稿件編號：OF1	利用免疫還原法定量法分析胚胎等級與析胚泡培養液中人絨毛膜促性腺激素之相對關係
臨時收件編號：2878	**Clinical application of immunomagnetic reduction for quantitative analysis of beta-subunit of human chorionic gonadotropin in blastocyst culture media to differentiate embryo quality** 李冠昇 [1] 胡玉銘 [1] 李國光 [1] 陳震宇 [1] 翁郁雯 [1] 林明輝 [1] 台北馬偕紀念醫院婦產部

論文發表方式：
口頭報告

論文歸類：
生殖內分泌

Study Question：To explore the possibility that using the immunomagnetic reduction (IMR) assay to quantitatively measure β-subunit of human chorionic gonadotropin (β-hCG) in blastocyst culture media to differentiate embryo quality.

Study Design, Size, Duration：This was a prospective case-control study form June 2015 to March 2016. including 28 samples of blastocyst culture media. We used single-step blastocyst culture and IMR assay to analyze β-hCG concentrations in culture media. Also,we explored the relationship between IMR signals of β-hCG and morphological grading of blastocysts.

Materials, Setting, Methods：After insemination, individual embryos were transferred to a 30-μL micro-droplet of one-step embryo culture medium (global, Life Global, Guilford, CT, USA) for culture to day 5 (blastocyst stage). Each 5-μL sample volume was drawn from the culture medium and diluted 25 times with phosphate buffered saline (PBS) solution (pH=7.4). We then sent the samples to our laboratory to measure the concentration of β-hCG using the IMR assay. At the same time, embryo morphological grading was assessed by two experienced embryologists who were blinded to the IMR results. The blastocyst morphology was graded based on the criteria established by Gardner and Schoolcraft [20]. The blastocysts were first graded according to their size.

Main Results：β-hCG concentration-dependent IMR signals were highly correlated with blastocyst morphological quality (Spearman correlation coefficient: 0.731). Receiver-operating characteristic curve analysis showed a cutoff IMR value to differentiate embryo quality of 0.873%

Conclusion：An IMR assay can quantitatively measure β-hCG in blastocyst culture media, and may be a potential clinical tool to assist in the assessment of good blastocyst quality before embryo transfer.

稿件編號：OF2	**試管嬰兒拮抗劑療程成熟卵子產出率(MOOR)的顯著預測因子**
	Significant predictors for mature oocyte output rate (MOOR) in COH with GnRH antagonist protocol
臨時收件編號：2809	賴宗炫 [1,2] 梁玉惠 [1] 林欣達 [1] 國泰綜合醫院婦產科 [1] 輔大醫學系 [2]

論文發表方式：
口頭報告

論文歸類：
生殖內分泌

Introduction:

What are the most important predictors for mature oocyte yield in controlled ovarian hyperstimulation (COH)? This important issue has not been concluded yet. In an effect to objectively evaluate the ratio of mature oocyte retrieved from antral follicles responsiveness to exogenous FSH, we define the mature oocyte output rate (MOOR) as the ratio between the number of MII oocytes retrieved and the antral follicle counts (AFC). The aim of this study was to explore the relationship between the clinical indicators and the MOOR, and to find out the significant predictors for MOOR in COH with GnRH antagonist protocol.

Materials and Methods:

This is a retrospective study. A total of 128 IVF patients with age from 28 to 43 y was enrolled between Aug 2016 and July 2017. The patients were assigned into two groups according to their MOOR. Group A: MOOR < 50% (n= 38)； Group B: MOOR >= 50% (n= 90). All the participants were treated with GnRH antagonist protocol for COH. When at least 3 follicle size reached > 18 mm, duo trigger (HCG + GnRH agonist) was administered and transvaginal oocyte retrieval was performed 36-38 h later. Follicular fluid were obtained during oocyte retrieval for further analysis. Serum AMH, day-2 FSH/LH/P4, day-hCG E2/LH/P4, intrafollicular VEGF and TGF-B were measured. AFC and the number of total and mature oocytes were recorded. Independent t test, univariate correlations, logistic regression and ROC curve were used for the statistical analysis. A P < 0.05 was considered significant.

Results:

There are significant differences in AMH, day-hCG E2 and LH level, the ratio of day-2 to day-hCG LH level, oocyte number and maturation rate between group A and B (P< 0.05). Logistic regression reveals AMH and the ratio of day-2 LH to day-hCG LH level are the most important predictors for MOOR (P< 0.05)(odds ratio: 2.468 VS 1.446). The computed ROC curve established that the cutoff value of AMH level and the ratio of day-2 LH to day-hCG LH level for predicting MOOR < 50% are 1.820 ng/ml (AUC= 0.680, sensitivity= 73.7%, specificity= 43.8%, P< 0.001) and 1.45 (AUC= 0.649, sensitivity= 65.6%, specificity= 46.7%, P< 0.05).

Conclusion:

AMH and the ratio of day-2 LH to day-hCG LH level are the significant predictors for MOOR in COH with GnRH antagonist protocol.

稿件編號： OF3	**卵子捐贈週期卵子玻璃化時間對存活率的影響** **The effect of oocyte vitrification time on survival rate in oocyte donation cycles**
臨時收件編號： 3108	陳秀惠 陳忠義 [1] 李宗賢 [123] 李俊逸 [123] 林秉瑤 [13] 黃俊嘉 [1] 李茂盛 [123] 茂盛醫院 [1] 中山醫學大學附設醫院婦產部 [2] 中山醫學大學醫研所 [3]
論文發表方式： 口頭報告	Objective: To assess the effects of oocyte vitrification time (the time to perform oocyte vitrification with respect to the time of hCG, cumulus denudation and oocyte pick-up (OPU)) on survival rate and the clinical outcomes in donation cycles. Materials and Methods: A retrospective study from a single in-vitro fertilization center in Lee Women's Hospital. Total 2820 vitrified oocyte from 122 egg donors were performed ICSI. There were 544 blastocyst performed PGT-A protocol. Exact times between hCG, OPU, denudation, vitrification, warming and ICSI were recorded. Logistic regression analysis and spearman's correlation analysis were performed to analysis the relation between the time of vitrification, oocyte survival rate, embryo quality and euploidy rates. The clinical pregnancy rates and cumulative pregnancy rates were also analyzed. Results: The survival rate, fertilization rate, good day 3 rate and good blastocyst rate were 94.0% (2651/2820), 88.3% (2341/2651), 56.3% (1317/2341) and 33.0% (772/2341), respectively. The euploidy rate of blastocyst was 42.3% (230/544). The clinical pregnancy rate (per embryo transfer) and cumulative pregnancy rate were 51.2% (43/84) and 70.0% (42/60), respectively. According to logistic regression analysis, the interval from hCG, OPU or denudation to vitrification time were not associated with the oocyte survival, fertilization, good blastocyst rates. According to correlation analysis, the oocyte survival rate correlated with fertilization rate (Spearman correlation coefficient $\rho = 0.221$; P =0.014) but not day 3 good embryo rate, good blastocyst rate and euploidy rate. Conclusions: Our results indicate that the survival rate of vitrified oocyte was not associated within a range of times between hCG-, OPU-, denudation and vitrification. The embryo quality and euploidy rate were not associated with survival rate, however, the fertilization rate was significantly affected by the survival rate in oocyte donation cycles.
論文歸類： 生殖內分泌	

稿件編號：OF4	囊胚發育延遲顯著降低單一整倍體胚胎移植之臨床懷孕率

Delayed blastulation significantly reduce the clinical pregnancy rate in euploid single embryo transfer cycles

臨時收件編號：2925

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論文發表方式： 口頭報告

論文歸類： 生殖內分泌

Developmental kinetics have been demonstrated to associate with clinical outcomes in patients undergoing IVF treatment. It is intriguing to investigate the association between morphokinetic parameters and pregnancy probabilities in PGT-A cycles. This study was approved by the Institutional Review Board of Chung Sun Medical University. From January 2017 to August 2018, a total of 92 consecutive patients < 38 years undergoing 107 euploid single embryo transfer (SET) cycles were enrolled. High-resolution next-generation sequencing (hr-NGS) was applied to identify euploid blastocysts, which were cultured in a time-lapse culture system. Univariate logistic regression analysis of this study revealed that the timing of start of blastulation (tSB) (odd ratio (OR) = 0.93, 95% confidence interval (CI) 0.88–0.99) and the timing of full blastulation (tB) (OR = 0.94, 95% CI 0.89–0.99) were negatively associated with the clinical pregnancy probability significantly. The areas under the curve of tSB and tB were 0.624 and 0.619, respectively. The cut-off values for tSB and tB were 79.5 h and 91.5 h post pronuclear fading (PNF). The clinical pregnancy rate was 72.1% (62/86) in the euploid blastocysts with tSB < 79.5 h and tB < 91.5 h. By contrast, the pregnancy rate greatly decreased to 22.2% (4/18) in euploidy blastocysts with tB > 91.5 h. In conclusion, this study clearly demonstrates that delays in blastulation appear to negatively associate with the clinical pregnancy probability of euploid SET cycles. Importantly, tSB and tB are potential to apply for non-invasive embryo selection.

稿件編號：OF5	**睡眠呼吸中止症與不孕**
	Association of obstructive sleep apnea with female infertility- A 13-year nationwide population-based retrospective study
臨時收件編號：2787	

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論文發表方式：
口頭報告

論文歸類：
生殖內分泌

Study Objectives: Obstructive sleep apnea (OSA) increases the risk of hypertension, type 2 diabetes mellitus (DM), cardiovascular diseases and stroke. In the previous study, we have shown that non apnea sleep disorder associates with increased risk of female infertility. However, the risk of OSA to female infertility has not been thoroughly understood. Our study aimed to determine whether OSA increases subsequent risk of female infertility.

Methods: Our study utilized the outpatient and inpatient data from Taiwan's National Health Insurance Research Database between 2000 and 2013. We enrolled 4,078 females aged 20 to 45 years old and diagnosed with female infertility in the end of 2013. 1,946 of them who matched our criteria were assigned to the study group. We retrospectively investigated those who had previous exposure to OSA and used multivariable logistic regression analysis to estimate the effects of OSA on female infertility.

Results: The OSA cohort had an adjusted hazard ratio (HR) of female infertility 2.154-fold higher than that of the cohort without sleep disorders. In the stratified age group, the OSA group had the highest impact on 31- to 35-year-olds, with an adjusted HR of 2.690 (p=0.049).

Conclusions: Our study provides a nationwide, population based, 13-year retrospective data demonstrating that OSA patients are at a higher risk of female infertility.

稿件編號： OF6	**研究早期胚胎著床位點的微核糖核酸表現及訊息傳遞途徑** **Study on microRNA performance and message delivery pathways in early embryo implantation sites**
臨時收件編號： 2826	蔡漢霓 [1] 鄭恩惠 [1] 陳建宏 [1] 黃俊嘉 [1,2,5] 李宗賢 [1,3,4] 林秉瑤 [1,3] 陳忠義 [1] 李茂盛 [1,2,3] 茂盛醫院 [1] 中國醫藥大學醫學檢驗生物技術系 [2] 中山醫學大學醫學研究所 [3] 中山醫學大學附設醫院婦產部 [4] 中台科技大學醫學檢驗生物技術系 [5]
論文發表方式： 口頭報告	Objective: Embryo implantation failure is a major limiting factor for early pregnancy and assisted reproduction. Implantation involves complex interactions between a receptive endometrium and a competent blastocyst. Signaling during implantation involves various genes and gene modifiers such as microRNAs； however, their regulatory mechanisms remain unclear.
論文歸類： 生殖內分泌	

Material and methods: The pseudo-pregnant mice were used to establish the early implantation model. Briefly, 48 hours after the blastocyst were implanted into one side of uterus, 1% Chicago blue dye was injected intravenously via the tail, and the mice were sacrificed after another 5 minutes. The implantation sites were visualized and separated from the uterus. Another side of uterus without embryos transfer was used as a control. The expression profiles of genes and microRNAs were determined by next-generation sequencing (NGS) and were compared among three groups: the uterus tissue with embryo removed (group A), the uterus tissue with embryo(group B), and the control group.

Results: Compared with control group, group A had 57 microRNAs with statistically significant changes. Group B had 103 microRNAs with statistically significant changes, and 45 of them were consistent with group A. Among the 45 microRNAs, there were10 microRNAs whose expression levels were inconsistent between the two groups, suggesting that the embryo might play an important role in the regulation of microRNAs. At the site of implantation, the expression profile of the Let-7 family of microRNAs was not consistent with previous studies, and may be due to different periods of observation. The expression profiles of microRNA-200 family, microRNA-30 family, and microRNA-17-92 cluster were the same as the previous studies. In addition, there were 200 and 118 genes with statistically significant changes found in group A and group B, respectively. The genes whose expression was changed in group A were mainly involved in the regulation of cell scaffold structure and cell cycle, while the genes in group B were more diverse, including the receptor, angiogenic genes, and embryonic development.

Conclusions: The results of our study provide promising insights into the mechanism of embryonic implantation and may guide the development of clinical therapeutics to improve the implantation of infertile women.

17β-雌二醇促進子宮內膜異位瘤基質細胞介白素-33（IL-33）和血管細胞粘附分子 1（VCAM-1）的表現

17β-estradiol promoted interleukin-33 (IL-33) and vascular cell adhesion molecule 1 (VCAM-1) expression in endometrial stromal cells derived from ovarian endometrioma

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Introduction : Endometriosis is a benign and chronic gynecologic disorder that affects women of reproductive age. Ovarian endometrioma is a cyst composed of endometrial tissue and is present in 20%-40% of patients with endometriosis. The pathogenesis of endometriosis is multifactorial. Current studies have shown that estrogen, immune and inflammatory mediators are closely related to the pathogenesis of endometriosis. Interleukin-33 (IL-33) is a new member of the IL-1 superfamily and is mainly expressed by stromal cells and up-regulated following pro-inflammatory stimulation. Previous studies showed that IL-33 concentrations were elevated in correlation with the progression of the endometriosis state, suggesting a relationship between IL-33 and the progression of endometriosis. Vascular cell adhesion molecule 1 (VCAM-1) is also well characterized in human immune responses. There is increasing evidence that VCAM-1 may play a pivotal role in the pathogenesis of endometriosis. In this study, we investigated the effect of 17β-estradiol on the expression of IL-33 and VCAM-1 genes in endometrial stromal cells derived from ovarian endometrioma (hOVEN-SCs).

Materials and methods : The hOVEN-SCs were treated with 1μM 17β-estradiol for two weeks. Gene expression was analyzed by Illumina Whole Genome Expression Arrays and reverse transcription polymerase chain reaction (RT-PCR).

Results : In this study, these 17β-estradiol-treated hOVEN-SCs were compared to hOVEN-SC using Illumina Whole Genome Expression Arrays. The results showed that the expression of 55 genes changed more than tenfold. Among these genes, 23 were up-regulated and 32 were down-regulated in 17β-estradiol-treated hOVEN-SCs as compared with hOVEN-SCs. Moreover, among those up-regulated genes related to immunity and inflammation, three genes (IL-33, VCAM-1 and IL-1β) are found to be common among them. Compared with hOVEN-SC, the expression of IL-33, VCAM-1 and IL-1β in 17β-estradiol-treated hOVEN-SC was 74.7-, 48.1- and 14.2-fold higher, respectively. We then validated the three genes using RT-PCR; nevertheless, only the expression of IL-33 and VCAM-1 tend to be differentially expressed. The results revealed that IL-33 and VCAM-1 expression in 17β-estradiol-treated hOVEN-SC were significantly higher than hOVEN-SC by RT-PCR (11.2- and 4.8-fold increase, respectively, for IL-33 and VCAM-1).

Conclusion : In short, our findings may provide a reference for studying the relationship between estrogen and human ectopic endometrial stromal cells for developing a new therapeutic strategy for endometriosis.

稿件編號： OF8 臨時收件編號： 2816	**探討影響子宮內注射自體血小板濃縮液療程之因子與其臨床結果** **To investigate the affecting factors of autologous platelet-rich plasma intrauterine infusion and the treatment clinical outcomes** 陳怡君 [1] 鄭恩惠 [1] 施惠馨 [1] 白依萍 [1] 黃俊嘉 [123] 林秉瑤 [14] 李宗賢 [45] 李茂盛 [145] 茂盛醫院 [1] 中國醫藥大學醫學檢驗生物技術系 [2] 中台科技大學醫學檢驗生物技術系 [3] 中山醫學大學醫學研究所 [4] 中山醫學大學附設醫院婦產部 [5]
論文發表方式： 口頭報告 論文歸類： 生殖內分泌	Objective: To evaluate whether platelet-rich plasma(PRP) treatment improved clinical outcomes for the women with thin endometrium during in-vitro fertilization and further investigated what factors affected the treatment. Materials and Methods: This is a prospective cohort study that perform in Lee Women's Hospital from Jan 2018 to Aug 2019. Total seventy-seven women had at least one IVF or FET canceled cycle resulted from thin endometrium were recruited in the study. All the patients were underwent PRP intrauterine infusion on the 11th-13th day of hormone replacement and repeat the PRP infusion after 48hrs. The autologous PRP were prepared from 20 ml whole blood without anticoagulant and total 1 ml of PRP was collected and infused into the uterine cavity through the IUI catheter. The primary outcome was endometrial expansion measurement after the intrauterine PRP infusion and the secondary outcome was the implantation rate clinical pregnancies and abortion rate. Results: After PRP infusion, total sixty-six cycles reached embryo transfer and eleven cycles were canceled because of the thin endometrium (Conclusions: PRP intrauterine infusion may improve the endometrium thickness and the clinical outcomes for the patients with thin endometrium during IVF, but the patients endometrium surgery history should be concern before treatment.

稿件編號：OF9	**雙酚 A 對濾泡刺激素誘導的顆粒細胞濾泡刺激素受體和連接蛋白 43 基因表現之影響**
臨時收件編號：2834	**The effect of BPA on FSH-induced FSH receptors and connexin 43 gene expression in granulosa cells** 王凱弘[1] 蔡青浣[1] 林大欽[1] 郭宗正[1.2] 台南郭綜合醫院 生殖醫學中心[1] 台南郭綜合醫院 婦產部[2]
論文發表方式：口頭報告	Introduction Follicular stimulating hormone (FSH) is an important hormone that regulates the development and maturation of ovarian follicles and granulosa cells (GCs). Since FSH acts exclusively through its receptor, the abundance of FSH receptors (FSHR) determines the sensitivity of GCs to FSH and its activity on these GCs. Connexin 43 (Cx43) is an important gap junction protein between GCs and oocyte communication. The expression of Cx43 increases with folliculogenesis, and a great deal of literature has demonstrated that FSH can increase the expression level of Cx43 in GCs. Bisphenol A (BPA), an estrogenic-like endocrine-disrupting chemical, is one of the most widely produced chemicals around the world. It has been associated with several female reproductive disorders. However, the effect of BPA exposure on GCs has been largely unexplored. The aim of this study was to understand BPA action in FSH-induced human GCs. Materials and methods The human GCs for analysis were collected from patients undergoing IVF procedures after controlled ovarian stimulation. FSHR and Cx43 were quantified by immunofluorescence staining and reverse transcription polymerase chain reaction (RT-PCR) analysis. Results In the present study, we found that the FSH treatment of GCs significantly increased FSHR and Cx43 gene expression in a dose-responsive manner, with doses ranging from 20-100 ng/mL. There was no significant difference in mRNA expression levels of FSHR and Cx43 between the FSH treatments of 80 and 100 ng/mL. Consequently, 80 ng/mL of FSH was chosen for the following experiments. Next, we analyzed the dose-dependent effect of BPA (concentration: 10^{-6}-10^{-10} M) on the FSH-induced GCs FSHR and Cx43 mRNA expression. Our current study showed that BPA-treated (concentration: 10^{-6} M) GCs significantly suppressed FSH-induced FSHR gene expression. Furthermore, BPA (concentration: 10^{-6} and 10^{-7} M) significantly inhibited the Cx43 gene expression of GCs induced by FSH. Conclusion In short, our study indicated that exposure of BPA to GCs affects FSH-induced FSHR and Cx43 mRNA expression. These results provide a basis for understanding the mechanisms by which BPA may contribute to the reproductive toxicity of GCs.
論文歸類：生殖內分泌	