

卵巢子宫内膜异位囊肿患者血清 APRIL 与 NDRG1 的水平表达及其临床价值研究

罗 亮, 许剑利, 程其军, 阴 莉 (自贡市第一人民医院妇产科, 四川自贡 643000)

摘要: **目的** 观察血清增殖诱导配体 (a proliferation inducing ligand, APRIL), N-myc 下游调节基因 1 (N-myc downstream regulated gene 1, NDRG1) 水平变化, 并分析其对卵巢子宫内膜异位囊肿 (ovarian endometriomas, OEM) 的诊断价值。**方法** 选取 2021 年 7 月~2022 年 7 月在自贡市第一人民医院就诊的 132 例 OEM 患者作为观察组, 并进行定期随访, 根据患者预后病情有无复发分为复发组 ($n=50$) 和未复发组 ($n=82$)。同期在该院体检的健康者 78 例为对照组。采用酶联免疫吸附法 (enzyme linked immunosorbent assay, ELISA) 检测血清中 APRIL 和 NDRG1 水平; 并对复发组和未复发组的一般资料进行比较; 采用 Logistic 回归分析影响 OEM 预后的相关因素; 用 Pearson 法分析 OEM 患者血清 APRIL 与 NDRG1 表达相关性; 绘制受试者工作特征 (receiver operating characteristic, ROC) 曲线分析血清 APRIL 和 NDRG1 对 OEM 的诊断价值。**结果** 与对照组相比, APRIL 水平 ($35.28 \pm 6.81\text{ng/ml}$ vs $26.37 \pm 3.19\text{ng/ml}$) 和 NDRG1 水平 ($124.39 \pm 15.67\mu\text{g/L}$ vs $9.67 \pm 10.82\mu\text{g/L}$) 升高, 差异具有统计学意义 ($t=10.864, 17.278$, 均 $P < 0.05$)。与未复发组比较, 复发组血清 APRIL ($40.38 \pm 7.88\text{ng/ml}$ vs $32.16 \pm 6.18\text{ng/ml}$) 和 NDRG1 ($132.04 \pm 19.83\mu\text{g/L}$ vs $119.73 \pm 13.16\mu\text{g/L}$) 水平升高, 差异具有统计学意义 ($t=6.668, 4.287$, 均 $P < 0.05$)。Logistic 回归分析显示, 血清 APRIL 和 NDRG1 水平是影响 OEM 患者预后的危险因素 (Wald $\chi^2=11.839, 28.437$, 均 $P < 0.001$)。Pearson 法分析结果显示, OEM 患者血清 APRIL 水平与 NDRG1 水平呈正相关 ($r=0.439, P<0.001$)。血清 APRIL, NDRG1 水平联合诊断 OEM 的曲线下面积 (AUC) 为 0.849, 灵敏度和特异度分别为 73.95%, 85.37%, 优于 APRIL 和 NDRG1 单独预测 ($Z=2.644, 2.094, P=0.008, 0.036$)。**结论** 子宫内膜异位囊肿患者血清 APRIL 和 NDRG1 水平升高, 二者联合对子宫内膜异位囊肿诊断具有较高的临床价值, 且与子宫内膜异位囊肿患者的预后密切相关。

关键词: 卵巢子宫内膜异位囊肿; 增殖诱导配体; N-myc 下游调节基因 1

中图分类号: R711.71; R392.11 文献标识码: A 文章编号: 1671-7414 (2024) 02-124-05

doi:10.3969/j.issn.1671-7414.2024.02.023

Expression of Serum APRIL and NDRG1 Levels in Patients with Ovarian Endometrioma and Their Clinical Value

LUO Liang, XU Jianli, CHENG Qijun, YIN Li

(Department of Obstetrics and Gynecology, Zigong First People's Hospital, Sichuan Zigong 643000, China)

Abstract: **Objective** To observe the changes in serum a proliferation inducing ligand (a proliferation inducing ligand, APRIL) and N-myc downstream regulated gene 1 (N-myc downstream regulated gene 1, NDRG1) levels, and analyze their diagnostic value for ovarian endometrioma (OEM). **Methods** From July 2021 to July 2022, 132 patients with OEM who visited Zigong First People's Hospital were regarded as the observation group, and regular follow-up was conducted. According to the prognosis of these patients, they were grouped into the recurrence group ($n=50$) and the non recurrence group ($n=82$). Meanwhile, 78 healthy individuals who had their medical checkups at the hospital during the same period were the control group. Enzyme linked immunosorbent assay (ELISA) was applied to detect serum APRIL and NDRG1 levels, and the general data of the recurrent and non recurrent groups were compared. Logistic regression analysis was applied to analyze the relevant factors affecting the prognosis of OEM. Pearson analysis was applied to explore the correlation between serum APRIL and NDRG1 levels in patients with OEM. Receiver operating characteristic (ROC) curve was applied to evaluate the diagnostic value of serum APRIL, NDRG1 levels and their combination for OEM. **Results** Compared with the control group, APRIL level ($35.28 \pm 6.81\text{ng/ml}$ vs $26.37 \pm 3.19\text{ng/ml}$) and NDRG1 level ($124.39 \pm 15.67\mu\text{g/L}$ vs $9.67 \pm 10.82\mu\text{g/L}$) in observation group were increased, and the differences were significant ($t=10.864, 17.278$, all $P<0.05$). Compared with the non recurrence group, the serum levels of APRIL ($40.38 \pm 7.88\text{ng/ml}$ vs $32.16 \pm 6.18\text{ng/ml}$) and NDRG1 ($132.04 \pm 19.83\mu\text{g/L}$ vs $119.73 \pm 13.16\mu\text{g/L}$) in the recurrence group

作者简介: 罗亮 (1988-), 男, 本科, 主治医师, 研究方向: 妇产科疾病, E-mail: fxdowhw@163.com。

通讯作者: 许剑利 (1971-), 女, 硕士, 主任医师, 研究方向: 妇科内分泌, E-mail: xujianli@163.com。

were increased, and the differences were significant ($t=6.668, 4.287$, all $P<0.05$). Logistic regression analysis showed that serum APRIL and NDRG1 levels were risk factors for the prognosis of patients with OEM (Wald $\chi^2=11.839, 28.437$, all $P<0.001$). Pearson method analysis results showed a positive correlation between serum APRIL level and NDRG1 level in patients with OEM ($r=0.439, P<0.001$). The area under the curve (AUC) of combined diagnosis of serum APRIL and NDRG1 levels in patients with OEM was 0.849, with a sensitivity and specificity of 73.95% and 85.37%, respectively, which was better than the single prediction of APRIL and NDRG1 ($Z=2.644, 2.094, P=0.008, 0.036$). **Conclusion** The serum levels of APRIL and NDRG1 were increased in patients with OEM. The combination of the two has high clinical value in the diagnosis of OEM, which may be closely related to the prognosis of patients with OEM.

Keywords: ovarian endometriomas; a proliferation inducing ligand; N-myc downstream regulated gene 1

卵巢子宫内膜异位囊肿 (ovarian endometriomas, OEM) 是一种多发于育龄女性的卵巢良性囊肿^[1-2]。OEM 临床症状主要表现为月经紊乱、严重痛经, 甚至盆腔粘连, 严重者会导致患者不孕, 严重影响患者家庭和生活^[3-4]。增殖诱导配体 (a proliferation inducing ligand, APRIL) 是肿瘤坏死因子超家族成员之一, 其编码基因位于染色体 17p13 上^[5]。已有研究报道, APRIL 可以促进肿瘤细胞的增殖和防止肿瘤细胞的凋亡^[6]。N-myc 下游调节基因 1 (N-myc downstream regulated gene1, NDRG1) 是 N-myc 下游调节基因 (Nmyc downstream regulated gene, NDRG) 家族成员之一, 定位于人染色体 9q24.3 上, 参与细胞生长分化、细胞周期、细胞增殖及凋亡等生物学过程^[7]。NDRG1 已经发现其在女性生殖系统肿瘤组织中存在异常表达并参与肿瘤的发生发展过程, 如子宫内膜癌^[8]。目前血清 APRIL 和 NDRG1 在 OEM 患者中的表达及临床意义相关研究涉及较少。本研究旨在探讨 OEM 患者血清 APRIL 和 NDRG1 表达水平及二者的临床诊断价值。

1 材料与方法

1.1 研究对象 选取 2021 年 7 月 ~ 2022 年 7 月在自贡市第一人民医院就诊的 132 例 OEM 患者作为观察组。年龄 20 ~ 55 (30.21 ± 6.27) 岁; 月经周期 20 ~ 29 (25.36 ± 3.61) 天。并进行一年定期随访, 根据患者预后复发情况分为复发组 ($n=50$) 和未复发组 ($n=82$)。纳入标准: ①符合 2015 年《子宫内膜异位症的诊治指南》中 OEM 的诊断标准^[9]; ②月经周期规律者; ③具有完整的病理资料者; ④随访完成者。排除标准: ①存在卵巢恶性肿瘤者; ②患有精神疾病, 无法正常交流者; ③存在多囊卵巢综合征等内分泌疾病者; ④存在其他免疫系统疾病者。选取同期在本院体检的健康者 78 例作为对照组, 年龄 19 ~ 52 (31.67 ± 6.18) 岁; 月经周期 19 ~ 28 (24.93 ± 3.01) 天。两组年龄和月经周期差异无统计学意义 ($t=1.639, 0.885$, 均 $P>0.05$), 具有可比性。本研究经过医院伦理委员会审核批准 (批准文号: 21051609), 研究对象或家属知情同意。

1.2 仪器与试剂 APRIL ELISA 试剂盒 [优利科

(上海) 生命科学有限公司]; NDRG1 ELISA 试剂盒 (温州科森生物科技有限公司); 酶标仪 [美谷分子仪器 (上海) 有限公司]。

1.3 方法

1.3.1 临床资料收集: 收集研究对象年龄、体质量指数等一般指标, 询问并记录患者是否存在痛经、是否有生育史等信息, 并通过腹腔镜检查记录囊肿位置以及囊肿最大径。

1.3.2 ELISA 检测血清中 APRIL, NDRG1 表达水平: 空腹采集 OEM 患者和健康体检者静脉血 3 ~ 5ml, 3 000r/min 离心 10min, 收集上清, -20°C 保存。采用 ELISA 检测血清 APRIL, NDRG1 水平, 实验操作步骤完全按照试剂盒的说明书进行。每个指标连续测量 3 次, 取平均值作为最终结果。

1.4 统计学分析 SPSS 25.0 处理数据。计量资料均符合正态分布, 用均数 \pm 标准差 ($\bar{x} \pm s$) 表示, 两组数据用 t 检验; 计数资料以 $n(\%)$ 表示, 采用 χ^2 检验进行组间比较; 采用 Logistic 回归分析影响 OEM 患者预后的影响因素; 血清 APRIL 与 NDRG1 表达的相关性采用 Pearson 相关分析; ROC 曲线分析血清 APRIL, NDRG1 以及二者联合对 OEM 的诊断效能, 并利用约登指数分析灵敏度及特异度。以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 观察组与对照组血清 APRIL, NDRG1 水平比较 与对照组比较, 观察组血清 APRIL ($35.28 \pm 6.81\text{ng/ml}$ vs $26.37 \pm 3.19\text{ng/ml}$), NDRG1 水平 ($124.39 \pm 15.67\mu\text{g/L}$ vs $89.67 \pm 10.82\mu\text{g/L}$) 均显著升高, 差异具有统计学意义 ($t=10.864, 17.278$, 均 $P<0.001$)。

2.2 复发组与未复发组一般资料比较 见表 1。复发组患者的年龄、囊肿位置、囊肿最大径、体质量指数与未复发组比较, 差异均无统计学意义 (均 $P>0.05$), 但复发组中痛经、生育史患者所占比例以及血清 APRIL, NDRG1 水平与未复发组比较, 差异具有统计学意义 (均 $P<0.05$)。

2.3 Logistic 回归分析卵巢子宫内膜异位囊肿预后的影响因素 见表 2。以 OEM 患者预后情况为因变量 (未复发=0, 复发=1), 以是否痛经 (否=0,

是=1)、是否有生育史(否=0,是=1)、血清 APRIL 水平(实测值),血清 NDRG1 水平(实测值)为自变量进行 Logistic 回归分析,结果表明血清

APRIL (OR=1.687, 95%CI: 1.252~2.272), NDRG1 (OR=2.385, 95%CI: 1.732~2.283) 是 OEM 预后的危险因素 (Wald χ^2 =11.839, 28.437, 均 $P < 0.001$)。

表 1 复发组与未复发组一般资料比较 [$n(\%)$, ($\bar{x} \pm s$)]

类别	n	复发组 ($n=50$)	未复发组 ($n=82$)	t/χ^2	P
年龄 (岁)					
< 30	56	22 (39.29)	34 (60.71)	0.082	0.775
≥ 30	76	28 (36.84)	48 (63.16)		
痛经					
有	72	21 (29.17)	51 (70.83)	5.109	0.024
无	60	29 (48.33)	31 (51.67)		
生育史					
有	79	36 (45.57)	43 (54.43)	4.946	0.026
无	53	14 (26.42)	39 (73.58)		
囊肿位置					
单侧	70	30 (42.86)	40 (57.14)	1.570	0.210
双侧	62	20 (32.26)	42 (67.74)		
囊肿最大径 (cm)					
< 3	68	24 (35.29)	44 (64.71)	0.398	0.528
≥ 3	64	26 (40.63)	38 (59.38)		
体质量指数 (kg/m^2)		22.49 \pm 3.29	23.16 \pm 3.57	1.077	0.283
APRIL (ng/ml)		40.38 \pm 7.88	32.16 \pm 6.18	6.668	0.001
NDRG1 ($\mu\text{g}/\text{L}$)		132.04 \pm 19.83	119.73 \pm 13.16	4.287	0.001

表 2 Logistic 回归分析卵巢子宫内膜异位囊肿预后的影响因素

因素	β	SE	Wald χ^2	P	OR	95%CI
痛经	0.281	0.231	1.484	0.223	1.325	0.843 ~ 2.084
生育史	0.063	0.216	0.085	0.771	1.065	0.697 ~ 1.626
APRIL	0.523	0.152	11.839	< 0.001	1.687	1.252 ~ 2.272
NDRG1	0.869	0.163	28.437	< 0.001	2.385	1.732 ~ 2.283

2.4 卵巢子宫内膜异位囊肿患者血清 APRIL 与 NDRG1 水平相关性 Pearson 相关性分析显示, OEM 患者血清 APRIL 与 NDRG1 表达水平呈显著正相关 ($r=0.439$, $P<0.001$)。

2.5 血清 APRIL, NDRG1 对卵巢子宫内膜异位囊肿患者的诊断价值 见图 1。ROC 曲线结果显示, 血清 APRIL 诊断 OEM 发生的 ROC 曲线下面积 (area under the curve, AUC) 为 0.738 (95%CI: 0.655~0.811), 灵敏度和特异度分别为 74.00%, 69.51%, 截断值为 35.40ng/ml; APRIL 诊断 OEM 发生的 AUC 为 0.747 (95%CI: 0.664~0.819), 灵敏度和特异度分别为 70.00%, 80.49%, 截断值为 130.95 $\mu\text{g}/\text{L}$; 两者联合检测的 AUC 为 0.849 (95%CI: 0.776~0.905), 灵敏度和特异度分别为 73.95%, 85.37%。

3 讨论

子宫内膜异位囊肿 (OEM) 指子宫内膜组织出现在子宫体以外的部位, 随着月经周期的变化呈现反复性出血。它会使卵巢皮层或髓质层发生病理性的改变, 从而加重盆腔粘连的严重程度, 甚至造成卵巢形态的丧失^[10-12]。OEM 发病原因复杂, 随着当代女性生活、工作压力的不断加剧, OEM 的发病率呈现不断上升的趋势^[13]。OEM 虽然是良性

疾病, 却具有类似恶性肿瘤的特征, 且 OEM 会降低生育能力, 术后复发风险大^[14]。因此深入研究 OEM 的发病机制, 寻找能够评估 OEM 的生物标志物具有重要意义^[15-16]。

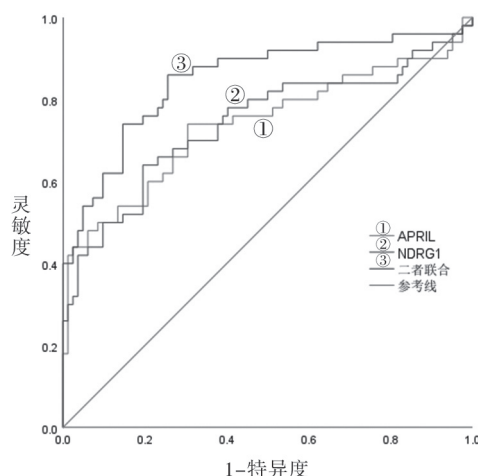


图 1 血清 APRIL, NDRG1 表达水平对卵巢子宫内膜异位囊肿患者的 ROC 曲线

增殖诱导配体 (APRIL) 作为肿瘤坏死因子超家族的成员与免疫疾病的发生、发展密切相关, APRIL 属于 II 型跨膜蛋白的一种, 会诱导肿瘤细胞的存活和增殖, 促进肿瘤细胞生长相关因子。研究发现 APRIL 是肿瘤坏死因子 (tumor necrosis factor,

TNF)超家族的成员之一,在多种肿瘤器官组织中异常表达^[5]。APRIL在多种恶性肿瘤中呈现高表达趋势,在正常组织中呈现低表达或者不表达的状态,FOULADSERESHT等^[17]报道,APRIL在脑膜瘤患者血清中呈现高表达状态;潘超等^[6]发现APRIL蛋白的表达可能与胃癌的发生、发展有关。本研究中,APRIL在观察组血清中表达水平显著高于对照组,提示APRIL可能与OEM的发生有关。未复发组患者血清APRIL表达水平显著低于复发组,且结合Logistic回归分析结果显示,血清APRIL是OEM预后的危险因素,提示APRIL与OEM的预后有关。其可能原因为APRIL作为一种细胞因子,需要与靶细胞受体结合发挥生物学作用,APRIL可能参与了与细胞增殖相关的信号通路的表达,从而促进OEM疾病的进展^[18]。NDRG1蛋白一般在上皮组织中表达,与细胞增殖以及细胞分化有关,当受到相关因素干扰时,会诱导其表达。已有研究报道NDRG1与肿瘤的发生发展密切相关,在多种肿瘤组织中发现NDRG1的表达发生改变,提出NDRG1可能成为肿瘤诊断以及肿瘤治疗的潜在靶点^[19-20]。本研究中,NDRG1在OEM患者血清中表达水平显著高于健康人群,提示NDRG1可能参与OEM疾病的发生;未复发组患者血清NDRG1表达水平显著低于复发组,且结合Logistic回归分析结果显示,血清NDRG1是OEM预后的危险因素,提示NDRG1水平有助于判断OEM患者预后情况。目前OEM的病因和发病机制并不十分清楚,研究报道,OEM患者分期越高其术后复发的可能性越大^[21]。本研究发现,OEM患者血清APRIL表达水平与NDRG1水平呈正相关,表明二者可能通过某些正向调控关系共同参与OEM的发生发展过程,但具体机制需要后续更深一步的研究。血清APRIL,NDRG1水平单独以及二者联合检测对OEM诊断具有临床价值,联合诊断价值更高,提示可以通过检测血清APRIL,NDRG1表达水平对OEM进行诊断,APRIL,NDRG1可以作为诊断OEM的血清标志物。

综上所述,血清APRIL,NDRG1在OEM患者中表达升高,二者联合检测诊断OEM有较高的临床价值,且二者与患者的预后密切相关,可以为患者的病情程度和预后情况提供参考。但本研究仍有不足之处,未深入探讨APRIL,NDRG1与OEM病理机制的关系,以及样本量有限,针对这些不足,后续会进一步加深研究。

参考文献:

[1] 中国医师协会妇产科医师分会,中华医学会儿科学分会妇产科学分会子宫内膜异位症协作组.子宫内膜异位症诊治指南(第三版)[J].中华妇产科杂志,2021,

56(12): 812-824.

- Chinese Obstetricians and Gynecologists Association, Cooperative Group of Endometriosis, Chinese Society of Obstetrics and Gynecology, Chinese Medical Association. Guideline for the diagnosis and treatment of endometriosis (Third edition)[J]. Chinese Journal of Obstetrics and Gynecology, 2021, 56(12): 812-824.
- [2] 冷金花,戴毅,李晓燕.子宫内膜异位症诊治新理念[J].中华妇产科杂志,2021,56(12): 831-835.
- LENG Jinhua, DAI Yi, LI Xiaoyan. New concept of diagnosis and treatment of endometriosis[J]. Chinese Journal of Obstetrics and Gynecology, 2021, 56(12): 831-835.
- [3] 舒丹,乔英琴,彭燕,等.卵巢子宫内膜异位囊肿治疗方式对卵巢功能及妊娠结局的影响[J].中国计划生育学杂志,2020,28(4): 561-565.
- SHU Dan, QIAO Yingqin, PENG Yan, et al. Influence of different treatment of ovarian endometriosis cyst on ovarian function and pregnancy outcomes[J]. Chinese Journal of Family Planning, 2020, 28(4): 561-565.
- [4] 薛乃瑞,李绪清,黄苗苗,等.卵巢子宫内膜异位囊肿剥除术对冻胚移植结局的影响[J].安徽医科大学学报,2019,54(5): 821-825.
- XUE Nairui, LI Xuqing, HUANG Miaomiao, et al. Effect of ovarian endometriosis cystectomy on the outcome of frozen embryo transplantation[J]. Acta Universitatis Medicinalis Anhui, 2019, 54(5): 821-825.
- [5] MAGLIOZZI R, MARASTONI D, CALABRESE M. The BAFF / April system as therapeutic target in multiple sclerosis[J]. Expert Opinion on Therapeutic Targets, 2020, 24(11): 1135-1145.
- [6] 潘超,冯永恒,朱宇,等.APRIL及PGR检测指标在胃炎、胃癌中的诊断价值分析[J].胃肠病学和肝病杂志,2019,28(6): 606-609.
- PAN Chao, FENG Yongheng, ZHU Yu, et al. Analysis of the diagnostic value of APRIL and PGR in gastritis and gastric cancer[J]. Chinese Journal of Gastroenterology and Hepatology, 2019, 28(6): 606-609.
- [7] AIKEMU B, SHAO Yanfei, YANG Guang, et al. NDRG1 regulates filopodia-induced colorectal cancer invasiveness via modulating CDC42 activity[J]. International Journal of Biological Sciences, 2021, 17(7): 1716-1730.
- [8] 荆羽萌,赵海潮,白丽娜,等.NDRG1通过上皮-间充质转化与子宫内膜样癌MELF浸润模式的相关研究[J].医学综述,2020,26(3): 491-497.
- JING Yumeng, ZHAO Haichao, BAI Lina, et al. Study on the relationship between the invasion pattern of the MELF and the transformation of NDRG1 through epithelial-mesenchymal[J]. Medical Recapitulate, 2020, 26(3): 491-497.
- [9] 中华医学会妇产科学分会子宫内膜异位症协作组.子宫内膜异位症的诊治指南[J].中华妇产科杂志,2015,56(3): 161-169.
- Cooperative Group of Endometriosis, Chinese Society of Obstetrics and Gynecology, Chinese Medical Association. Guideline for the diagnosis and treatment of endometriosis[J]. Chinese Journal of Obstetrics and Gynecology, 2015, 56(3): 161-169.

- [10] 裘陆平, 朱卫平, 余飞成, 等. 多模态磁共振成像在卵巢子宫内膜异位囊肿诊断中的应用观察[J]. 中国妇幼保健, 2020, 35(1): 163-166.
QIU Luping, ZHU Weiping, YU Feicheng, et al. Application of multimodal magnetic resonance imaging in diagnosis of ovarian endometriosis cyst[J]. Maternal and Child Health Care of China, 2020, 35(1): 163-166.
- [11] 甘金裕, 褚伯良. 促性腺激素释放激素激动剂预处理对卵巢子宫内膜异位囊肿腹腔镜手术患者卵巢功能的影响[J]. 中国妇幼保健, 2020, 35(2): 243-245.
GAN Jinyu, CHU Bailiang. Effect of gonadotropin-releasing hormone agonist pretreatment on ovarian function of patients with ovarian endometriosis cyst laparoscopic surgery[J]. Maternal and Child Health Care of China, 2020, 35(2): 243-245.
- [12] 黄骊莉, 郭晶晶, 徐花, 等. 化瘀消癥汤保留灌肠术后辅助治疗中重度卵巢子宫内膜异位囊肿的临床观察[J]. 中国医师杂志, 2020, 22(9): 1407-1410.
HUANG Lili, GUO Jingjing, XU Hua, et al. Clinical observation of Huayu Xiaozheng decoction retention enema for the adjuvant treatment of moderate and severe ovarian endometrioma after surgery[J]. Journal of Chinese Physician, 2020, 22(9): 1407-1410.
- [13] 张汉涛, 何好超, 王国彪. 超声介入穿刺与腹腔镜手术治疗卵巢子宫内膜异位囊肿的效果比较[J]. 哈尔滨医药, 2020, 40(5): 424-426.
ZHANG Hantao, HE Haochao, WANG Guobiao. Comparison of the effects of ultrasound interventional puncture and laparoscopic surgery for ovarian endometriotic cyst[J]. Harbin Medical Journal, 2020, 40(5): 424-426.
- [14] OTTOLINA J, SCHIMBERNI M, MAKIEVA S, et al. Early-life factors, in-utero exposures and endometriosis risk: a meta-analysis[J]. Reproductive Biomedicine Online, 2020, 41(2): 279-289.
- [15] ANASTASIU C V, MOGA M A, ELENA NECULAU A, et al. Biomarkers for the noninvasive diagnosis of endometriosis: state of the art and future perspectives[J]. International Journal of Molecular Sciences, 2020, 21(5): 1750.
- [16] CAI Wei, YANG Jule, LIU Yini, et al. Association between phthalate metabolites and risk of endometriosis: a meta-analysis[J]. International Journal of Environmental Research and Public Health, 2019, 16(19): 3678.
- [17] FOULADSERESHT H, ZIAEE S M, ERFANI N, et al. Serum levels of APRIL increase in patients with glioma, meningioma and schwannoma[J]. Asian Pacific Journal of Cancer Prevention, 2019, 20(3): 751-756.
- [18] YANG Jia, ZHOU Jiaojiao, WANG Xin, et al. Risk factors for severe acute kidney injury among patients with rhabdomyolysis[J]. BMC Nephrology, 2020, 21(1): 498.
- [19] SKEDSMO F S, ESPENES A, TRANULIS M A, et al. Impaired NDRG1 functions in Schwann cells cause demyelinating neuropathy in a dog model of Charcot-Marie-Tooth type 4D[J]. Neuromuscular Disorders, 2021, 31(1): 56-68.
- [20] CHEKMAREV J, AZAD M G, RICHARDSON D R. The oncogenic signaling disruptor, NDRG1: molecular and cellular mechanisms of activity[J]. Cells, 2021, 10(9): 2382.
- [21] 张璇, 赵爱琴, 邹丹, 等. 子宫内膜异位症患者血清 miR-455 和 FABP4 表达水平及临床意义[J]. 现代检验医学杂志, 2022, 37(4): 49-52, 158.
ZHANG Xuan, ZHAO Aiqin, ZOU Dan, et al. Expression level and clinical significance of serum miR-455 and FABP4 in patients with endometriosis[J]. Journal of Modern Laboratory Medicine, 2022, 37(4): 49-52, 158.

收稿日期: 2023-08-17

修回日期: 2023-11-13

(上接第22页)

- [13] ZHU Yingping, XU Leilai, MA Weirong, et al. Research on radiosensitivity of the protein kinase B signaling pathway in cervical cancer[J]. Computational and Mathematical Methods in Medicine, 2021, 2021: 6350038.
- [14] MIAO Zhifeng, SUN Jingxu, ADKINS-THREATS M, et al. DDIT4 licenses only healthy cells to proliferate during injury-induced metaplasia[J]. Gastroenterology, 2021, 160(1): 260-271, e10.
- [15] NAKI M, GOURDOMICHALI O, ZONKE K, et al. APEX2-mediated proximity labeling resolves the DDIT4-interacting proteome[J]. International Journal of Molecular Sciences, 2022, 23(9): 5189.
- [16] DING Fadian, HONG Xiaoping, FAN Xiangqun, et al. DDIT4 novel mutations in pancreatic cancer[J]. Gastroenterology Research and Practice, 2021, 2021: 6674404.
- [17] HU Tao, WANG Fengmiao, HAN Guanghui. LncRNA PSMB8-AS1 acts as ceRNA of miR-22-3p to regulate DDIT4 expression in glioblastoma[J]. Neuroscience Letters, 2020, 728: 134896.
- [18] LÜ Xiaoqian, HU Yuting, WANG Lina, et al. DDIT4 mediates the proliferation-promotive effect of IL-34 in human monocytic leukemia cells[J]. Blood Sci, 2021, 3(2): 48-56.
- [19] ZHANG Chunyan, TANG Bingxiang, HU Jianping, et al. Neutrophils correlate with hypoxia microenvironment and promote progression of non-small-cell lung cancer[J]. Bioengineered, 2021, 12(1): 8872-8884.
- [20] FOLTYN M, LUGER A L, LORENZ N I, et al. The physiological mTOR complex 1 inhibitor DDIT4 mediates therapy resistance in glioblastoma[J]. British Journal of Cancer, 2019, 120(5): 481-487.
- [21] LI Wenyang, HU Sheng, TIAN Chunfang, et al. TRIP4 transcriptionally activates DDIT4 and subsequent mTOR signaling to promote glioma progression[J]. Free Radical Biology and Medicine, 2021, 177: 31-47.

收稿日期: 2023-07-15

修回日期: 2023-10-26