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## 目 次

### 临床研究

- 不明原因复发性自然流产患者分泌期子宫内膜  
树突状细胞数量分析 .....徐士儒 刘苏 李玉叶等 89  
子痫前期胎盘组织中尾型同源框基因 2 的  
表达及意义 .....孙曼 宋贵玉 郑欣等 96

### 实验研究

- 人胎盘间充质干细胞移植通过降低超氧化物歧化酶 1 和  
解耦联蛋白 -2 的表达提高卵巢功能 .....相丽 马会明 何艳桃等 101

### 流行病学研究

- 体外受精 - 胚胎移植女性患者心理韧性及  
其影响因素研究 .....马胜男 肖红 柳鸣等 109

### 循证医学

- 移植前宫腔灌注人绒毛膜促性腺激素对于体外受精 -  
胚胎移植妊娠结局影响的 Meta 分析 .....张乐 吴亮 于医萍等 115

### 临床报道

- 小泛素样修饰蛋白 1 和 P53 的表达与子宫  
平滑肌瘤发生的相关性研究 .....诸葛丽芳 周坚红 曲凡等 122  
高通量测序技术在复发性流产病因  
诊断中的应用 .....张影 向卉芬 徐祖滢等 127  
预防性子官动脉栓塞术用于胎盘前置状态的  
中期妊娠终止的回顾性分析 .....王彩燕 姚晓英 黄紫蓉 131  
长效高效可逆避孕方法在高危人工流产后的应用 .....汪莉 135

### 个案报道

- 染色体平衡易位伴不良孕史 3 例 .....朱海波 王科 张静等 139  
节育器膀胱内异位伴结石形成 1 例报道 .....裴芳利 黄爽 陈思达等 142

### 综 述

- 高孕激素状态下促排卵——一种新的促排卵方案 .....奚倩雯 匡延平 147  
人乳腺癌易感基因突变和卵巢储备  
下降的探讨 .....喻意 雷小云 王嘉宁等 152  
外源物暴露所致卵巢发育毒性相关  
发生机制的研究进展 .....倪媛 吕丰 邹文等 158  
复发性流产的免疫学因素研究进展 .....秦诗 高玉平 165  
父代饮食运动及应激通过精子中小非编码  
RNA 对子代表型的影响 .....孙婷也 吴铃 吕祁峰 170

《中华生殖与避孕杂志》第一届编委会成员名单 ..... 134

《中华生殖与避孕杂志》杂志稿约 ..... 封三

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## CONTENTS IN BRIEF

### Clinical Study

Quantitative analysis of uterine dendritic cells in secretory phase of women with unexplained recurrent spontaneous abortion..... 89

*Xu Shiru, Liu Su, Li Yuye, et al*

Expression and significance of caudal-related homeobox transcription factor 2 in placenta of patients with preeclampsia..... 96

*Sun Man, Song Guiyu, Zheng Xin, et al*

### Laboratory Study

Effects of human placenta mesenchymal stem cell transplantation on superoxide dismutase 1 and uncoupling protein-2 in the treatment of premature ovarian failure in rats..... 101

*Xiang Li, Ma Huiming, He Yantao, et al*

### Epidemiological Study

The resilience and its influencing factors in women undergoing *in vitro* fertilization-embryo transfer treatment..... 109

*Ma Shengnan, Xiao Hong, Liu Ming, et al*

### Evidence-based Medicine

Effect of intrauterine infusion of human chorionic gonadotropin before embryo transfer on pregnancy outcomes in *in vitro* fertilization: a Meta-analysis ..... 115

*Zhang Le, Wu Liang, Yu Yiping, et al*

### Clinical Report

Expression and clinical significance of small ubiquitin-like modifier-1 and P53 protein in uterine leiomyosarcoma ..... 122

*Zhuge Lifang, Zhou Jianhong, Qu Fan, et al*

Application of next generation sequencing in etiological diagnosis of recurrent spontaneous abortion ..... 127

*Zhang Ying, Xiang Huiifen, Xu Zuying, et al*

A retrospective analysis of prophylactic uterine arterial embolization for second-trimester pregnancy termination with placenta previa..... 131

*Wang Caiyan, Yao Xiaoying, Huang Zirong*

Application of long acting reversible contraceptive after induced abortion with high-risk factors..... 135

*Wang Li*

### Case Report

Three cases of chromosome balanced translocation associated with adverse pregnancy history..... 139

*Zhu Haibo, Wang Ke, Zhang Jing, et al*

A case report of vesical calculus caused by an ectopic intrauterine device..... 142

*Pei Fangli, Huang Shuang, Chen Sida, et al*

### Review

Progesterin primed ovarian stimulation—a new stimulation regimens ..... 147

*Xi Qianwen, Kuang Yanping*

Breast cancer susceptibility gene mutations and decreased ovarian reserve... 152

*Yu Yi, Lei Xiaoyun, Wang Jianing, et al*

Research progress on the related mechanisms of ovary developmental toxicity caused by exposure to xenobiotics..... 158

*Ni Yuan, Lyu Feng, Zou Wen, et al*

Process in immune etiology of recurrent spontaneous abortion ..... 165

*Qin Shi, Gao Yuping*

The hereditary impaction of paternal diet, exercise and stress on filial generation through small non-coding RNAs in the sperm..... 170

*Sun Tingye, Wu Ling, Lyu Qifeng*

# 不明原因复发性自然流产患者分泌期子宫内膜树突状细胞数量分析

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**【摘要】** 目的 研究子宫内膜树突状细胞(DC)在不明原因复发性自然流产(uRSA)患者分泌期子宫内膜的表达情况。方法 根据子宫内膜形态学 Noyes 标准, 对在本中心就诊的 uRSA 患者(uRSA 组,  $n=113$ )与男性因素不孕患者(对照组,  $n=35$ )进行子宫内膜分期; 以 CD1a 与 CD83 分别作为子宫内膜未成熟树突状细胞(iDC)与成熟树突状细胞(mDC)的表面标志物, 并利用免疫组织化学技术检测患者分泌期子宫内膜 CD1a 与 CD83 阳性细胞的数量, 并通过 Vectra<sup>®</sup> 自动病理成像定量分析系统分别计算其阳性细胞率。结果 uRSA 组分泌期子宫内膜 CD1a 阳性细胞率无明显变化, 而 CD83 阳性细胞率  $[(2.03 \pm 1.60)\%]$  显著高于对照组  $[(0.81 \pm 1.11)\%, P=0.000]$ ; 两组患者子宫内膜 CD1a 阳性细胞率从分泌早期到中期均呈递减趋势, 而 CD83 阳性细胞率从分泌早期到中期均呈递增趋势; 与对照组相比, uRSA 组子宫内膜 CD1a 阳性细胞率在分泌早期和中期均无明显变化, 而 uRSA 组子宫内膜 CD83 阳性细胞率在分泌早期  $[(1.64 \pm 1.20)\%]$  和中期  $[(2.20 \pm 1.60)\%]$  均显著高于对照组  $[(0.17 \pm 0.11)\%, P=0.000; (0.63 \pm 0.78)\%, P=0.000]$ 。结论 uRSA 组患者子宫内膜分泌早期和中期 CD83 阳性细胞率异常升高, 提示其可能影响子宫内膜容受性, 从而导致妊娠失败。

**【关键词】** 不明原因复发性自然流产(uRSA); 子宫内膜树突状细胞(uDC); CD1a; CD83

**基金项目:** 深圳市科技计划项目(JCYJ20170307140647669); 深圳市卫生计生系统科研项目(201606063)

**Quantitative analysis of uterine dendritic cells in secretory phase of women with unexplained recurrent spontaneous abortion** Xu Shiru, Liu Su, Li Yuye, Chen Cong, Lin Jiayin, Zeng Yong

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**【Abstract】 Objective** To explore the uterine dendritic cell (uDC) levels in the secretory phase of patients with unexplained recurrent spontaneous abortion (uRSA). **Methods** The expression of CD1a and CD83 in the endometrium of women with uRSA (113 cases) and infertility women with male factors (35 cases) were detected by immunohistochemical staining technique. The percentages of CD1a<sup>+</sup> and CD83<sup>+</sup> cells were measured by Vestra® automatic pathological imaging quantitative analysis system. **Results** There was no significant difference in the proportion of CD1a<sup>+</sup> cells in the secretory phase of patients with uRSA and control group. However, the percentage of CD83<sup>+</sup> cells in the secretory phase of patients with uRSA [(2.03±1.60)%] was significantly higher than that in control group [(0.81±1.11)%,  $P=0.000$ ]. In addition, the percentages of CD83<sup>+</sup> cells during early- [(1.64±1.20)%] and mid-secretory phase [(2.20±1.60)%] from uRSA group were significantly higher than those in control group [(0.17±0.11)%,  $P=0.000$ ; (0.63±0.78)%,  $P=0.000$ , respectively]. The percentage of CD1a<sup>+</sup> cells was gradually decreased through the early- and mid-secretory phase in both groups, while the percentage of CD83<sup>+</sup> cells was gradually increased. **Conclusion** The abnormal elevation of uterine CD83<sup>+</sup> cells in early- and mid-secretory phase of patients with uRSA may affect the endometrial receptivity, which may lead to pregnancy failure.

**【Key words】** Unexplained recurrent spontaneous abortion (uRSA); Uterine dendritic cell (uDC); CD1a; CD83

**Fund program:** Basic Research Program of Shenzhen (JCYJ20170307140647669); The Science and Technology Project of Health and Family Planning Commission of Shenzhen Municipality (201606063)

# 子痫前期胎盘组织中尾型同源框基因 2 的表达及意义

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**【摘要】**目的 研究子痫前期 (preeclampsia, PE) 患者胎盘组织中尾型同源框基因 2(CDX2) 表达与早孕绒毛和正常足月妊娠者之间的差异及其临床意义。方法 选取 2015 年 9 月—2016 年 4 月期间于本院分娩的 PE 孕妇 30 例, 选择同期早孕妊娠孕妇 30 例和正常足月妊娠妇女 30 例。采用 Real-time PCR 方法检测患者的胎盘组织 CDX2 mRNA 的表达, Western blotting 及免疫组织化学方法检测胎盘组织中蛋白的表达及蛋白定位。结果 ① RT-PCR 技术显示, PE 患者胎盘组织中 CDX2 mRNA 的表达水平 ( $0.385 \pm 0.065$ ) 低于早孕妊娠 ( $1.880 \pm 0.235$ ) 和正常足月妊娠组 ( $1.015 \pm 0.184$ ), 差异有统计学意义 ( $P < 0.05$ )。② Western blotting 显示, PE 患者胎盘组织中 CDX2 蛋白表达水平 ( $0.276 \pm 0.029$ ) 显著低于早孕妊娠组 ( $0.658 \pm 0.059$ ) 和正常足月妊娠组 ( $0.478 \pm 0.136$ ), 差异有统计学意义 ( $P < 0.05$ )。③ 免疫组织化学 SP 法显示, 正常早孕妊娠、正常妊娠者胎盘和 PE 胎盘组织均有 CDX2 表达, 主要表达在合体滋养细胞细胞质中, 在 PE 中 CDX2 表达明显降低。结论 CDX2 下调可能参与 PE 的发病, 提示其可能参与了滋养细胞的增殖、浸润和胎盘形成。

**【关键词】**尾型同源框基因 2(CDX2); 胎盘; 滋养细胞; 子痫前期 (PE)

**基金项目:** 辽宁省自然科学基金项目资助 (2011225017); 国家自然科学基金面上项目资助 (81370735)

**Expression and significance of caudal-related homeobox transcription factor 2 in placenta of patients with preeclampsia** Sun Man, Song Guiyu, Zheng Xin, Yang Yun, Qiao Chong

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**【Abstract】 Objective** To investigate the expression of caudal-related homeobox transcription factor 2 (*CDX2*) and its role in placenta of patients with preeclampsia (PE). **Methods** Thirty cases of PE women who delivered in our hospital from September 2015 to April 2016 were recruited. Thirty cases of the first trimester and 30 cases of full-term birth women at the same period were also recruited. Reverse transcription (RT)-PCR was used to detect the expression of *CDX2* mRNA in placenta. Western blotting was used to detect the expression of CDX2 protein in placenta. Immunohistochemistry SP method was applied to detect the expression and the location of CDX2 in placenta. **Results** ① RT-PCR showed that the *CDX2* mRNA expression was significantly lower in PE ( $0.385 \pm 0.065$ ) than that in the first trimester ( $1.880 \pm 0.235$ ) and full-term birth ( $1.015 \pm 0.184$ ) women groups. There was a significant difference ( $P < 0.05$ ). ② Western blotting showed that the CDX2 protein expression was significantly lower in the placenta of PE ( $0.276 \pm 0.029$ ) than in the first trimester ( $0.658 \pm 0.059$ ) and full-term birth women ( $0.478 \pm 0.136$ ) ( $P < 0.05$ ). ③ Immunohistochemical detection showed that the CDX2 protein was expressed in the placentas of full-term birth women and PE women of the first trimester. The expression of CDX2 in placenta mainly distributed in the cytoplasm of placental syncytiotrophoblasts. The expression of CDX2 was significantly decreased in PE group. **Conclusion** The down-regulation of CDX2 may be involved in the pathogenesis of PE, suggesting that it may be involved in trophoblast proliferation, invasion and placental formation.

**【Key words】** Caudal-related homeobox transcription factor 2 (*CDX2*); Placenta; Trophoblast; Preeclampsia (PE)

**Fund program:** Liaoning Provincial Natural Science Foundation (2011225017); National Natural Science Foundation of China (81370735)

# 人胎盘间充质干细胞移植通过降低超氧化物歧化酶 1 和解耦联蛋白 -2 的表达提高卵巢功能

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**【摘要】**目的 探讨人胎盘间充质干细胞(hPMSC)移植治疗对环磷酰胺所致卵巢早衰(POF)模型SD大鼠超氧化物歧化酶1(SOD1)和解耦联蛋白-2(UCP-2)表达的影响。方法 将60只雌性SD大鼠随机分为4组( $n=15$ ): 空白对照组, POF模型组, 治疗对照组, hPMSC移植组。以首计量50 mg/kg、维持剂量8 mg/kg连续14 d给大鼠腹腔注射环磷酰胺溶液建立POF模型, 观察大鼠动情周期变化, 采用ELISA方法测定血清中雌二醇( $E_2$ )、促卵泡生成素(FSH)、抗苗勒氏管激素(AMH)、活性氧族(ROS)、8-羟基脱氧鸟苷(8-OHdG)水平; HE染色方法检测卵巢组织形态学及卵泡计数, VG染色法观察卵巢组织纤维化情况; 采用免疫组织化学和Western blotting法测定SOD1和UCP-2蛋白表达。结果 ELISA结果显示: 模型组血清FSH水平 $[(10.60 \pm 1.0) \text{ IU/L}]$ 明显高于空白对照组 $[(5.83 \pm 0.92) \text{ IU/L}]$ ( $P < 0.01$ ), 而 $E_2$ 、AMH水平 $[(35.52 \pm 10.27) \text{ ng/L}]$ 、 $[(2\ 090.6 \pm 397.5) \text{ ng/L}]$ 则明显低于空白对照组 $[(65.62 \pm 3.76) \text{ ng/L}]$ 、 $[(3\ 636.39 \pm 204.46) \text{ ng/L}]$ , 差异有统计学意义( $P < 0.01$ )。与空白对照组相比hPMSC移植组血清中ROS和8-OHdG升高( $P < 0.05$ )。卵泡计数显示hPMSC移植组闭锁卵泡数 $(5.36 \pm 1.11)$ 显著低于治疗对照组 $(8.01 \pm 2.22)$ 和POF模型组 $(11.21 \pm 1.69)$ ( $P < 0.05$ )。与治疗对照组相比, hPMSC移植组中ROS和8-OHdG显著下降( $P < 0.05$ )。VG染色显示, 与治疗对照组比, hPMSC移植组纤维化面积比例显著降低( $P < 0.05$ )。Western blotting结果显示, 与治疗对照组相比, hPMSC移植组中SOD1和UCP-2蛋白表达量显著下降( $P < 0.05$ ), 而hPMSC移植组与对照组则差异无统计学意义( $P > 0.05$ ); 免疫组织化学结果显示模型组中SOD1和UCP-2蛋白表达相较于治疗对照组是降低的, 而hPMSC移植组相较于空白对照组则差异无统计学意义。结论 hPMSC移植改善POF模型SD大鼠氧化应激, 降低SOD1及UCP-2表达, 起到保护卵巢线粒体功能的作用。

**【关键词】**人胎盘间充质干细胞(hPMSC); 超氧化物歧化酶1(SOD1)/解耦联蛋白-2(UCP-2)表达; 卵巢早衰(POF); 大鼠

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**Effects of human placenta mesenchymal stem cell transplantation on superoxide dismutase 1 and uncoupling protein-2 in the treatment of premature ovarian failure in rats**

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**【Abstract】 Objective** To investigate the effects of human placenta mesenchymal stem cell (hPMSC) transplantation on superoxide dismutase 1 (SOD1) and uncoupling protein-2 (UCP-2) in the treatment of premature ovarian failure in rats. **Methods** Sixty SD female rats with normal estrous cycle were randomly divided into four groups ( $n=15$ ): blank control group, POF model group, treatment control group, and hPMSC transplantation group. It was determined the ROS levels and 8-OHdG of serum by ELISA method. The ovarian tissue fibrosis was detected by VG staining method; The expression of SOD1 and UCP-2 protein was detected by Western blotting and immunohistochemical staining. **Results** Serum FSH level in the model group [ $(10.60 \pm 1.0)$  IU/L] was significantly higher than that in blank control group [ $(5.83 \pm 0.92)$  IU/L] ( $P < 0.01$ ), while  $E_2$  and AMH levels in the model group [ $(35.52 \pm 10.27)$  ng/L,  $(2\ 090.6 \pm 397.5)$  ng/L] were significantly lower than those in blank control group [ $(65.62 \pm 3.76)$  ng/L,  $(3\ 636.39 \pm 204.46)$  ng/L] ( $P < 0.01$ ). The count of the atretic follicle in hPMSC transplantation group ( $5.36 \pm 1.11$ ) was lower than that in treatment control group ( $8.01 \pm 2.22$ ) and POF model group ( $11.21 \pm 1.69$ ) ( $P < 0.05$ ). Compared with the blank control group, the serum ROS was increased in the model group and the treatment control group ( $P < 0.05$ ); compared with the treatment control group, there was a significant change in ROS and 8-OHdG in the hPMSC transplantation group ( $P < 0.05$ ). VG staining showed that the ovarian tissue fibrosis in the model group was obvious, and after hPMSC transplantation there was a significant reduction compared with that in the treatment control group. The expression of SOD1 and UCP-2 protein has a statistical decrease in the hPMSC transplantation group compared with the treatment control group ( $P < 0.05$ ). **Conclusion** hPMSC transplantation may regulate the mitochondrial ROS synthesis and decrease oxidative stress by decreasing the expression of SOD1 and UCP-2 in rats.

**【Key words】** Human placenta mesenchymal stem cell (hPMSC); Premature ovarian failure (POF); Superoxide dismutase 1 (SOD1)/uncoupling protein 2 (UCP-2); Rats

**Fund program:** National Natural Science Foundation of China (81360095)



# 体外受精 - 胚胎移植女性患者心理韧性及其影响因素研究

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**【摘要】** 目的 探讨接受体外受精 / 卵胞质内单精子注射 - 胚胎移植 (*in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer, IVF/ICSI-ET) 女性患者影响心理韧性的因素。方法 采用一般资料调查表、心理韧性量表、一般自我效能感量表、简易应对方式量表、领悟社会支持量表对进行 IVF/ICSI-ET 的 189 例女性患者进行问卷调查。结果 IVF/ICSI-ET 女性患者的心理韧性总分为  $(61.4 \pm 11.7)$  分, 显著低于国内普通人群 [ $(65.4 \pm 13.9)$  分] ( $P < 0.05$ ), 一般自我效能、积极应对方式、家庭内支持状况、文化程度、不孕类型、治疗周期数及不孕原因是心理韧性的主要影响因素, 共同解释了 IVF/ICSI-ET 女性患者心理韧性 63.00% 的变异。结论 IVF/ICSI-ET 女性患者心理韧性总体水平较差, 医护人员应采取针对性的心理干预措施来提高其心理韧性, 改善其心理健康状况, 提高治疗效果。

**【关键词】** 体外受精 / 卵胞质内单精子注射 - 胚胎移植 (IVF/ICSI-ET); 心理韧性; 影响因素

**The resilience and its influencing factors in women undergoing *in vitro* fertilization-embryo transfer**

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**【Abstract】 Objective** To investigate the resilience and influencing factors in women undergoing *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) treatment. **Methods** A total of 189 women who undergoing IVF/ICSI-ET were asked to independently complete some questionnaires, including Connor-Davidson Resilience Scale, General Self-Efficacy Scale, Simplified Coping Style Questionnaire, Perceived Social Support Scale and a questionnaire about demographics. **Results** The average score of resilience was  $(61.4 \pm 11.7)$ , significantly lower than the general population  $(65.4 \pm 13.9)$  ( $P < 0.05$ ). Multiple stepwise regression analysis indicated that the self-efficacy, positive coping style, family support, education level, type of infertility, treatment cycles and the causes of infertility significantly affected resilience and explained variance of 63.00%. **Conclusion** Women undergoing IVF/ICSI-ET treatment demonstrated particularly low resilience level. Clinicians should take corresponding measures to improve their resilience, then improve their mental state and treatment outcomes.

**【Key words】** *In vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET); Resilience; Influencing factors

# 移植前宫腔灌注人绒毛膜促性腺激素对于体外受精 - 胚胎移植妊娠结局影响的 Meta 分析

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**【摘要】** 目的 评价移植前宫腔灌注人绒毛膜促性腺激素 (hCG) 是否能影响体外受精 - 胚胎移植 (IVF-ET) 患者的妊娠结局。方法 计算机检索 PubMed、EMBase、ISI Web of Science、Cochrane Library、中国知网全文数据库 (CNKI)、中国生物医学文献数据库 (CBM)、万方和维普等数据库, 查找关于宫腔灌注 hCG 对于妊娠结局的影响的研究, 检索年限自建库至 2017 年 7 月, 对检索到的文献按照纳入和排除标准进行筛选、质量评价和数据提取, 采用 RevMan5.3 软件进行数据分析。结果 共纳入符合要求的 12 个随机对照研究, 灌注组与对照组相比, 临床妊娠率 ( $OR=1.24$ , 95%  $CI=1.08\sim 1.43$ ) 和种植率 ( $OR=1.21$ , 95%  $CI=1.00\sim 1.46$ ) 组间差异有统计学意义, 活产率 ( $OR=1.05$ , 95%  $CI=0.81\sim 1.36$ ) 和流产率 ( $OR=1.02$ , 95%  $CI=0.78\sim 1.34$ ) 组间差异有统计学意义。其中移植卵裂期胚胎的患者, 移植前宫腔灌注  $\geq 500$  IU 的 hCG, 与对照组相比, 种植率 ( $OR=1.61$ , 95%  $CI=1.32\sim 1.97$ )、临床妊娠率 ( $OR=1.46$ , 95%  $CI=1.26\sim 1.70$ ) 和活产率 ( $OR=1.52$ , 95%  $CI=1.27\sim 1.84$ ) 差异具有统计学意义。结论 移植前宫腔灌注 hCG 能够改善不孕症患者胚胎移植的妊娠结局。

**【关键词】** 人绒毛膜促性腺激素 (hCG); 宫腔灌注; 胚胎移植; 妊娠结局; Meta 分析

**Effect of intrauterine infusion of human chorionic gonadotropin before embryo transfer on pregnancy outcomes in *in vitro* fertilization: a Meta-analysis**

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**【Abstract】 Objective** To determine whether intrauterine human chorionic gonadotropin (hCG) infusion before embryo transfer impacts the *in vitro* fertilization-embryo transfer (IVF-ET) pregnancy outcomes. **Methods** Databases included PubMed, EMBase, ISI Web of Science Cochrane Library, CNKI, Wanfang and VIP were searched for the study of the effect of hCG on pregnancy outcome. The retrieval period was from the date of database construction to July 2017. The literature screening according to the inclusion and exclusion criteria, followed by quality evaluation and data extraction. The RevMan 5.3.5 software was used for data analysis. **Results** Twelve randomized controlled trials were analyzed. The results showed that there was a significant increase in clinical pregnancy rates ( $OR=1.24$ , 95%  $CI=1.08-1.43$ ) and implantation rate ( $OR=1.21$ , 95%  $CI=1.00-1.46$ ) in intrauterine hCG group compared with control group, but no significant difference in live birth rate ( $OR=1.05$ , 95%  $CI=0.81-1.36$ ) and abortion rate ( $OR=1.02$ , 95%  $CI=0.78-1.34$ ). Subgroup analysis showed that, for the patients who received the intrauterine hCG  $\geq 500$  IU before cleavage stage embryo transfer, the implantation rate ( $OR=1.61$ , 95%  $CI=1.32-1.97$ ), the clinical pregnancy rates ( $OR=1.46$ , 95%  $CI=1.26-1.70$ ) and the live birth rate ( $OR=1.52$ , 95%  $CI=1.27-1.84$ ) were greater than those in controls. **Conclusion** The intrauterine perfusion of hCG can improve pregnancy outcomes of patients with embryo transfer.

**【Key words】** Human chorionic gonadotropin (hCG); Intrauterine infusion; Embryo transfer; Pregnancy outcomes; Meta analysis

## 小泛素样修饰蛋白 1 和 P53 的表达与子宫平滑肌肉瘤发生的相关性研究

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**【摘要】** 目的 了解小泛素样修饰蛋白(SUMO)-1、P53 蛋白在子宫平滑肌肉瘤中的表达及其临床意义。方法 收集 2006 年 3 月—2012 年 3 月期间接受手术治疗的 20 例子宫平滑肌肉瘤, 29 例良性子宫平滑肌瘤, 采用免疫组织化学 Envision 法检测各组织中 SUMO-1 和 P53 蛋白的表达, 对收集的 20 例子宫平滑肌肉瘤患者进行电话随访预后情况。结果 SUMO-1、P53 在子宫平滑肌肉瘤组中阳性表达率分别为 85%、30%; 在子宫平滑肌瘤组中阳性表达率分别为 52% 和 0%; 子宫平滑肌肉瘤组中的 SUMO-1 阳性表达率明显高于子宫平滑肌瘤组 ( $P<0.01$ ); 子宫平滑肌瘤组中的 P53 阳性表达率明显高于子宫平滑肌肉瘤组 ( $P<0.01$ ); 子宫平滑肌瘤中 SUMO-1 与 P53 蛋白表达无明显相关性; SUMO-1、P53 蛋白的表达分别与子宫平滑肌瘤预后均无相关性 ( $P>0.05$ )。结论 P53 可能与子宫平滑肌肉瘤的发生机制相关, 并对子宫平滑肌瘤与子宫平滑肌肉瘤有一定的鉴别诊断价值; SUMO-1 可能与子宫平滑肌肉瘤的发生密切相关。

**【关键词】** 小泛素样修饰蛋白(SUMO)-1; P53; 子宫平滑肌瘤; 子宫平滑肌肉瘤; 免疫组织化学  
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**Expression and clinical significance of small ubiquitin-like modifier-1 and P53 protein in uterine leiomyosarcoma**

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**【Abstract】 Objective** To learn the expression and significance of small ubiquitin-like modifier (SUMO)-1 and P53 protein in uterine leiomyosarcoma. **Methods** From March 2006 to March 2012, 20 cases of uterine leiomyosarcoma and 29 cases of uterine leiomyoma were collected. Immunohistochemical Envision method was used to detecte the expression level of SUMO-1 and P53 in 49 cases with uterine sarcoma, and prognosis was followed up by telephone in 20 cases of uterine leiomyosarcoma. **Results** The positive expression rates of SUMO-1 and P53 in uterine leiomyosarcoma were 85% and 30%, respectively; the positive expression rates of SUMO-1 and P53 in uterine leiomyoma were 52% and 0%, respectively; the positive expression rate of SUMO-1 in uterine leiomyosarcoma was significantly higher than that in uterine leiomyoma ( $P<0.01$ ); the positive expression rate of P53 in uterine leiomyosarcoma was significantly higher than that in uterine leiomyoma ( $P<0.01$ ); the expressions of SUMO-1 and P53 protein in uterine leiomyosarcoma were not associated with prognosis ( $P>0.05$ ).

**Conclusion** P53 may be implicated in the pathogenesis of uterine leiomyosarcoma and is useful in differentiating uterine leiomyosarcoma from uterine leiomyoma. SUMO-1 could be closely related to the occurrence of uterine leiomyosarcoma.

**【Key words】** Small ubiquitin-like modifier (SUMO)-1; P53; Uterine leiomyoma; Uterine leiomyosarcoma; Immunohistochemistry

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## 高通量测序技术在复发性流产病因诊断中的应用

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**【摘要】** 目的 探讨高通量测序(next generation sequencing, NGS)技术对复发性流产(recurrent spontaneous abortion, RSA)患者流产绒毛组织进行全基因组拷贝数变异分析中的价值。方法 选取RSA患者252例,收集其流产绒毛组织,采用NGS技术对绒毛组织行全基因组拷贝数变异(copy number variants, CNVs)。结果 252例流产绒毛组织均成功获得检测结果,检测成功率为100%,共124例(49.21%)检测出拷贝数异常,其中整条染色体拷贝数增加或减少98例,嵌合体3例,部分染色体片断拷贝数增加或减少23例,包括微重复型10例,微缺失型4例,混合型9例,共包含微缺失/微重复片段33个。与CNV数据库比较,这33个片段中,共包含29个与早期流产、胚胎停育相关的致病性CNVs。结论 NGS技术可用于RSA绒毛组织的染色体拷贝数变异分析。该方法检测率高、分辨率高,尤其可以检测出亚显微结构的染色体异常,对RSA患者的遗传咨询及生育指导具有重要意义。

**【关键词】** 高通量测序(NGS); 复发性流产(RSA); 绒毛组织染色体; 拷贝数变异(CNVs)

**Application of next generation sequencing in etiological diagnosis of recurrent spontaneous abortion**

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**【Abstract】 Objective** To investigate the value of next generation sequencing (NGS) in chromosomal analysis of recurrent spontaneous abortion (RSA) villus, and to provide guidance for genetic counseling, clinical diagnosis and treatments of RSA. **Methods** A total of 252 patients with RSA were enrolled. The villi tissues were collected and the whole genome copy number variants (CNVs) was detected by NGS technique. **Results** All of 252 abortion villus were successfully analyzed. The success rate was 100%. Clinically significant chromosomal abnormalities were detected in 124 of the villus (49.21%, 124/252), which included 98 abnormal CNVs of the whole chromosome, 3 mosaicism and 23 partial anomalies. In structural anomalies, 10 villus were micro-duplication, 4 were micro-deletion and 9 were mixed. Compared with CNVs database, a total of 29 pathogenic CNVs associated with early abortion and embryo stop were found in 23 villi tissues with structural abnormal chromosomes. **Conclusion** NGS for chromosomal copy number variants analysis of recurrent miscarriages have a high detection rate and resolution, particularly can detect submicroscopic chromosomal abnormalities. It is important for genetic counseling and reproductive instruction in patients with RSA.

**【Key words】** Next generation sequencing (NGS); Recurrent spontaneous abortion (RSA); Chromosome analysis of villus; Copy number variants (CNVs)



· 临床报道 ·

## 预防性子宫动脉栓塞术用于胎盘前置状态的中期妊娠终止的回顾性分析

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**【摘要】** 目的 探讨终止胎盘前置状态中期妊娠前行预防性子宫动脉栓塞术的可行性。方法 回顾性分析 2011 年 1 月—2017 年 1 月期间于本院计划生育科住院的因胎盘前置状态或胎盘植入行预防性子宫动脉栓塞术终止中期妊娠 24 例患者资料。结果 24 例患者中 1 例子宫动脉栓塞术失败, 予以剖宫取胎术终止妊娠, 其余 23 例子宫动脉栓塞术成功, 成功率为 95.8%。6 例在预防性子宫动脉栓塞术后 1~3 d 内产生规律宫缩并娩出胎儿, 17 例患者应用了不同的引产方法终止妊娠。无严重不良反应发生。结论 预防性子宫动脉栓塞术用于终止胎盘前置状态的中期妊娠是有效、安全、可行的。

**【关键词】** 子宫动脉栓塞术; 胎盘前置状态; 终止中期妊娠

**A retrospective analysis of prophylactic uterine arterial embolization for second-trimester pregnancy termination with placenta previa** Wang Caiyan, Yao Xiaoying, Huang Zirong

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**【Abstract】 Objective** To investigate the feasibility of prophylactic uterine artery embolization for second-trimester pregnancy termination with placenta previa. **Methods** The cases of prophylactic uterine artery embolization for second-trimester pregnancy termination with placenta previa were retrospectively analyzed in our hospitals from January 2011 to January 2017. **Results** There were 24 patients of second-trimester pregnancy termination with placenta previa received prophylactic uterine artery embolization. One failed and underwent cesarean delivery. The others (95.8%) succeeded. Six patients delivered the fetal and placenta 1–3 d after uterine artery embolization. Totally 17 patients needed labor induction. No serious adverse event happened. **Conclusion** Prophylactic uterine arterial embolization for second-trimester pregnancy termination with placenta previa is effective, safe and feasible.

**【Key words】** Uterine arterial embolization; Placenta previa; Second-trimester pregnancy termination

## 长效高效可逆避孕方法在高危人工流产后的应用

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**【摘要】**目的 探讨高危人工流产后落实长效高效可逆避孕措施(long acting reversible contraception, LARC)是否能降低非意愿妊娠及重复流产。**方法** 对行人工流产的妇女中具有高危因素的妇女随访流产后第1、第3、第6个月LARC方法的使用情况和再次妊娠情况。**结果** 685例人工流产女性中,高危人工流产女性共372例(54.31%),其中年龄 $\leq 20$ 岁64例(17.20%),1年内 $\geq 2$ 次流产或半年内终止妊娠者共74例(19.89%), $\geq 3$ 次人工流产者213例(57.25%);带器妊娠7例(1.88%),哺乳期11例(2.96%),稽留流产3例(0.81%)。术后6个月随访结果显示:年龄 $\leq 20$ 岁者,术后立即落实LARC的女性半年内未发生重复人工流产,而术后未立即落实LARC的女性半年内的重复流产率为57.70%(15/26)。两者比较,差异有统计学意义( $P<0.05$ )。1年内 $>2$ 次流产或半年内终止妊娠者术后立即落实LARC方法的女性半年内重复流产率为8.33%(2/24),未立即落实者半年内重复流产率为43.33%(13/30),两者比较,差异有统计学意义( $P<0.05$ )。 $\geq 3$ 次人工流产者术后立即落实LARC者半年内重复人工流产率为1.82%(1/55),术后未立即落实者半年内重复人工流产率为26.14%(23/88),两者比较差异有统计学意义( $P<0.05$ )。**结论** 提高人工流产术后LARC立即落实率,能有效提高避孕措施的持续使用率,降低重复人工流产及非意愿妊娠的发生。

**【关键词】** 高危因素; 人工流产; 避孕; 长效高效可逆避孕(LARC)方法

**Application of long acting reversible contraceptive after induced abortion with high-risk factors** Wang Li  
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**【Abstract】 Objective** To investigate whether the use of long acting reversible contraception (LARC) post-abortion in the high-risk factors of induced abortion can reduce the unwanted pregnancy and repeat abortion after induced abortion with high risk factors. **Methods** The study collects women with high-risk factors of induced abortion. And these women were followed up for 3 times: 1 month post-abortion, 3-month post-abortion, 6-month post-abortion. These women responded about LARC use and whether pregnancy again. **Results** Among the 685 induced abortion, 372 (54.31%) were high-risks induced abortion, 64 (17.20%) were  $\leq 20$  years old, 74 (19.89%) underwent abortion more than twice in one year or terminate pregnancy in half a year, 213 (57.25%) underwent induced abortion more than three times, 7 (1.88%) were pregnant with IUD, 11 (2.96%) were in lactation, 3 (0.18%) had missed abortion. The 6-months follow-up results indicated that the women  $\leq 20$  years old, who immediately use LARC post-abortion did not have repeated abortion in half a year, who did not use LARC immediately had a repeated abortion rate of 57.70% (15/26), there was a significant difference between the two groups ( $P < 0.05$ ). The women terminate pregnancy in half a year or induced abortion more than 2 times in one year, who immediately use LARC post-abortion had a repeated abortion rate of 8.33% (2/24), who did not use LARC immediately had a repeated abortion rate of 43.33% (13/30) ( $P < 0.05$ ). The women induced abortion 3 times or more, who immediately use LARC post-abortion had 1.82% (1/55) induced abortion, who did not use LARC immediately had 26.14% (23/88) repeated abortion, there was a significant difference between the two groups ( $P < 0.05$ ). **Conclusion** Promote the rate of LARC use immediately after induced abortion to increase the continuous application rate and follow-up rate of the effective contraception, reduce the repeated and unwanted pregnancies.

**【Key words】** High-risk factors; Induced abortion; Contraception; Long acting reversible contraception (LARC)

## 染色体平衡易位伴不良孕史 3 例

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**【摘要】** 目的 报道 3 例染色体平衡易位伴不良孕史的病例。方法 应用 G 显带技术对 3 例伴有不良孕史的女性患者进行染色体核型分析, 检测到核型异常后用荧光原位杂交技术 (FISH) 进行验证。结果 3 例患者均为平衡易位, 核型分别为  $t(3;5)(p13;q13.3)$ 、 $inv(4)(p16q13)$  和  $ins(4;7)(p15.2;q32q34)$ , 后用 FISH 验证结果与核型分析相符, 经查询国内外权威数据库均未见 3 例异常核型相同报道。结论 平衡易位是不明原因反复流产的重要因素之一, 携带者再次妊娠应积极配合医生进行产前诊断。

**【关键词】** 平衡易位; 不良孕史

· 个案报道 ·

**Three cases of chromosome balanced translocation associated with adverse pregnancy history** Zhu Haibo, Wang Ke, Zhang Jing, Deng Jianping

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**【Abstract】 Objective** To report three cases of chromosomal balance translocation with adverse pregnancy history. **Methods** The chromosome karyotype analysis of 3 female patients with the history of adverse pregnancy was performed using G-banding technique and fluorescence *in situ* hybridization (FISH) was used to verify the nuclear abnormality. **Results** All three patients were chromosomal balance translocation and the nuclear types were t(3;5)(p13;q13.3), inv(4)(p16q13) and ins(4;7)(p15.2;q32q34), the results of the FISH test were consistent with the nuclear type analysis, and the same report of the three abnormal karyotypes had not been searched before. **Conclusion** The balance translocation is one of the important factors for recurrent miscarriage, and the carrier should be actively cooperating with the doctor for prenatal diagnosis.

**【Key words】** Balance translocation; Adverse pregnancy history

## 节育器膀胱内异位伴结石形成 1 例报道

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**【摘要】目的** 探讨宫内节育器(IUD)异位发生的原因、诊断及防范措施,并通过查阅文献总结部分不同情况下异常 IUD 的取器方式,为减少临床 IUD 异位及取器并发症提供参考资料。**方法** 对本院 1 例经宫腔镜、膀胱镜、大力碎石术成功取出节育器膀胱内异位并结石形成病例进行详细分析,并查阅相关文献学习总结。**结果** IUD 膀胱内异位并结石形成是放置宫内节育器的罕见并发症,一旦发生不仅可致避孕失败,而且增加取器困难及取器过程中子宫穿孔、大出血、周围脏器损伤等并发症的发生。**结论** 采用微创的宫腔镜联合膀胱镜下碎石及取器方案,可减少 IUD 膀胱内异位并结石形成患者手术的并发症,并可提高取器安全性及成功率。

**【关键词】** 宫内节育器(IUD); 异位; 膀胱结石; 宫腔镜; 膀胱镜

· 个案报道 ·

**A case report of vesical calculus caused by an ectopic intrauterine device** Pei Fangli, Huang Shuang, Chen Sida, Zeng Cheng

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**【Abstract】 Objective** To investigate the reason, diagnosis and preventive measures of the ectopic intrauterine device (IUD) and summarize the treatment methods of it under different circumstances, in order to provide reference for the decrease of ectopic intrauterine device and complications of dislodgment of abnormal IUD. **Methods** The study reported and analyzed retrospectively a case of vesical calculus induced by an ectopic intrauterine device which was taken out by the hysteroscopy, cystoscopy and lithotripsy successfully, and then reviewed the referring to related literatures. **Results** The ectopic IUD of the bladder came with vesical calculus is a rare complication of IUD, which will not only cause the contraceptive failure, but also increase the difficulty of removing the IUD and the occurrence of complications such as uterine perforation, massive bleeding and peripheral organ injury during the process of taking out the device. **Conclusion** The dislodgment of abnormal IUD and calculus by hysteroscopy combined with cystoscopy lithotripsy, which is safe, effective, but minimally invasive and small damaged, could reduce the operative complications and improve the safety and success rate.

**【Key words】** Intrauterine device (IUD); Ectopic; Vesical calculus; Hysteroscopy; Cystoscopy



## 高孕激素状态下促排卵——一种新的促排卵方案

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**【摘要】** 随着胚胎冷冻技术的进步, 全部胚胎冷冻策略得以实现, 高孕激素状态下促排卵 (progestin primed ovarian stimulation, PPOS) 成为可能。PPOS 的理论基础是基于高孕激素能抑制黄体生成素 (luteinizing hormone, LH) 峰及人类卵泡募集的多个卵泡波模式, 其包括利用内源性天然高孕激素的黄体期促排卵, 应用外源性孕激素类药物的卵泡期高孕激素状态下促排卵, 及其衍生而来的一系列方案。这些方案在国内外的研究中都已被证明能有效抑制 LH 峰, 且能获得有发育潜能的胚胎, 但对于其卫生经济学效益等仍有待研究。本文就此方案目前的研究进展作一综述。

**【关键词】** 全部胚胎冷冻; 体外受精 - 胚胎移植 (IVF-ET); 控制性超促排卵 (COH); 黄体期促排卵; 高孕激素状态下促排卵 (PPOS)

**Progestin primed ovarian stimulation—a new stimulation regimens** Xi Qianwen, Kuang Yanping

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**【Abstract】** With the improvements of freezing embryos techniques for assisted reproductive technology (ART), freezing all the embryos after controlled ovarian hyperstimulation (COH) is realized. Thanks to the freeze-all policy, progesterone is actually used as part of the protocol, which we called the progestin primed ovarian stimulation (PPOS). The physiological principles of PPOS are the use of progesterone to block the luteinizing hormone (LH) surge and waves of folliculogenesis during the menstrual cycle. There are two ways of using progesterone, whether it be endogenous, as in luteal phase, or exogenous, as in the follicular phase. These two methods and a variety of stimulation protocols derived from them have already been proved that they do not affect the number of oocytes collected or the quality of the embryos obtained both in normal responders and poor responders, while being effective in blocking the LH surge. However, their medical and economic significance remains to be demonstrated. This paper makes a review of the progress of this new ovarian stimulation protocol here.

**【Key words】** Freeze-all policy; *In vitro* fertilization-embryo transfer (IVF-ET); Controlled ovarian hyperstimulation (COH); Luteal phase stimulation; Progestin primed ovarian stimulation (PPOS)

## 人乳腺癌易感基因突变和卵巢储备下降的探讨

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**【摘要】** 人乳腺癌易感基因 (*BRCA*)1 和 *BRCA*2 的表达产物 BRCA1 和 BRCA2 蛋白是毛细血管扩张性共济失调突变基因 (*ATM*) 介导的 DNA 损伤修复信号通路成员, 对 DNA 双链断裂同源重组修复至关重要。*BRCA* 突变很大程度上增加了女性罹患乳腺癌、卵巢癌的风险。但对于 *BRCA* 突变产生的非癌症影响仍旧知之甚少。近年来有研究表明 *BRCA* 突变携带的女性可能出现卵巢储备下降。若 *BRCA* 突变与卵巢储备下降存在因果关系, 则不仅有助于揭示遗传参与的卵巢衰老机制, 甚至提示 *BRCA* 有望作为卵巢早衰的易感因素之一, 有助于卵巢早衰的早期诊断。本文就近年来国内外的相关研究, 对 *BRCA* 突变和卵巢储备功能下降作一探讨。

**【关键词】** 人乳腺癌易感基因 (*BRCA*); 卵巢储备下降 (DOR); 卵母细胞衰老; DNA 损伤修复; 抗苗勒管激素 (AMH); 卵巢早衰

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**Breast cancer susceptibility gene mutations and decreased ovarian reserve** Yu Yi, Lei Xiaoyun, Wang Jianing, Xu Ying

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**【Abstract】** Breast cancer susceptibility gene (*BRCA*)1 and *BRCA*2 are members of the *ATM*-mediated DNA damage signalling pathway which are integral in the repair of DNA double strand breaks through homologous recombination. *BRCA* germline mutations substantially increase the risk of breast and ovarian cancer. But the non-cancer-related implications still remain less-known. A number of studies suggest that ovarian reserve may be reduced in *BRCA* mutation carriers. If the causal relationship between *BRCA* mutations and diminished ovarian reserve (DOR) is confirmed, it helps not only to recover the mechanism of ovarian aging but also the early diagnosis for premature ovarian failure (POF). Here is to make a review of the reseach status of *BRCA* germline mutation and diminished ovarian reserve.

**【Key words】** Breast cancer susceptibility gene (*BRCA*); Diminished ovarian reserve (DOR); Oocyte aging; DNA damage repair; Anti-Müllerian homone (AMH); Premature ovarian failure (POF)

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## 外源物暴露所致卵巢发育毒性相关发生机制的研究进展

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**【摘要】** 卵巢的结构和功能对于女性生育力的维系具有重要意义, 大量流行病学调查和动物实验研究表明, 孕期所接触的多种外源物, 如有机挥发物等的环境毒物、含有可卡因等成分的药物、吸烟或过量饮用酒及咖啡等不良生活习惯, 不仅影响母体健康, 更会对其子代的卵巢发育、功能维护及成年后生殖健康产生不利影响。故就孕期外源物暴露对子代卵巢发育的影响及其机制作一综述。

**【关键词】** 卵巢发育; 孕期外源物暴露; 神经内分泌; 下丘脑-垂体轴

**Research progress on the related mechanisms of ovary developmental toxicity caused by exposure to xenobiotics** Ni Yuan, Lyu Feng, Zou Wen, Yang Jing, Wang Hui

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**【Abstract】** The structure and function of ovary is of great significance to the maintenance of female fertility. A large number of epidemiological surveys and animal studies have shown that a variety of exogenous substances exposure during pregnancy not only affect the mother's health, but also adversely affect the offspring's ovarian development, ovarian function, and adult reproductive health. Exogenous substances constrain environmental toxicants such as organic volatile, drugs containing cocaine, smoking, excessive drinking and coffee. This article reviews the influence of prenatal xenobiotic exposure to ovarian development and the potential mechanisms.

**【Key words】** Ovarian development; Prenatal xenobiotic exposure; Neuroendocrine; Hypothalamic-pituitary axis

## 复发性流产的免疫学因素研究进展

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**【摘要】** 复发性流产 (recurrent spontaneous abortion, RSA) 是指连续 $\geq 2$ 次的自然流产, 且常发生于同一妊娠月份, 临床发病率约 1%~5%。除美国妇产科医师协会 (ACOG)、皇家妇产科医师学会 (RCOG) 已明确提出的病因如染色体异常、母体生殖道异常、母体内分泌异常、生殖道感染、血栓形成倾向等, 约 80% 与免疫因素相关。近年来研究者根据免疫学发病机制将 RSA 分为自身免疫型和同种免疫型两大类, 前者可能由于自身抗体针对内皮细胞、滋养细胞及种植前胚胎导致妊娠失败, 后者则可能与母-胎界面免疫失衡有关。本文将分别从这 2 个方面就 RSA 免疫学发病机制进行综述。

**【关键词】** 复发性流产 (RSA); 免疫; 病因; 诊断

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**【Abstract】** Recurrent spontaneous abortion (RSA) is defined as two or more consecutive miscarriages generally occurred in the same gestation period. It affects about 1%–5% of females at childbearing ages. Except for multiple causes for RSA been identified, such as chromosome abnormalities, maternal genital malformation, endocrine dysfunction, reproductive tract infections, thrombophilia, according to the American College of Obstetricians and Gynecologists (ACOG) and the Royal College of Obstetricians and Gynecologists (RCOG), there are still 80% of risk factors related to immunology. Recently, RSA has been classified into two categories: autoimmune and alloimmune. Some autoantibodies may lead to pregnancy loss by targeting at vascular endothelial cells, trophoblastic cells and preimplantation embryos while alloimmune RSA may associate with the imbalance of immune interactions at the maternal-fetal interface. This article reviewed the two types of RSA respectively on the basis of immunological pathogenesis.

**【Key words】** Recurrent spontaneous abortion (RSA); Immune factors; Etiology; Diagnose



## 父代饮食、运动及应激通过精子中小非编码 RNA 对子代表型的影响

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**【摘要】**跨代遗传是指环境因素通过对亲代生殖细胞(精子、卵子)的改变,将遗传信息传递给子代,调节子代特定器官和组织中的基因表达,从而影响子代的生长发育和某些疾病的发生、发展。DNA 甲基化和组蛋白修饰参与其中,微小 RNA(miRNA)、小片段干扰 RNA(siRNA)、Piwi 蛋白相作用的 RNA(piRNA)、tRNA 来源片段(tRFs)在内的小非编码 RNA(sncRNA)在跨代遗传中扮演了重要角色。不同的饮食摄入方式,包括高脂饮食和饥饿饮食等,分别通过改变精子中 miRNA、tsRNA(tRFs 中的一种)或 siRNA 的含量对后代肥胖及糖代谢产生影响;针对父代小鼠的运动干预则可导致精子中 miRNA 的改变,从而影响后代肥胖及糖代谢表型。此外,在持续慢性应激作用下,父代小鼠精子中 miRNA 及 piRNA 的表达发生改变,进而影响子代小鼠的行为、代谢和应激反应。本文对这 4 类 sncRNA 及其受父代环境影响经精子跨代遗传的研究进展作了逐一概述。

**【关键词】**跨代遗传; 精子; 小非编码 RNA; 饮食; 运动; 应激

**The hereditary impact of paternal diet, exercise and stress on filial generation through small non-coding RNAs in the sperm** Sun Tingye, Wu Ling, Lyu Qifeng

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**【Abstract】** Transgenerational inheritance is the transmission of hereditary information from one generation of an organism to the next generation via germ cells (sperm, oocytes), by which affect the offspring's phenotype and disease development. Mechanistically, altered DNA methylation and histonemodifications have been implicated in the transgenerational phenotype transmission. Small non-coding RNAs (sncRNAs), including microRNA (miRNA), small interfering RNA (siRNA), piwi-interacting RNA (piRNA) and tRNA-derived small RNA (tRFs), play important roles in mediating this transgenerational effects. Paternal factors, including diet, exercise and stress, influence offsprings through small non-coding RNAs. For instance, it has been shown that different diets, such as high-fat diet and starvation will affect offsprings' obesity and glucose metabolism through the change of miRNA, tsRNA or siRNA in sperm; exercise intervention targeted for paternal mouse will cause miRNA change in sperm to affect descendents' phenotypes including obesity and glucose metabolism. Under continuous chronic stress, the experssion of miRNA and piRNA in paternal mouse will change. In this paper, we will review and summarize the roles of these four sncRNAs' transgenerational effect to mediate paternal environmental information.

**【Key words】** Transgenerational inheritance; Sperm; Small non-coding RNA (sncRNA); Diet; Exercise; Stress