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反复呼吸道感染患儿血清微量元素及体液免疫水平测定及临床意义

杨剑敏 高 原 姜林林 马 展 张 泓△

（上海市儿童医院检验科 上海 200062）

摘要 目的:探讨反复呼吸道感染患儿血清微量元素及体液免疫水平测定及其临床意义。**方法**:选取 2016 年 1 月至 2017 年 1 月在我院接受治疗的反复呼吸道感染患儿 64 例作为观察组,另外选取同期来我院体检的健康儿童 60 例作为对照组,比较两组儿童血清微量元素钙(Ca)、铁(Fe)、铜(Cu)、锌(Zn)、镁(Mg)等的水平、体液免疫因子免疫球蛋白 A(IgA)、免疫球蛋白 M(IgM)、免疫球蛋白 G(IgG)水平及血清补体 C3、C4、C5 水平,并分析其相关性。**结果**:观察组患儿血清 Ca、Fe、Zn 水平显著低于对照组儿童(P＜0.05),两组儿童血清 Cu、Mg 水平比较差异无统计学意义(P＞0.05)。观察组患儿血清 IgA、IgM、IgG 水平低于对照组儿童(P＜0.05)。两组儿童血清补体 C3、C4、C5 水平比较差异无统计学意义(P＞0.05)。经 Pearson 相关性分析可得:反复呼吸道感染患儿血清 Ca、Fe、Zn 与血清 IgA、IgM、IgG 水平呈正相关(P＜0.05)。**结论**:反复呼吸道感染患儿存在血清 Ca、Fe、Zn 微量元素缺乏及血清 IgA、IgM、IgG 水平降低现象,且它们之间具有正相关关系,可能共同促进反复呼吸道感染的发生。

关键词:反复呼吸道感染;微量元素;体液免疫;补体

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Children with Recurrent Respiratory Tract Infection: Determination and Clinical Significance of Serum Trace Elements and Humoral Immunity

YANG Jian-min, GAO Yuan, JIANG Lin-lin, MA Zhan, ZHANG Hong△

(Department of Laboratory Medicine, Children's Hospital of Shanghai, Shanghai, 200062, China)

ABSTRACT Objective: To investigate the determination and clinical significance of serum trace elements and humoral immunity in children with recurrent respiratory tract infection. **Methods:** A total of 64 children with recurrent respiratory tract infection, who were treated in Children's Hospital of Shanghai from January 2016 to January 2017, were chosen as observation group;in addition,60 healthy children who received physical examination in this hospital, as control group during the same period.The levels of serum trace elements calcium (Ca), iron (Fe), copper (Cu), zinc (Zn) and magnesium (Mg),humoral immune factors of immunoglobulin A (IgA), immunoglobulin M (IgM), immunoglobulin G (IgG) levels, and serum levels of complement C3, C4, and C5 were compared between the two groups,and the correlation among them was analyzed. **Results:** The serum levels of Ca, Fe and Zn in the observation group were significantly lower than those in the control group (P<0.05). There was not statistically significant in serum Cu and Mg levels between the two groups (P>0.05). The serum levels of IgA, IgM and IgG in the observation group were significantly lower than those in the control group (P<0.05). There were not statistical differences in the levels of serum complement C3, C4 and C5 between the two groups (P>0.05).Pearson correlation analysis showed that the levels of serum Ca, Fe and Zn were positively related to serum IgA, IgM and IgG levels in children with repeated respiratory infection (P<0.05). **Conclusion:** Deficiency of trace elements in serum Ca, Fe and Zn and the decrease of serum IgA, IgM and IgG levels were found in children with recurrent respiratory tract infection,and there is a positive correlation between them, which may jointly promote the occurrence of recurrent respiratory tract infections.

Key words: Recurrent respiratory tract infection; Trace elements; Humoral immunity; Complement

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前言

反复呼吸道感染是儿科常见病与多发病，发病率高达 15.6%~18.4%,不仅给儿童带来了痛苦,同时也影响了儿童的生长与发育,应给予及时诊治[1-3]。目前,反复呼吸道感染的发病机制尚未完全明确,多数患儿经过抗炎、抗感染治疗后病情可以好转,但在特定诱因下还可发病,给临床治疗带来了困难。有研究表明，小儿免疫力低下是造成反复呼吸道感染的重要原因[4,5]。体液免疫是免疫系统的重要组成部分,主要包括抗体和补体,在抗感染中起到重要作用。同时有研究报道,微量元素缺乏也是引起小儿抵抗力低下的重要因素[6,7]。钙(Calcium,Ca)、铁(Iron,Fe)、铜(Copper,Cu)、锌(Zinc,Zn)、镁(Magnesium,Mg)等是机体重要的微量元素,与小儿生长发育、造血、骨骼形成、蛋白和基因合成有密切关系[8-10]。但关于微量元素缺乏与体液

作者简介:杨剑敏(1972-),女,大专,主管技师,从事儿童血液学及体液检验方面的研究,E-mail: lcx95674@163.com

△ 通讯作者:张泓(1963-),女,硕士,主任技师,从事实验室管理及微生物检验方面的研究,E-mail: tyggfj@163.com

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免疫是否在反复呼吸道感染中同时作用仍缺乏相关研究。为进一步探讨反复呼吸道感染患儿血清微量元素变化以及与体液免疫水平关系，我们进行了对照研究，现报道如下。

1 资料与方法

1.1 一般资料

选取 2016 年 1 月至 2017 年 1 月在我院接受治疗的反复呼吸道感染患儿 64 例作为观察组，纳入标准：(1)所有患者符合全国小儿呼吸疾病学术会议制定的反复呼吸道感染诊断标准[11]，年发病次数≥ 8 次；(2)患儿年龄 2~14 岁；(3)患儿未在疾病发病状态；(4)患儿法定监护人对研究知情同意。排除标准：(1)心脏、肺、呼吸道先天性畸形者；(2)先天性免疫功能异常者；(3) 近期服用过影响免疫功能和微量元素药物者。其中男 38 例，女 26 例，年龄 2～14 岁，平均年龄(5.87± 1.86)岁。另选取同期来我院体检的健康儿童 60 例作为对照组，其中男 35 例，女 25 例，年龄 2~14 岁，平均年龄(5.31± 1.92)岁。两组儿童性别、年龄比较均无统计学差异(P＞0.05)，组间存在可比性。本研究经我院伦理委员批准。

1.2 研究方法

1.2.1 血液标本的采集 观察组患儿入院后采集清晨空腹外周静脉血 5 mL，对照组儿童于体检当日采集空腹外周静脉血 5 mL，置于试管中，静置 30 min，以 4000 r/min 转速离心 10 min，离心半径为 6 cm，取上清液，所有标本于 30 min 内送检。

1.2.2 血清微量元素检查 应用原子吸收法测定患儿血清 Ca、Fe、Cu、Zn、Mg 等微量元素水平，仪器为博晖石墨炉元素分析仪和 RH5500 原子吸收光谱仪，试剂盒采用 BOHUI 创新光电技术股份有限公司，具体操作严格按照试剂盒说明书进行。

1.2.3 体液免疫因子的检测 应用免疫散色比浊法测定受试儿童血清免疫球蛋白 A(Immunoglobulin A，IgA)、免疫球蛋白 M（ImmunoglobulinM，IgM)、免疫球蛋白 G(Immunoglobulin G，IgG)及血清补体 C3、C4、C5 水平。仪器为 BNII 全自动蛋白分析仪，试剂盒购自西门子有限公司，具体操作严格按照试剂盒说明书进行。

1.3 观察指标

比较两组儿童血清微量元素 Ca、Fe、Cu、Zn、Mg 等的水平、体液免疫因子 IgA、IgM、IgG 水平及血清补体 C3、C4、C5 水平，并分析其相关性。

1.4 统计学方法

本研究数据均采用 SPSS25.0 软件进行统计学分析，计数资料以比或率(%)表示，采用 x^2 检验，计量资料以均数± 标准差($\bar{x}\pm s$)表示，采用 t 检验，其中相关性予以 Pearson 相关性分析，P＜0.05 表明数据比较差异具有统计学意义。

2 结果

2.1 两组儿童血清微量元素水平比较

观察组患儿血清 Ca、Fe、Zn 水平显著低于对照组儿童(P＜0.05)，两组儿童血清 Cu、Mg 水平比较差异无统计学意义(P＞0.05)。见表 1。

表 1 两组儿童血清微量元素水平比较(mmol/L，$\bar{x}\pm s$)

Table 1 Comparison of serum trace elements of children in two groups(mmol/L，$\bar{x}\pm s$)

Groups	n	Ca	Fe	Cu	Zn	Mg
Observation group	64	0.82± 0.26	5.22± 0.79	25.11± 3.59	64.81± 7.83	1.78± 0.49
Control group	60	1.71± 0.28	9.68± 0.65	25.20± 3.79	112.43± 10.64	1.82± 0.43
t	-	4.783	6.392	0.603	14.328	0.847
P	-	0.000	0.000	0.505	0.000	0.383

2.2 两组儿童血清 IgA、IgM、IgG 水平比较

观察组患儿血清 IgA、IgM、IgG 水平低于对照组儿童(P＜0.05)。见表 2。

表 2 两组儿童血清 IgA、IgM、IgG 水平比较(g/L，$\bar{x}\pm s$)

Table 2 Comparison of serum IgA, IgM and IgG levels of children in two groups(g/L, $\bar{x}\pm s$)

Groups	n	IgA	IgM	IgG
Observation group	64	1.68± 0.35	1.83± 0.77	7.34± 2.12
Control group	60	2.42± 0.38	2.01± 0.57	12.34± 3.33
t	-	4.263	3.128	6.647
P	-	0.008	0.040	0.000

2.3 两组儿童血清补体 C3、C4、C5 水平比较

两组儿童血清补体 C3、C4、C5 水平比较无统计学差异(P＞0.05)。见表 3。

2.4 反复呼吸道感染患儿血清微量元素与免疫因子及补体的相关性分析

经 Pearson 相关性分析可得：反复呼吸道感染患儿血清 Ca、Fe、Zn 与血清 IgA、IgM、IgG 水平呈正相关(P＜0.05)，与血清补体 C3、C4、C5 水平无相关性(P＞0.05)，反复呼吸道感染患儿血清血清 Cu、Mg 水平与血清 IgA、IgM、IgG 水平及血清补体 C3、C4、C5 水平均无相关性(P＞0.05)。见表 4。

表 3 两组儿童血清补体 C3、C4、C5 水平比较(g/L, $\bar{x}\pm s$)

Table 3 Comparison of serum C3, C4, C5 levels of children in two groups(g/L, $\bar{x}\pm s$)

Groups	n	C3	C4	C5
Observation group	64	1.45± 0.38	1.75± 0.27	1.44± 0.22
Control group	60	1.43± 0.25	1.71± 0.22	1.48± 0.23
t	-	0.643	0.835	0.632
P	-	0.518	0.128	0.445

表 4 反复呼吸道感染患儿血清微量元素与免疫因子及补体的相关性分析

Table 4 Correlation analysis of serum trace elements and immune factors and complement in children with recurrent respiratory tract infection

Indexs	IgA		IgM		IgG		C3		C4		C5	
	r	P	r	P	r	P	r	P	r	P	r	P
Ca	0.463	0.000	0.585	0.000	0.543	0.000	0.142	0.128	0.095	0.423	0.114	0.182
Fe	0.597	0.000	0.532	0.000	0.512	0.000	0.108	0.224	0.128	0.305	0.098	0.351
Zn	0.523	0.000	0.481	0.000	0.505	0.000	0.097	0.307	0.105	0.285	0.112	0.128
Cu	0.108	0.428	0.124	0.125	0.056	0.721	0.135	0.310	0.058	0.825	0.032	0.692
Mg	0.103	0.482	0.098	0.512	0.072	0.628	0.128	0.428	0.124	0.125	0.158	0.182

3 讨论

小儿反复呼吸道感染是儿童高发疾病，以 2~6 岁儿童最为常见。患儿临床表现为反复出现发热、咳嗽、流涕、喷嚏等症状，病程迁延，临床治愈较为困难，时间长者可引发小儿哮喘、贫血、心脏病等，严重影响患儿身体健康[12]。目前对于小儿反复呼吸道感染的发病机制仍未完全明确，一般认为该病与遗传、感染因素及免疫功能缺陷等有密切关系[13,14]，尤其是患儿免疫力低下是引起反复呼吸道感染的重要因素。近年来有研究发现，微量元素缺乏可以导致小儿免疫力低下，并引发多种疾病，在小儿反复呼吸道感染发病中可能起到重要作用[15-17]。

本研究通过对反复呼吸道感染患儿和健康儿童的比较发现，观察组患儿血清 Ca、Fe、Zn 水平显著低于对照组儿童（P＜0.05），两组儿童血清 Cu、Mg 水平比较差异无统计学意义（P＞0.05）。Ca、Fe、Cu、Zn、Mg 是机体重要的微量元素，在儿童生长发育、组织形成、创伤修复等过程中起到重要作用[18]。其中 Ca 是牙齿和骨骼的主要成分，也是小儿发育中的重要微量元素，它可以参与蛋白质合成、心电生理反应、骨骼肌收缩等，同时也是细胞行使正常功能的重要物质[19,20]。当机体钙缺乏时可以影响蛋白质合成和细胞组织功能，降低机体免疫力[21]。而 Fe 是血红蛋白的重要组成成分，同时也参与生物呼吸功能[22]。而 Zn 则与细胞分裂、核酸和蛋白质合成有密切关系[23]。本研究中反复呼吸道感染患儿 Ca、Fe、Zn 水平降低，提示 Ca、Fe、Zn 在反复呼吸道感染发病中起到重要作用。而两组儿童血清 Cu、Mg 水平比较差异无统计学意义，提示 Cu、Mg 与反复呼吸道感染关系不密切。

本研究还对两组儿童体液免疫水平进行了比较。儿童身体正处在生长发育时期，各器官、系统功能尚不完善。其中体液免疫主要包括特异性体液免疫系统和非特异性体液免疫系统。前者主要是由 B 细胞产生的免疫球蛋白，包括 IgA、IgM、IgG 等，而后者则是体液内存在的补体成分，包括 C1、C2、C3 等。本研究中观察组患儿血清 IgA、IgM、IgG 水平低于对照组儿童（P＜0.05）。其中 IgA 主要分布于机体口腔、呼吸道、肠道粘膜等，具有抑制病原体增殖，调节吞噬功能的作用，当机体发生感染时，可造成 IgA 大量消耗，免疫功能降低[24,25]。而 IgM 是特异性免疫系统的主要成员，主要在新生儿出生后形成[26]。IgG 则是可以通过胎盘的唯一一种免疫球蛋白，具有中和内外毒素，调节吞噬细胞的功能[27]。本研究结果提示反复呼吸道感染的发生与血清 IgA、IgM、IgG 水平降低有关。补体是存在于机体体液中的具有酶活性的蛋白质，其数量众多，在炎症反应、免疫细胞活化、中和毒素、杀伤病原体中起到重要作用[28]。目前关于反复呼吸道感染患儿血清补体水平报道结果不一。Racette SD 等[29]研究报道反复呼吸道感染患儿血清补体 C3、C4 水平显著升高，并认为血清补体 C3、C4 在反复呼吸道感染发病中起到重要作用。而 Fauroux B 等 [30] 则报道反复呼吸道感染患儿血清补体 C3、C4 与健康儿童无明显差异。本研究中两组儿童血清补体 C3、C4、C5 水平比较无统计学差异（P＞0.05），与 Fauroux B 等报道相符。我们认为血清补体非特异性免疫的重要成分，其水平与感染性疾病的发生有关，但发生感染后可快速升高，而感染结束后可迅速恢复至正常水平。而本研究选择的反复呼吸道感染患儿未在疾病发病状态，因此血清补体 C3、C4、C5 水平并未明显升高。本研究经 Pearson 相关性分析可得：反复呼吸道感染患儿血清 Ca、Fe、Zn 与血清 IgA、IgM、IgG 水平呈正相关，提示反复呼吸道感染患儿 Ca、Fe、Zn 微量元素水平与血清 IgA、IgM、IgG 水平存在关系，Ca、Fe、Zn 微量元素缺乏可能通过 IgA、IgM、IgG 影响体液免疫功能，导致小儿体液免疫功能降低，引发反复呼吸感染。

综上所述，反复呼吸道感染患儿存在血清 Ca、Fe、Zn 微量元素缺乏及血清 IgA、IgM、IgG 水平降低现象，它们之间具有正相关关系，Ca、Fe、Zn 微量元素缺乏可能通过 IgA、IgM、IgG

影响体液免疫功能,共同促进反复呼吸道感染的发生。

参 考 文 献(References)

[1] Paśnik J. Vaccines nonspecific-immunostimulation in patients with recurrent respiratory infections[J]. Otolaryngol Pol, 2016, 70(6): 31-39

[2] Zhang X, Ding F, Li H, et al. Low Serum Levels of Vitamins A, D, and E Are Associated with Recurrent Respiratory Tract Infections in Children Living in Northern China:A Case Control Study [J]. PLoS One, 2016, 11(12): e0167689

[3] Woicka-Kolejwa K, Zaczeniuk M, Majak P, et al. Food allergy is associated with recurrent respiratory tract infections during childhood [J]. Postepy Dermatol Alergol, 2016, 33(2): 109-113

[4] Braido F, Melioli G, Candoli P, et al. The bacterial lysate Lantigen B reduces the number of acute episodes in patients with recurrentinfections of the respiratory tract: the results of a double blind, placebo controlled, multicenter clinical trial [J]. Immunol Lett, 2014, 162(2 Pt B): 185-193

[5] Vaccaro M, Salpietro C, Foti A, et al. Pityriasis rotunda with recurrent respiratory infections [J]. G Ital Dermatol Venereol, 2017, 152(2): 190-191

[6] van Kessel DA, Hoffman TW, van Velzen-Blad H, et al. Response to pneumococcal vaccination in mannose-binding lectin-deficient adults with recurrentrespiratory tract infections[J]. Clin Exp Immunol, 2014, 177(1): 272-279

[7] Nicolai A, Frassanito A, Nenna R, et al. Risk Factors for Virus-induced Acute Respiratory Tract Infections in Children Younger Than 3 Years and Recurrent Wheezing at 36 Months Follow-Up After Discharge[J]. Pediatr Infect Dis J, 2017, 36(2): 179-183

[8] 高超,吴永利,刘君婷,等.血清微量元素与多动症患儿行为症状的相关性研究[J].现代生物医学进展, 2016, 16(29): 5727-5729, 5719
Gao Chao, Wu Yong-li, Liu Jun-ting, et al. A Study on the Relationship Between the Trace Elements of Serum and Behavioral in Children with ADHD [J]. Progress in Modern Biomedicine, 2016, 16 (29): 5727-5729, 5719

[9] Klein LD, Breakey AA, Scelza B, et al. Concentrations of?trace elements in human milk: Comparisons among women in Argentina, Namibia, Poland, and the United States [J]. PLoS One, 2017, 12(8): e0183367

[10] 马丽娟,周林.儿童微量元素的检测及其价值分析[J].中华检验医学杂志, 2016, 39(4): 240-242
Ma Li-juan, Zhou Lin. Detection of trace elements in children and its clinical value [J]. Chinese Journal of Laboratory Medicine, 2016, 39 (4): 240-242

[11] 唐秀英,李莉,席向红,等.儿童反复呼吸道感染与免疫球蛋白及IgG亚类的相关性研究[J].中国儿童保健杂志, 2016, 24(8): 873-876
Tang Xiu-ying, Li Li, Xi Xiang-hong, et al. Correlation study between recurrent respiratory tract infections and immunoglobulin and IgG subclass in children [J]. Chinese Journal of Child Health Care, 2016, 24(8): 873-876

[12] Esposito S, Rosazza C, Sciarrabba CS, et al. Inhaled Antibiotic Therapy for the Treatment of Upper Respiratory Tract Infections[J]. J Aerosol Med Pulm Drug Deliv, 2017, 30(1): 14-19

[13] Korona-Glowniak I, Maj M, Siwiec R, et al. Molecular Epidemiology of Streptococcus pneumoniae Isolates from Children with Recurrent UpperRespiratory Tract Infections [J]. PLoS One, 2016, 11 (7): e0158909

[14] Esposito S, Rosazza C, Sciarrabba CS, et al. Inhaled Antibiotic Therapy for the Treatment of Upper Respiratory Tract Infections[J]. J Aerosol Med Pulm Drug Deliv, 2017, 30(1): 14-19

[15] Saad K, Abo-Elela MG, El-Baseer KA, et al. Effects of bovine colostrum on recurrent respiratory tract infections and diarrhea in children[J]. Medicine (Baltimore), 2016, 95(37): e4560

[16] Toivonen L, Karppinen S, Schuez-Havupalo L, et al. Burden of Recurrent Respiratory Tract Infections in Children: A Prospective Cohort Study[J]. Pediatr Infect Dis J, 2016, 35(12): e362-e369

[17] Takhar RP, Bunkar M, Jain S, et al. Tracheal diverticulum: an unusual cause of chronic cough and recurrent respiratory infections [J]. Tuberk Toraks, 2016, 64(1): 77-82

[18] Yakoob MY, Lo CW. Nutrition (Micronutrients) in Child Growth and Development: A Systematic Review on Current Evidence, Recommendations and Opportunities for Further Research [J]. J Dev Behav Pediatr, 2017, 38(8): 665-679

[19] Egeland GM, Skurtveit S, Sakshaug S, et al. Low Calcium Intake in Midpregnancy Is Associated with Hypertension Development within 10 Years after Pregnancy: The Norwegian Mother and Child Cohort Study[J]. J Nutr, 2017, 147(9): 1757-1763

[20] Ludwa IA, Falk B, Ward WE, et al. Mechanical, biochemical, and dietary determinants of the functional model of bone development of the radius in children and adolescents [J]. Appl Physiol Nutr Metab, 2017, 42(7): 780-787

[21] 侯安存.关于补钙的研究进展[J].临床和实验医学杂志, 2016, 15 (18): 1862-1865
Hou An-cun. Research Progress on calcium supplementation [J]. Journal of Clinical and Experimental Medicine, 2016, 15 (18): 1862-1865

[22] Nguyen PH, Gonzalez-Casanova I, Young MF, et al. Preconception Micronutrient Supplementation with Iron and Folic Acid Compared with Folic Acid Alone Affects Linear Growth and Fine Motor Development at 2 Years of Age: A Randomized Controlled Trial in Vietnam[J]. J Nutr, 2017, 147(8): 1593-1601

[23] Liu X, Piao J, Zhang Y, et al. Assessment of Zinc Status in School-Age Children from Rural Areas in China Nutrition and Health Survey 2002 and 2012[J]. Biol Trace Elem Res, 2017, 178(2): 194-200

[24] Janssen WJ, Nierkens S, Sanders EA, et al. Antigen-specific IgA titres after 23-valent pneumococcal vaccine indicate transient antibody deficiency disease in children [J]. Vaccine, 2015, 33(46): 6320-6326

[25] Gustafson CE, Higbee D, Yeckes AR, et al. Limited expression of APRIL and its receptors prior to intestinal IgA plasma cell development during human infancy[J]. Mucosal Immunol, 2014, 7(3): 467-477

[26] Chandy S, Kirubanandhan L, Hemavathy P, et al. Serovar prevalence of Leptospira in semirural India and the development of an IgM-based indirect ELISA[J]. J Infect Dev Ctries, 2017, 11(3): 234-241

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cell activity and multidrug resistance of $CD44^+CD24^-$/lowbreast cancer stem cells[J]. Chinese Journal of Tissue Engineering Research, 2016, 20(32): 4758-4763

[12] Choy C, Ansari KI, Neman J, et al. Cooperation of neurotrophin receptor TrkB and Her2 in breast cancer cells facilitates brain metastases[J]. Breast Cancer Res, 2017, 19(1): 51

[13] Sciortino M, Camacho-Leal MDP, Orso F, et al. Dysregulation of Blimp1 transcriptional repressor unleashes p130Cas/ErbB2 breast cancerinvasion[J]. Sci Rep, 2017, 7(1): 1145

[14] Federico L, Chong Z, Zhang D, et al. A murine preclinical syngeneic transplantation model for breast cancer precision medicine [J]. Sci Adv, 2017, 3(4): e1600957

[15] Gao Y, Cai A, Xi H, et al. Ring finger protein 43 associates with gastric cancer progression and attenuates the stemness of gastric cancer stem-like cells via the Wnt-β/catenin signaling pathway [J]. Stem Cell Res Ther, 2017, 8(1): 98

[16] Liu H, Wang YJ, Bian L, et al. $CD44^+/CD24^+$ cervical cancer cells resist radiotherapy and exhibit properties of cancer stem cells [J]. Eur Rev Med Pharmacol Sci, 2016, 20(9): 1745-1754

[17] Nami B, Donmez H, Kocak N. Tunicamycin-induced endoplasmic reticulum stress reduces in vitro subpopulation and invasion of $CD44^+/CD24^-$ phenotype breast cancer stem cells [J]. Exp Toxicol Pathol, 2016, 68(7): 419-426

[18] Zheng Z, Shao N, Weng H, et al. Correlation between epidermal growth factor receptor and tumor stem cell markers CD44/CD24 and their relationship with prognosis in breast invasive ductal carcinoma [J]. Med Oncol, 2015, 32(1): 275

[19] Tramm T, Kim JY, Leibl S, et al. Expression of C-KIT, CD24, CD44s, and COX2 in benign and non-invasive apocrine lesions of the breast[J]. Virchows Arch, 2016, 469(3): 285-295

[20] Kapucuo ğ lu N, Bozkurt KK, Ba ş pınar Ş , et al. The clinicopathological and prognostic significance of CD24, CD44, CD133, ALDH1 expressions in invasive ductal carcinoma of the breast: CD44/CD24 expression in breast cancer [J]. Pathol Res Pract, 2015, 211(10): 740-747

[21] Hsieh CH, Hsiung SC, Yeh CT, et al. Differential expression of CD44 and CD24 markers discriminates the epitheliod from thefibroblastoid subset in a sarcomatoid renal carcinoma cell line: evidence suggestingthe existence of cancer stem cells in both subsets as studied with sorted cells[J]. Oncotarget, 2017, 8(9): 15593-15609

[22] Ghuwalewala S, Ghatak D, Das P, et al. CD44 (high)CD24 (low) molecular signature determines the Cancer Stem Cell and EMT phenotype in Oral Squamous Cell Carcinoma [J]. Stem Cell Res, 2016, 16(2): 405-417

[23] Salomon S, Guignant C, Morel P, et al. Th17 and CD24hiCD27+ regulatory B lymphocytes are biomarkers of response to biologics in rheumatoid arthritis[J]. Arthritis Res Ther, 2017, 19(1): 33

[24] Kim MH, Kim MH, Kim KS, et al. In vivo monitoring of $CD44^+$ cancer stem-like cells by γ-irradiation in breast cancer[J]. Int J Oncol, 2016, 48(6): 2277-2286

[25] Zheng J, Zhao S, Yu X, et al. Simultaneous targeting of CD44 and EpCAM with a bispecific aptamer effectively inhibits intraperitoneal ovarian cancer growth[J]. Theranostics, 2017, 7(5): 1373-1388

[26] Zeng JF, Ma XQ, Wang LP, et al. MicroRNA-145 exerts tumor-suppressive and chemo-resistance lowering effects by targeting CD44 in gastric cancer [J]. World J Gastroenterol, 2017, 23 (13): 2337-2345

[27] PLOS ONE Staff. Correction: CD90 and CD24 Co-Expression Is Associated with Pancreatic Intraepithelial Neoplasias [J]. PLoS One, 2017, 12(4): e0176804

[28] Yang N, Zhou TC, Lei XX, et al. Inhibition of Sonic Hedgehog Signaling Pathway by Thiazole Antibiotic Thiostrepton Attenuates the $CD44^+/CD24^-$ Stem-Like Population and Sphere-Forming Capacity in Triple-Negative Breast Cancer[J]. Cell Physiol Biochem, 2016, 38(3): 1157-1170

[29] Da Cruz Paula A, Leitão C, Marques O, et al. Molecular characterization of $CD44^+/CD24^-/Ck^+/CD45^-$ cells in benign and malignant breastlesions[J]. Virchows Arch, 2017, 470(3): 311-322

[30] Chen Y, Song J, Jiang Y, et al. Predictive value of CD44 and CD24 for prognosis and chemotherapy response in invasive breast ductal carcinoma[J]. Int J Clin Exp Pathol, 2015, 8(9): 11287-11295

（上接第 296 页）

[27] França CT, Li Wai Suen CSN, Carmagnac A, et al. IgG antibodies to synthetic GPI are biomarkers of immune-status to both Plasmodium falciparum and Plasmodium vivax malaria in young children[J].Malar J, 2017, 16(1): 386

[28] 臧丹丹,张家祥,叶良平,等.药疹患者血清 Th22 细胞相关细胞因子和补体蛋白水平变化研究 [J]. 中华皮肤科杂志, 2016, 49(11): 781-784

Zang Dan-dan, Zhang Jia-xiang, Ye Liang-ping, et al. Changes in serum levels of Th22 cell-related cytokines and complements in patients with drug eruption before and after treatment [J]. Chinese Journal of Dermatology, 2016, 49(11): 781-784

[29] Racette SD, Wijewickrama RC, Jayaprakash V, et al. Correlation of Symptoms,Clinical Signs,and Biomarkers of Inflammation in Postsurgical Chronic Rhinosinusitis [J]. Ann Otol Rhinol Laryngol, 2017, 126(6): 455-462

[30] Fauroux B, Sim ões EAF, Checchia PA, et al. The Burden and Long-term Respiratory Morbidity Associated with Respiratory Syncytial Virus Infection in Early Childhood [J]. Infect Dis Ther, 2017, 6(2): 173-197