

doi: 10.13241/j.cnki.pmb.2018.13.023

胃癌组织中 Bag-1 蛋白表达特点及与临床病理学特征、预后的关系*

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摘要 目的:探讨 Bcl-2 相联系的抗凋亡基因 1(Bag-1)蛋白在胃癌组织中的表达及与患者临床病理学特征、预后的关系。**方法:**选取病理科收集的 79 例胃癌组织及 30 例癌旁组织,标本收集时间 2010 年 2 月至 2013 年 12 月,采用免疫组化 SP 染色检测两组标本中的 Bag-1 蛋白表达水平,并分析 Bag-1 蛋白表达与胃癌患者临床病理学、预后的关系。**结果:**胃癌组织中的 Bag-1 蛋白阳性表达率 65.82%显著的高于癌旁组织的 13.33%($P<0.05$);Bag-1 蛋白阳性表达的胃癌患者 3 年生存率 30.77%显著的低于阴性表达患者的 55.56%($P<0.05$);Bag-1 蛋白阳性和阴性表达的患者 1 年以及 2 年生存率相差不大,差异无统计学意义($P>0.05$);Bag-1 蛋白阳性表达的胃癌患者 3 年生存率 30.77%显著的低于阴性表达患者的 55.56%($P<0.05$)。**结论:**胃癌组织中的 Bag-1 蛋白高表达,并且与患者的胃癌临床分期和淋巴结转移以及预后有关。

关键词: Bag-1 蛋白;胃癌;病理学特征;预后

中图分类号: R735.2 **文献标识码:** A **文章编号:** 1673-6273(2018)13-2512-05

The Relationship between the Expression of Bag-1 Protein and the Occurrence, Development and Prognosis of Gastric Carcinoma*

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ABSTRACT Objective: To investigate the expression of Bcl-2 related anti apoptosis gene 1 (Bag-1) protein in gastric carcinoma and its relationship with clinicopathological features and prognosis of the patients. **Methods:** Selection of Pathology, collected 79 cases of gastric carcinoma and 30 cases of adjacent tissue samples were collected from February 2010 to December 2013, by using SP immunohistochemical staining in two groups. The expression level of Bag-1 protein, and analyze the relationship between Bag-1 protein expression and clinical pathology in patients with gastric cancer and prognosis. **Results:** The positive expression of Bag-1 protein in gastric cancer rate of 65.82% was significantly higher than that in the adjacent tissues 13.33% ($P<0.05$); lower than the negative expression of Bag-1 protein expression in gastric cancer patients 3 year survival rate of 30.77% patients was 55.56% ($P<0.05$); the expression of Bag-1 and negative expression in 1 years, 2 years survival rate difference statistical significance ($P>0.05$); lower than the negative expression of Bag-1 protein expression in gastric cancer patients 3 year survival rate of 30.77% patients was 55.56% ($P<0.05$). **Conclusion:** High expression of Bag-1 protein in gastric cancer tissues is related to the clinical stage, lymph node metastasis and prognosis of gastric cancer.

Key words: Bag-1 protein; Gastric cancer; Pathological features; Prognosis

Chinese Library Classification(CLC): R735.2 **Document code:** A

Article ID: 1673-6273(2018)13-2512-05

近年来相关研究显示,胃癌的发病率维持在较高的水平,部分地区的发病率可达 233-455/10 万人左右^[1,2]。临床上胃癌的远期临床预后比较差,患者病死率较高,而通过对于胃癌发病的生物学机制的研究探讨,能够为胃癌的诊断和治疗提供详实的理论基础。越来越多的研究显示,分子生物学水平的改变,可能影响胃癌癌细胞早期增殖异常、凋亡抑制,促进细胞的增殖速度的增加,增加癌细胞早期发生风险^[3,4]。Bcl-2 相联系的抗凋亡基因 1(Bcl-2 related anti apoptosis gene 1, Bag-1)是抗凋亡家族成员,其对于癌细胞转录调控相关基因的抗凋亡作用,能够持续性促进癌细胞早期增殖的风险,增加癌细胞的侵袭或者

转移的能力^[5,6]。为了进一步揭示 Bag-1 在胃癌发生发展过程中的作用,本次研究选取病理科收集的 79 例胃癌组织及 30 例癌旁组织,揭示了相关指标的异常表达变化,重点分析了相关指标与胃癌患者临床病理特征的关系。详见下文报道。

1 对象与方法

1.1 研究对象

选取病理科收集的 79 例胃癌组织及 30 例癌旁组织,标本收集时间 2010 年 2 月至 2013 年 12 月。胃癌组,男 41 例、女 38 例,年龄 43~77 岁,平均 62.5 ± 10.4 岁,病理分化程度:16

* 基金项目:湖南省科技计划资助项目(2016JJ3165)

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(收稿日期:2017-12-25 接受日期:2018-01-26)

例患者高分化、20例患者中分化、43例患者低分化或未分化,其中49例患者淋巴结转移,临床分期:其中20例TNM I期、27例患者TNM II期、26例患者TNM III期、6例患者TNM IV期;病灶部位:胃窦部32例、胃体部24例、胃底部11例。癌旁组织,男22例、女18例,年龄45~75岁,平均 60.9 ± 11.4 岁。胃癌组和癌旁组的年龄、性别比较无统计学显著性($P>0.05$)。

1.2 病例入选排除标准

1.2.1 入选标准 (1)胃癌的诊断主要通过腹部超声、CT、超声胃镜检查证实;(2)患者年龄 ≤ 79 岁;(3)病理学标本来源于术前活检、术后切除组织;(4)既往无放疗化疗治疗史;(5)基础资料完整能进行统计分析。

1.2.2 排除标准 (1)患者病理学资料不完整者;(2)发生远处转移的胃癌患者;(3)合并其他部位恶性肿瘤者。

1.3 免疫组化染色

采用石蜡切片3毫米常规脱蜡至水,并将之置于3%双氧水室温孵育5 min,通过去离子水冲洗9 min(每次3 min),采用牛奶液体封闭5 min,然后添加 Bag-1 蛋白抗体(鼠来源,南京碧云天生物科技有限公司)37℃孵育2h,采用PBS缓冲液冲洗15 min(每次5 min),滴加HRP标记的二抗(兔来源,罗氏检测公司),然后37℃孵育30 min,采用PBS冲洗3次(5 min/

次),最后加入南京泰康生物科技有限公司生产的NBT/BCIP色剂显色、封片,最后于上海精密仪器有限公司生产的电子显微镜下观察。

1.4 结果判断

计分标准:Bag-1蛋白在细胞核中呈黄色或棕褐色等深色表达,(1)其中褐色及更深的色彩判断为3分、棕黄色判断为2分、淡黄色着色判断为1分、无色判断为0分;(2)依据阳性染色细胞比例:阳性染色细胞占比达到 $\leq 10\%$ 判断为1分、阳性染色细胞占比达到11%~50%判断为2分、阳性染色细胞占比达到51%~75%判断为3分、阳性染色细胞占比达到 $>75\%$ 判断为4分,总分 <3 分判断为阴性、总分 ≥ 3 分判断为阳性。

1.5 统计学方法

本文采用SPSS19.0分析,年龄等资料用($\bar{x} \pm s$)描述,t检验;表达率等百分率资料实施 χ^2 检验; $P<0.05$;差异有统计学显著性。

2 结果

2.1 两组标本中 Bag-1 蛋白表达情况比较

胃癌组织中的 Bag-1 蛋白阳性表达率65.82%显著的高于癌旁组织的13.33%($P<0.05$);(表1)。

表1 两组标本中 Bag-1 蛋白表达情况比较

Table1 Comparison of Bag-1 protein expression of specimens in two groups

Specimen type	n	-	+	++	+++	positive rate(%)
Gastric carcinoma	79	27	26	24	2	52(65.82)
Adjacent tissue	30	26	4	0	0	4(13.33)
χ^2						23.98
P						<0.001

2.2 Bag-1 蛋白与患者年龄、性别及其他临床病理特征的关系

经分析,TNM分期越高、发生淋巴结转移的胃癌患者 Bag-1 蛋白阳性表达率越高($P<0.05$),胃癌组织中的 Bag-1 蛋

白阳性表达率与患者的年龄、性别、CEA水平、肿瘤部位、肿瘤大小、分化程度无关($P>0.05$);(表2)。

表2 患者胃癌组织中 Bag-1 蛋白表达情况与其临床病理学特征的关系

Table 2 Relationship between Bag-1 protein and clinicopathological features in patients with gastric cancer

Clinicopathological features	Positive of Bag-1 (n=52)		Negative of Bag-1 (n=27)		χ^2	P
	n		n			
Age (year)					0.437	0.509
≥ 60	31	59.62%	14	51.85%		
<60	21	40.38%	13	48.15%		
Gender					0.913	0.339
Male	29	55.77%	12	44.44%		
Female	23	44.23%	15	55.56%		
CEA ($\mu\text{g/L}$)					0.729	0.393
>5.0	34	65.38%	15	55.56%		
≤ 5.0	18	34.62%	12	44.44%		
Tumor location					0.239	0.888

表 2 患者胃癌组织中 Bag-1 蛋白表达情况与其临床病理学特征的关系(续表)

Table 2 Relationship between Bag-1 protein and clinicopathological features in patients with gastric cancer

Clinicopathological features	Positive of Bag-1 (n=52)		Negative of Bag-1 (n=27)		χ^2	P
	n		n			
Gastric fundus	9	17.31%	4	14.81%	1.606	0.205
body of stomach	19	36.54%	9	33.33%		
Gastric antrum	24	46.15%	14	51.85%		
Tumor size					1.649	0.199
<5 cm	29	55.77%	11	40.74%		
≥ 5 cm	23	44.23%	16	59.26%		
Differentiation degree					5.383	0.020
well+moderately	21	40.38%	15	55.56%		
poorly	31	59.62%	12	44.44%		
Lymph node metastasis					11.235	0.001
Yes	37	71.15%	12	44.44%		
No	15	28.85%	15	55.56%		
TNM staging						
staging I + II	24	46.15%	23	85.19%		
staging III+IV	28	53.85%	4	14.81%		

2.3 胃癌组织中 Bag-1 蛋白表达对患者预后的影响

Bag-1 蛋白阳性表达的胃癌患者 3 年生存率 30.77% 显著低于阴性表达患者的 55.56% ($P < 0.05$); Bag-1 蛋白阳性和阴

性表达的患者 1 年以及 2 年生存率差异无统计学意义 ($P > 0.05$); (表 3)。

表 3 Bag-1 蛋白表达患者的生存率比较

Table 3 Comparison of survival rates in patients with Bag-1 protein expression

Bag-1 Protein expression	n	1 year	2 year	3 year
positive	52	47(90.38)	34(65.38)	16(30.77)
negative	27	25(92.59)	21(77.78)	15(55.56)
χ^2		0.107	1.291	4.579
P		0.743	0.256	0.032

3 讨论

胃癌的现阶段临床上总体治疗有效率不足 25%, 包括手术或者联合放化疗等综合性治疗措施的临床病情缓解率较低^[7,8]。同时对于胃癌的早期发病缺乏有效的筛查指标, 虽然 CA125 等上皮肿瘤糖蛋白成分能够在一定程度上提高胃癌的诊断效率^[9,10], 但其筛查的灵敏度或者特异度等局限性仍然较为明显。本次研究对于分子生物学相关指标的研究, 具有下列几个方面的显示意义: (1) 能够为胃癌的分子诊断学提供新的研究方向; (2) 能够为揭示胃癌的发病原因提供基础, 并为后续临床药理学实验提供治疗靶点。

分子生物学水平的异常近年来被认为是影响恶性肿瘤发生的核心因素, 分子水平的表达调控异常, 增加了癌细胞过度

扩增的风险, 导致癌细胞的正常分化或者促凋亡过程明显失常^[11,12]。Bag-1 作为抗凋亡家族成员, 其对于癌细胞细胞周期的影响, 促进了癌细胞的增殖速度的提高, 降低的了细胞程序性凋亡的发生, 并减少了癌细胞的凋亡比例。Bag-1 对于癌细胞分化成熟的抑制作用, 提高了癌细胞对于血管内皮或者淋巴管内皮的粘附能力, 对于恶性肿瘤的进展具有一定的促进作用^[13-16]。近年来相关基础理论方面的研究也提示, Bag-1 不仅能够影响癌细胞的凋亡, 同样可以在干预细胞肿瘤相关蛋白的转录翻译、癌细胞的变形能力, 降低消化系统上皮细胞排列的极性等方面发挥作用^[17-19]。回顾国内外已有的相关临床研究^[20-23], 部分研究探讨了 Bag-1 的在胃癌患者中的流行病学数据, 特别是对于相关异常阳性表达的分析, 但缺乏对于 Bag-1 与胃癌患者临床预后的关系研究。

本次研究发现,在胃癌患者中存在明显的 Bag-1 蛋白表达,提示 Bag-1 蛋白与胃癌的发生发展中可能起到一定作用,Bag-1 蛋白的高表达能够从下列几个方面促进胃上皮细胞的恶性肿瘤的发生^[24-26]:(1)Bag-1 蛋白抑制了癌细胞的凋亡,胃癌癌细胞凋亡诱导因子 a 的表达明显下降;(2)Bag-1 蛋白影响到了癌细胞的分化成熟功能,低分化或者异常分化水平的癌细胞比例明显上升。贾静等^[27,28]研究者在探讨了 123 例样本量的胃癌患者的蛋白水平的相关因子改变后发现,在胃腺癌或者鳞癌患者中,Bag-1 蛋白的阳性表达率均可上升 25%以上,并且病程越长、病情进展速度越快的患者相关指标阳性表达率也明显越高。临床分期较晚或者发生了明显的淋巴结转移的患者中,Bag-1 蛋白的表达阳性率往往较高,这主要可以从下列几个方面进行理解^[29,30]:(1)Bag-1 蛋白提升了癌细胞粘附淋巴结内皮细胞的能力,从而提高了癌细胞从淋巴结转移的风险;(2)Bag-1 蛋白能够增加癌细胞对于临床正常胃壁组织的浸润,特别是增加了癌细胞对于远处器官的侵袭风险,增加了临床分期。但本次研究并未发现 Bag-1 蛋白的表达与胃癌患者 CEA 水平、肿瘤部位、肿瘤大小、分化程度等的关系,提示 Bag-1 蛋白对于胃癌患者的肿瘤起源部位或者肿瘤细胞的分化调控的影响并不大。组合相关蛋白表达与患者临床预后的关系研究发现,胃癌患者 Bag-1 蛋白的阳性表达能够影响其 3 年生存率。本次研究的创新性在于探讨了蛋白水平表达与患者生存预后的关系。综上所述,胃癌组织中的 Bag-1 蛋白高表达,同时与患者的临床病理特征等因素密切相关。

参考文献(References)

- [1] Wang P, Zhang K, Zhang Q, et al. Effects of quercetin on the apoptosis of the human gastric carcinoma cells [J]. Toxicology in Vitro, 2012, 26(2): 221-228
- [2] Wang T, Xuan X, Li M, et al. Astragalus saponins affect proliferation, invasion and apoptosis of gastric cancer BGC-823 cells[J]. Diagnostic Pathology, 2013, 8(1): 90-92
- [3] Wan D, Shen S, Fu S, et al. miR-203 suppresses the proliferation and metastasis of hepatocellular carcinoma by targeting oncogene ADAM9 and oncogenic long non-coding RNA HULC[J]. Anti-cancer agents in medicinal chemistry, 2015, 16(4): 414
- [4] Jeganathan N, Dan P, Jin Z, et al. Rac1-mediated cytoskeleton rearrangements induced by intersectin-1s deficiency promotes lung cancer cell proliferation, migration and metastasis [J]. Molecular Cancer, 2016, 15(1): 59
- [5] 余洁丽,邱宇安,刘利艳,等. RNA 干扰 Nodal 基因对胃癌细胞凋亡及血管生成的影响[J].实用癌症杂志, 2017, 32(03): 401-404
Yu Jie-li, Qiu Yu-an, Liu Li-yan, et al. Effect of RNA Interference Targeting Nodal Gene on Apoptosis in Gastric Carcinoma Cell and Angiogenesis[J]. The Practical Journal of Cancer, 2017, 32(03): 401-404
- [6] 李佳,王东旭,张辰新,等. 抗凋亡蛋白 Mcl-1、Survivin 和 Bag-1 在肠化、不典型增生和胃癌中的表达及意义[J].解放军预防医学杂志, 2015, 33(06): 608-610
Li Jia, Wang Dong-xu, Zhang Chen-xin, et al. Expression of Mcl-1, Survivin and Bag-1 in human intestinal metaplasia, dysplasia and gastric cancer and its clinical significance [J]. Journal of Preventive Medicine of Chinese People's Liberation Army, 2015, 33(06): 608-610
- [7] 陆晟,燕敏,李琛,等. 老年胃癌患者临床病理特征与术后并发症危险因素的分析[J].中华胃肠外科杂志, 2016, 19(5): 514-521
Lu Sheng, Yan Min, Li Chen, et al. Analysis of clinicopathological features and risk factors for postoperative complications in the elderly gastric cancer patients [J]. Chinese Journal of Gastrointestinal Surgery, 2016, 19(5): 514-521
- [8] Allemanni C, Weir H K, Carreira H, et al. Global surveillance of cancer survival 1995-2009: analysis of individual data for 25 676 887 patients from 279 population-based registries in 67 countries (CONCORD-2)[J]. Lancet, 2015, 385(9972): 977-1010
- [9] Zhu Z, Chen Z, Chen C, et al. Opposite variation tendencies of serum CA724 levels in patients with colon and rectal carcinoma [J]. Molecular & Clinical Oncology, 2014, 2(1): 139-145
- [10] Li Y, Li D J, Chen J, et al. Application of Joint Detection of AFP, CA19-9, CA125 and CEA in Identification and Diagnosis of Cholangiocarcinoma [J]. Asian Pacific Journal of Cancer Prevention Apjcp, 2015, 16(8): 3451
- [11] Rew J. Capsaicin induces apoptosis and modulates MAPK signaling in human gastric cancer cells [J]. Molecular Medicine Reports, 2013, 24(05): 56-58
- [12] Luo X, Liu B, Dai Z, et al. Expression of apoptosis-associated microRNAs in ethanol-induced acute gastric mucosal injury via JNK pathway[J]. Alcohol, 2013, 47(6): 481-493
- [13] 曹建桥,王冠华,杨文君,等. 宁夏回族自治区回、汉族食管胃交界部腺癌临床病理特征对比分析 1524 例 [J]. 世界华人消化杂志, 2015, 23(12): 1949-1955
Cao Jian-qiao, Wang Guan-hua, Yang Wen-jun, et al. Clinical and pathological characteristics of adenocarcinoma of the esophagogastric junction in Hui and Han patients from Ningxia Hui Autonomous Region: Analysis of 1524 cases [J]. World Chinese Journal of Digestology, 2015, 23(12): 1949-1955
- [14] 陈慧,詹俊,于钟,等. 食管-胃连接部恶性肿瘤 218 例临床病理特征和预后分析[J].中华消化杂志, 2015, 35(5): 328-332
Chen Hui, Zhan Jun, Yu Zhong, et al. Clinical-pathological features and prognosis analysis of 218 esophagogastric junction malignant tumor[J]. Chinese Journal of Digestion, 2015, 35(5): 328-332
- [15] Dixon M, Mahar A L, Helyer L K, et al. Prognostic factors in metastatic gastric cancer: results of a population-based, retrospective cohort study in Ontario [J]. Gastric Cancer Official Journal of the International Gastric Cancer Association & the Japanese Gastric Cancer Association, 2016, 19(1): 150
- [16] Davidson B, Valborg Reinertsen K, Trinh D, et al. BAG-1/SODD, HSP70, and HSP90 are potential prognostic markers of poor survival in node-negative breast carcinoma[J]. Hum Pathol, 2016, 54:64-73
- [17] 欧阳小明,吴坤河,曾涛. 剔除 Bcl-2 基因对胃癌细胞 HGC-27 凋亡及 5-氟尿嘧啶敏感性的影响 [J]. 实用医学杂志, 2015, 31(15): 2423-2426
Ouyang Xiao-ming, Wu Kun-he, Zeng Tao. Effect of Bcl-2 knockdown on apoptosis and drug sensitivity of 5-FU in the gastric carcinoma HGC-27 cells [J]. The Journal of Practical Medicine, 2015, 31(15): 2423-2426
- [18] 季涛,徐向明,谭洪武. 胃癌变过程中凋亡基因生存素及 Bcl-2 的

- 表达与幽门螺杆菌感染相关性研究 [J]. 中华医院感染学杂志, 2015, 25(08): 1707-1709
- Ji Tao, Xu Xiang-ming, Tan Hong-wu. The research of the relationship between the expression of survivin and Bcl-2 and Hp infections during the course of gastric canceration[J]. Chinese Journal of Nosocomiology, 2015, 25(08): 1707-1709
- [19] Davidson B, Reinertsen K V, Trinh D, et al. BAG-1/SODD, HSP70, and HSP90 are potential prognostic markers of poor survival in node-negative breast carcinoma[J]. Human Pathology, 2016, 54:64-73
- [20] Gong D, Zhang Z, Zhang Y, et al. Expressions of p-STAT3, Survivin and Mcl-1 in gastric carcinoma tissues and their clinical significances [J]. Chinese Journal of Clinicians, 2015
- [21] Papadakis E S, Barker C R, Syed H, et al. The Bag-1 inhibitor, Thio-2, reverses an atypical 3D morphology driven by Bag-1L overexpression in a MCF-10A model of ductal carcinoma in situ[J]. Oncogenesis, 2016, 5(4): e215
- [22] Ozfiliz P, Kizilboga T, Demir S, et al. Bag-1 promotes cell survival through c-Myc-mediated ODC upregulation that is not preferred under apoptotic stimuli in MCF-7 cells [J]. Cell Biochemistry & Function, 2015, 33(5): 293
- [23] Fei M A, Zheng L Z, Jian-Chun G U, et al. Effects of Bag1 expression inhibition on cell growth and chemotherapy sensitivity in gastric cancer [J]. Journal of Shanghai Jiaotong University, 2014, 34 (3): 308-313
- [24] Amini N, Spolverato G, Kim Y, et al. Clinicopathological features and prognosis of gastric cardia adenocarcinoma: A multi-institutional U.S. study[J]. Journal of Surgical Oncology, 2015, 111(3): 285-292
- [25] Fei M A, Zheng L Z, Jian-Chun G U, et al. Effects of Bag1 expression inhibition on cell growth and chemotherapy sensitivity in gastric cancer[J]. Journal of Shanghai Jiaotong University, 2014, 34(3): 308-313
- [26] Li P, Wang Y D, Cheng J, et al. Association between polymorphisms of BAG - 1, and XPD, and chemotherapy sensitivity in advanced non-small-cell lung cancer patients treated with vinorelbine combined cisplatin regimen[J]. Tumor Biology, 2015, 36(12): 9465-9473
- [27] 贾静, 陈剑, 王华, 等. 胃肝样腺癌临床病理、免疫表型及预后分析 [J]. 临床与实验病理学杂志, 2014, 30(04): 443-446
- Jia Jing, Chen Jian, Wang Hua, et al. Clinicopathological features, immunophenotype and prognosis of gastric adenocarcinoma [J]. Chinese Journal of Clinical and Experimental Pathology, 2014, 30 (04): 443-446
- [28] 孟锐, 杨力, 刘雅琦, 等. 早期胃癌临床病理特征与淋巴结转移的关系 [J]. 实用医学杂志, 2015, 31(8): 1272-1274
- Meng Rui, Yang Li, Liu Ya-qi, et al. Relationship between clinicopathological features and lymph node metastasis in early gastric cancer[J]. The Journal of Practical Medicine, 2015, 31(8):1272 -1274
- [29] 伍冬梅, 李春鸣. Bcl-2, Bax 在胃癌及胃癌前病变中的表达与细胞凋亡的关系 [J]. 遵义医学院学报, 2014, 37(02): 201-203
- Wu Dong-mei, Li Chun-ming. Relationship between Bcl-2 and Bax expressions in gastric carcinoma and precancerous lesions and apoptosis[J]. Journal of zunyi medical university, 2014, 37(02): 201-203
- [30] Huang B, Zhou H, Lang X, et al. Expression of BAG-1 is closely related to cell differentiation and TNM stage in esophageal cancer and its downregulation inhibits the proliferation and invasion of human esophageal carcinoma cells[J]. Oncology Reports, 2014, 32(4): 1441-1446

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- [27] Uprety P, Lindsey JC, Levin MJ, et al. Inflammation and Immune Activation in Antiretroviral-Treated Human Immunodeficiency Virus Type 1-Infected African Infants and Rotavirus Vaccine Responses[J]. J Infect Dis, 2017, 215(6): 928-932
- [28] Li PQ, Zhang L. Study on the Change of Erythrocyte Immune and Serum Inflammatory Factors of Children with Rotavirus Enteritis[J]. Journal of Chengdu Medical College, 2014, 9(04): 389-391
- [29] Basile JI, Kviatcovsky D, Romero MM, et al. Mycobacterium tuberculosis multi-drug-resistant strain M induces IL-17+ IFN γ - CD4 $^{+}$ T cell expansion through an IL-23 and TGF- β -dependent mechanism in patients with MDR-TB tuberculosis [J]. Clin Exp Immunol, 2017, 187(1): 160-173
- [30] Dong H, Qu S, Chen X, et al. Changes in the cytokine expression of peripheral Treg and Th17 cells in children with rotavirus enteritis[J]. Exp Ther Med, 2015, 10(2): 679-682
- [31] Lai ML. Effect of Zinc Gluconate Auxiliary Therapy on Myocardial Injury, Immune Function and Serum Inflammatory Factors of Children with Rotavirus Enteritis [J]. Chinese Journal of Medical Guide, 2015, 17(06): 583-585+588