference in the colon mucosa tissues only in the Jiechangning group ( $P<0.05$ ). The serum IL-4 level in the SASP group and the Jiechangning group was increased compared with that in the colitis control group, with significant difference only in the Jiechangning group ( $P<0.05$ ). There was no difference in IL-4 level in the colon mucosa tissues whether treated or not ( $P>0.05$ ). IL-10 level both in the serum and the colon mucosa tissues in the SASP group and the Jiechangning group was increased compared with that in the colitis model group, with significant difference (all  $P<0.05$ ). There was no difference in the expression level of cytokines IL-2, IFN- $\gamma$ , IL-4, and IL-10 both in the serum and the colon mucosa tissues between the SASP group and the Jiechangning group (all  $P>0.05$ ). Conclusion: DSS can break the balance of Th1/Th2 expression in the colon. Jiechangning enema can

## 扩展功能

### 本文信息

- Supporting info
- PDF(2975KB)
- [HTML全文]
- 参考文献[PDF]
- 参考文献

### 服务与反馈

- 把本文推荐给朋友
- 加入我的书架
- 加入引用管理器
- 引用本文
- Email Alert
- 文章反馈
- 浏览反馈信息

### 本文关键词相关文章

- 溃疡性结肠炎
- 结肠宁灌肠剂
- I类T辅助细胞/II类T辅助细胞
- 葡聚糖硫酸钠
- 大鼠模型

### 本文作者相关文章

- 彭小青
- 李夏雨
- 王玮
- 李楠
- 马健
- 沈守荣

### PubMed

- Article by PENG Xiaoqing
- Article by LI Xiayu
- Article by WANG Wei
- Article by LI Nan
- Article by MA Jian
- Article by SHEN Shourong
- Article by

ameliorate DSS-induced acute experimental colitis in rats by decreasing IFN- $\gamma$  level and increasing IL-10 level both in the serum and the colon mucosa tissues to regulate the Th1/Th2 balance and improve immunity.

Keywords: ulcerative colitis Jiechangning enema helper T cells-1/helper T cells-2 dextran sulfate sodium rat model

收稿日期 2013-03-02 修回日期 网络版发布日期

DOI: 10.3969/j.issn.1672-7347.2013.10.008

基金项目:

通讯作者: 沈守荣,Email: 35403-ssr@163.com

作者简介: 彭小青,硕士,医师,主要从事溃疡性结肠炎机制的研究。

作者Email: 35403-ssr@163.com

## 参考文献:

1. Bouguen G, Chevaux JB, Peyrin-Biroulet L. Recent advances in cytokines: therapeutic implications for inflammatory bowel diseases [J]. *World J Gastroenterol*, 2011, 17(5): 547-556.
2. Bitiren M, Karakilcik AZ, Zerim M, et al. Protective effects of selenium and vitamin E combination on experimental colitis in blood plasma and colon of rats [J]. *Biol Trace Elem Res*, 2010, 136(1): 87-95.
3. Whittam CG, Williams AD, Williams CS. Murine colitis modeling using dextran sulfate sodium (DSS) [J]. *J Vis Exp*, 2010, 35: 1-3.
4. Kozlowski C, Jeet S, Beyer J, et al. An entirely automated method to score DSS-induced colitis in mice by digital image analysis of pathology slides [J]. *Dis Model Mech*, 2013, 6(3): 855-865.
5. Cooper HS, Murthy SN, Shah RS, et al. Clinicopathologic study of dextran sulfate sodium experimental murine colitis [J]. *Lab Invest*, 1993, 69(2): 238-249.
6. Hirata I, Yasumoto S, Toshina K, et al. Evaluation of the effect of pyrrolidine dithiocarbamate in suppressing inflammation in mice with dextran sodium sulfate-induced colitis [J]. *World J Gastroenterol*, 2007, 13(11): 1666-1671.
7. Yao J, Wang JY, Liu L, et al. Anti-oxidant effects of resveratrol on mice with DSS-induced ulcerative colitis [J]. *Arch Med Res*, 2010, 41(4): 288-294.
8. Yan Y, Kolachala V, Dalmaso G, et al. Temporal and spatial analysis of clinical and molecular parameters in dextran sodium sulfate induced colitis [J]. *PLoS One*, 2009, 4(6): e6073.
9. Hall LJ, Faivre E, Quinlan A, et al. Induction and activation of adaptive immune populations during acute and chronic phases of a murine model of experimental colitis [J]. *Dig Dis Sci*, 2011, 56(1): 79-89.
10. Lim BO. Efficacy of wogonin in the production of immunoglobulins and cytokines by mesenteric lymph node lymphocytes in mouse colitis induced with dextran sulfate sodium [J]. *Biosci Biotechnol Biochem*, 2004, 68(12): 2505-2511.
11. Boyman O, Sprent J. The role of interleukin-2 during homeostasis and activation of the immune system [J]. *Nat Rev Immunol*, 2012, 12(3): 180-190.
12. Chavez AR, Buchser W, Basse PH, et al. Pharmacologic administration of interleukin-2 [J]. *Ann N Y Acad Sci*, 2009, 1182: 14-27.
13. Inoue S, Matsumoto T, Iida M, et al. Characterization of cytokine expression in the rectal mucosa of ulcerative colitis: correlation with disease activity [J]. *Am J Gastroenterol*, 1999, 94(9): 2441-2446.
14. Dong Z, Du L, Xu X, et al. Aberrant expression of circulating Th17, Th1 and Tc1 cells in patients with active and inactive ulcerative colitis [J]. *Int J Mol Med*, 2013, 31(4): 989-997.
15. Choi SY, Hur SJ, An CS, et al. Anti-inflammatory effects of *Inonotus obliquus* in colitis induced by dextran sodium sulfate [J]. *J Biomed Biotechnol*, 2010, 2010: 943516-943521.
16. Roberts-Thomson IC, Fon J, Uylaki W, et al. Cells, cytokines and inflammatory bowel disease: a clinical perspective [J]. *Expert Rev Gastroenterol Hepatol*, 2011, 5(6): 703-716.
17. Liu L, Guo Z, Lv Z, et al. The beneficial effect of *Rheum tanguticum* polysaccharide on protecting against diarrhea, colonic inflammation and ulceration in rats with TNBS-induced colitis: the role of macrophage mannose receptor in inflammation and immune response [J]. *Int Immunopharmacol*, 2008, 8(11): 1481-1492.
18. 任科雨, 卢放根, 吴小平, 等. 嗜酸乳杆菌对小鼠结肠炎的疗效及结肠黏膜转录因子表达的影响 [J]. *世界华人消化杂志*, 2009, 17(22): 2251-2258. REN Keyu, LU Fanggen, WU Xiaoping, et al. Clinical efficacy of *Lactobacillus acidophilus* against experimental murine colitis and its effects on the expression of STAT1, T-bet and GATA3 [J]. *World Chinese Journal of Gestology*, 2009, 17(22): 2251-2258.
19. 邓长生, 夏冰. 炎症性肠病 [M]. 2版. 北京: 人民卫生出版社, 2006: 60-68. DENG Changsheng, XIA Bin. *Inflammatory bowel disease* [M]. 2nd ed. Beijing: People's Medical Publishing House, 2006: 60-68.
20. van Kampen C, Gaudie J, Collins SM. Proinflammatory properties of IL-4 in the intestinal microenvironment [J]. *Am J Physiol Gastrointest Liver Physiol*, 2005, 288(1): G111-117.

21. Fiocchi C. Inflammatory bowel disease: etiology and pathogenesis [J] . *Gastroenterology*, 1998, 115(1): 182-205.
22. Coburn LA, Gong X, Singh K, et al. L-arginine supplementation improves responses to injury and inflammation in dextran sulfate sodium colitis [J] . *PLoS One*, 2012, 7(3): e33546.
23. Zenewicz LA, Antov A, Flavell RA. CD4 T-cell differentiation and inflammatory bowel disease [J] . *Trends Mol Med*, 2009, 15(5): 199-207.
24. Presser K, Schwinge D, Wegmann M, et al. Coexpression of TGF-beta1 and IL-10 enables regulatory T cells to completely suppress airway hyperreactivity [J] . *J Immunol*, 2008, 181(11): 7751-7758.
25. Sanchez-Fidalgo S, Cardeno A, Villegas I, et al. Dietary supplementation of resveratrol attenuates chronic colonic inflammation in mice [J] . *Eur J Pharmacol*, 2010, 633(1-3): 78-84.
26. Steidler L, Hans W, Schotte L, et al. Treatment of murine colitis by *Lactococcus lactis* secreting interleukin-10 [J] . *Science*, 2000, 289(5483): 1352-1355.
27. Lindsay JO, Sandison A, Cohen P, et al. IL-10 gene therapy is therapeutic for dextran sodium sulfate-induced murine colitis [J] . *Dig Dis Sci*, 2004, 49(7-8): 1327-1334.
28. Kim JY, Cho MK, Choi SH, et al. Inhibition of dextran sulfate sodium (DSS)-induced intestinal inflammation via enhanced IL-10 and TGF-beta production by galectin-9 homologues isolated from intestinal parasites [J] . *Mol Biochem Parasitol*, 2010, 174(1): 53-61.

本刊中的类似文章

1. 王玮, 周艳宏, 李夏雨, 沈守荣. 巨噬细胞在溃疡性结肠炎癌变中的作用[J]. *中南大学学报(医学版)*, 2012,37(6): 637-641