稿件編號：OF3

臨時稿件編號：
0618

在縮時攝影培養下男性不孕症的早期胚胎發育型態變化

Male factor infertility and its impact on early embryonic morphokinetic parameters observed under time-lapse imaging incubator

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論文發表方式：
口頭報告

論文歸類：
生殖內分泌

Objective: Whether there is an effect of male factor infertility (MFI) on early morphokinetic parameters obtained during embryonic culture in a time-lapse imaging (TLI) incubator

Study Design, Size and Duration: This is a single center, retrospective cohort study conducted between April 2019 to May 2021. A total of 373 embryos were analyzed, including 157 embryos derived from couples (n=48) with a diagnosis of MFI, and 216 embryos from couples with other, non-MFI diagnosis of infertility (n=39).

Materials and Methods: Data from 373 embryos cultured to the 8-cell stage in a TLI-monitored incubator were retrospectively reviewed. Embryos derived from the sperm of men with MFI were compared with those derived from patients with other, non-MFI diagnosis of infertility. Markers of early embryo development included P1: pronuclei fading time (tPNf) to first cytokinesis (t2), P2: time from 2–3 cells (t2-t3), P3: 3–4 cells (t4-t3), (P4) 4–5 cells (t5-t4), (P5) 5-8 cells (t8-t5), and tPNf to 8 cell embryo stage (t8-tPNf).
Results: Antral follicle counts (AFCs), anti-Müllerian hormone (AMH) levels, and ages of both the men and women in MFI couples were comparable to that of couples with other, non-MFI diagnosis of infertility. ICSI was utilized in all embryos of couples with MFI, and 25% of embryos in couples with non-MFI infertility (non-MFI ICSI group). 75% of embryos of non-MFI couples underwent IVF (non-MFI IVF group). When all embryos of MFI and non-MFI groups were compared, a shorter time for 3 to 4 cell division of 0.54 hours (p=0.02) was seen in the MFI group, but the overall time from tPNf to 8-cell stage embryo development was comparable (t8-tPNf difference: -0.82 hours, p=0.41). Similarly, when only embryos fertilized via ICSI were analyzed, a shorter 3 to 4 cell division time by 1.36 hours was seen (p=0.02) in those with MFI, but no significant difference was seen in the overall t8-tPNf times (t8-tPNf difference: -2.13 hours, p=0.21). When the MFI group was compared to the non-MFI IVF group, or when comparing different fertilization (ICSI vs. IVF) in the non-MFI group, no significant difference in any parameter of early embryo development was demonstrated.

Conclusion: Our findings show that MFI had no impact on overall parameter of early embryogenesis, despite a shorter 3 to 4 cell division time of early embryogenesis in embryos of couples with MFI compared to non-MFI, and non-MFI ICSI groups. Furthermore, a comparison between different fertilization methods within the non-MFI groups showed that whilst no significant differences was seen in times of early embryogenesis between non-MFI ICSI vs. IVF, a trend towards delayed embryo development was seen when ICSI was utilized.

台灣婦產科醫學會 111 年度年會暨學術研討會

論文摘要

稿件編號：OF4

臨時稿件編號：
0594

正常卵巢反應族群在試管嬰兒新鮮胚胎移植週期個別化早期停止使用黃體支持

Individualized early stop of luteal phase support in IVF/ICSI fresh embryo transfer cycles in normal ovarian responders

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論文發表方式：
口頭報告

論文歸類：
生殖內分泌

Objective: To evaluate the best cut-off value of progesterone (P4) serum level which could determine early stop of luteal phase support (LPS) after in vitro fertilization (IVF)/ intracytoplasmic sperm injection (ICSI) fresh embryo transfer (ET) fresh embryo transfer (ET) cycles in patient of normal ovarian response.
Design: Retrospective cohort study between Jan. 2010 and Dec. 2020 in single tertiary medical center.
Materials and Methods:
Women (n=1221) who underwent IVF/ICSI fresh ET cycle after standard controlled ovarian stimulation (COS) and ovum pick-up (OPU) with subsequent LPS by one tube of Crinone (8% P4 vaginal gel) and 4 mg of estradiol valerate twice a day. The LPS were started 2 days after OPU (day 0) and lasted for 14 days (day 16) until pregnancy test was positive, which was defined as serum β-HCG ≥20 mIU/mL. The pregnant women were divided into two groups dependent on different doctor's ideas: the control group kept using LPS ≥ 9th week, and the early stop group ceased the LPS at ≤ 6th weeks.
A received operative curve (ROC) based on the maximization of Yuden index was applied twice for identifying the best cut-off values of the P4 level on day 16 in all women and on day 23 in all pregnant women in recognizing the 12th week ongoing pregnancy status respectively. Using the best cut-off values of the P4 level at day 16 (primary) and day 23 (secondary), we categorized our infertile patients into condition of ''with CLR (corpus luteum rescue)'' and ''without CLR''.
Results:
There were no significant differences in age, parity, hormone data, stimulation duration, number of oocytes retrieved, and number of embryos transferred between the early stop group and control group. A total of 677(55.4%) women were confirmed as pregnancy on day16. Among them, 179(26.4%) women in the control group, and 498 (73.6%) women in the study group. There were 529 (78.1%) women with primary CLR (P4 >21.2 ng/ml) and 148 (21.9%) women without primary CLR (P4 ≤ 21.2 ng/ml). Total 595 woman had gestational sac presentation, and there were 547 (91.9%) women with secondary CLR (P4 > 35.1 ng/ml) and 48 (8.1%) women without secondary CLR (P4 ≤ 35.1 ng/ml).
The area under the curve (AUC) of ROC is 0.92 for primary CLR and 0.763 for secondary CLR, which refer to highly and moderately predictive model respectively. In women with primary CLR, compared to control group, no significant risk was noted in early stop group with miscarriage rate (OR = odds ratio, 1.14; 95% CI = confidence interval, 0.49-2.61). The same condition was noted in patients with secondary CLR (OR, 1.45; 95% CI, 0.63-3.37). In women without primary CLR, compared to control group, early stop group had significant higher risk in miscarriage (OR, 2.72; 95% CI, 1.19-6.23). A similar outcome was also noted in patients without secondary CLR (OR, 2.71; 95% CI, 1.08-6.78).
Conclusion:
Our study indicates that individualized early stop of LPS ≤ 6th weeks of pregnancy for infertile patients of normal ovarian response in IVF/ICSI fresh ET cycles is safe if the patient achieves primary or secondary CLR. While early stop of LPS for patients without CLR may increase the risk of miscarriage.

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論文摘要

稿件編號：OF5

臨時稿件編號：
0545

分段體外受精併冷凍胚胎移植合併藥物、手術與海扶刀在子宮肌腺症病人之治療成效

Efficacy of medical, surgical therapies and high-intensity focused ultrasound for segmented in vitro fertilization and frozen embryo transfer in patients with adenomyosis

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論文發表方式：
口頭報告

論文歸類：
生殖內分泌

Objective: To determine the best therapeutic strategy for segmented in vitro fertilization (IVF) and frozen embryo transfer (FET) in patients with adenomyosis by comparing the fertility outcomes.

Methods: The retrospective study included 120 cases of women with adenomyosis undergoing segmented IVF and FET in Chang Gung Memorial Hospital from January 2020 to December 2021. Adenomyosis was diagnosed by sonographic exam and an elevated cancer antigen 125 (CA-125). Depending on imaging findings, the patients were further classified into focal and diffuse types. FET cycles following either medical treatment alone (group A), surgical intervention with or without medical treatment (group B), and high-intensity focused ultrasound (HIFU) with or without medical treatment (group C) were compared.

Results: Early follicular hormone profiles, treatment outcomes of adenomyosis (changes in CA-125 and size of adenomyoma) were obtained. IVF outcomes including stimulation duration (day), total dosage of gonadotropin (IU), estradiol on hCG day (pg/mL), number of retrieved oocytes, mature oocyte rate (%), fertilization rate (%), number of transferred embryos, clinical pregnancy rate (%), median time to conceive (months) would be compared.

Conclusion: For patients with adenomyosis opting for IVF cycle segmentation, treatment strategy may differ depending on severity of adenomyosis. For focal adenomyosis, patients may benefit the most from accepting both medical treatment and adenomyomectomy. However, for diffuse disease, cycle segmentation with medicine and HIFU therapy may result in greater fertility outcome.

稿件編號：OF6

臨時稿件編號：
0625

應用高光譜成像於胚胎品質人工智慧預測模型之研發
Research and Development of Artificial Intelligence Prediction Model for Embryo Quality by Hyperspectral Imaging

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論文發表方式：
口頭報告

論文歸類：
生殖內分泌

不孕症已為全球性危機，不孕症療程重點即在於胚胎品質檢測，目前主要的胚胎品質檢測方法可區分為胚胎影像、胚胎縮時攝影與胚胎著床前染色體篩檢(Preimplantation Genetic Screening, PGS)。然而，胚胎影像及胚胎縮時攝影需透過胚胎師主觀判斷篩選品質，故不同的醫院和胚胎師可能會有不同的判斷品質結果，而 PGS 是至今普遍的胚胎染色體檢測方式，但此方法卻可能對胚胎造成傷害。因此發展不同於上述的非侵入式檢測的技術具有其重大意義。

高光譜成像 (Hyperspectral Imaging, HSI) 為光譜學與成像技術的結合，透過收集不同時間及不同波段波長下的連續波段光譜，可呈現定性和定量多種物理特徵，已被廣泛應用於分析複雜的結構。於臨床醫學上，分析特定的波段對應的胚胎發育的光譜資訊也許有助於胚胎細胞之研究。

本研究使用 HSI 方法拍攝人體胚胎高光譜影像，並對高光譜影像進行影像處理以得到 26 種細節影像，接著結合人工智慧(Artificial Intelligence, AI)對 26 種細節影像進行訓練和預測，發展非侵入式的胚胎檢測技術。本研究使用受精後時數(Hours Post Insemination, hpi)24 小時胚胎高光譜影像預測 72 hpi 胚胎品質，結果顯示不同的細節影像能提供卷積神經網路(Convolution Neural Network, CNN)模型不同的資訊而可用於預測，最高預測正確率能達到 87.50%，此外，更在 AI 預測模型中使用影像擴增技術增加訓練資料量以提升各模型之預測準確率，最後，本研究將所有達 87.50%預測正確率的組合歸納統整，期望此些組合能幫助其它胚胎細胞研究快速發展最佳預測率的 CNN 模型。

本研究證實胚胎的高光譜影像比單一波長的影像提供更多的資訊，有助於 CNN 模型辨別胚胎的品質，且 26 種細節影像之處理使層數較少之 CNN 模型能得到較佳的預測結果，有效減少資料運算量與運算時間，由結果也初步證實高光譜成像 AI 預測模型應用於胚胎品質預測之可行性，亦說明了此模型未來的發展潛力與應用價值。

稿件編號：OF7

臨時稿件編號：
0609

金屬蛋白酶組織抑制因子 2 之基因多型性與婦女進行試管嬰兒療程臨床結果相關

Tissue inhibitors of metalloproteinases 2 gene polymorphisms associated with clinical outcomes of women undergoing in vitro fertilization

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論文發表方式：
口頭報告

論文歸類：
生殖內分泌

Objective:
Matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs), involved in the mechanism of extracellular matrix proteolysis, have the ability to regulate the degradation of extracellular matrix and play a key role in trophoblasts invasion. The aim of this study was to examine the effects of single-nucleotide polymorphisms (SNPs) in the MMPs and TIMPs genes of clinical outcomes of women undergoing in vitro fertilization (IVF).
Material and methods:
A prospective study was composed of 1014 women undergoing their first fresh IVF cycle with non-donor in Lee Women's Hospital from January 2014 to December 2015. DNA was extracted from the peripheral blood of all participants, and the SNPs were genotyped by real-time polymerase chain reaction. The effects of the following three single nucleotide polymorphisms (SNPs) on IVF outcomes were explored: TIMP1 (rs4898 C/T), TIMP2 (rs2277698 C/T) and MMP2 (rs243865 C/T). The SNP genotype, correlation with clinical pregnancy, embryo implantation, abortion and live birth rates of IVF were analyzed.
Results:
In the analysis of 1014 patients attempting their first cycle of IVF, TIMP1 and MMP2 gene polymorphisms were no significant difference in clinical outcomes. For TIMP2 polymorphisms, wild genotype (CC) had higher clinical pregnancy rate (34.8% v.s 28.0%; p=0.032), embryo implantation rate (19.4% v.s 15.4%; p=0.009), live birth rate (29.8% v.s 22.1%; p=0.006), and lower abortion rate (7.0% v.s 17.1%; p=0.005) compare with CT/TT genotype.
Conclusions:
This study showed that the minor T allele of TIMP2 (rs2277698 C/T) SNP polymorphisms (CT/TT) was associated with poor clinical outcomes. The mechanism of TIMP2 gene T allele affected the outcome of IVF remains to be determined. Further studies should focus on the mechanism of these associations in a larger, more heterogeneous cohort.

稿件編號：OF8

臨時稿件編號：
0459

精蟲去氧核醣核酸碎片化對於試管嬰兒授卵療程的囊胚染色體非整倍體之影響
Impact of sperm DNA fragmentation on blastocyst aneuploidy from patients undergoing IVF oocyte donation cycles

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論文發表方式：
口頭報告

論文歸類：
生殖內分泌

Objective: Sperm DNA fragmentation is a known etiology for male infertility. The aim of this study was to assess the relationship between sperm DNA fragmentation on blastocyst aneuploidy from patients undergoing IVF oocyte donation cycles.

Materials and Methods: This study collected 24 infertile patients undergoing IVF oocyte donation cycles in Lee women's hospital from Feb. 2019 and Nov. 2020. Sperm samples were identified sperm DNA fragmentation by terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay. Blastocysts were subjected to trophectoderm biopsy and pre-implantation genetic testing for aneuploidies (PGT-A) by next-generation sequencing (NGS).

Results: According to sperm DNA fragmentation index (DFI), IVF oocyte donation cycles were divided into 3 groups: group 1: DFI>=15% (n=5); group 2: 8%<=DFI<15% (n=13); group 3: DFI<8% (n=6). Blastocyst formation rate in group 1 were significantly lower than group 3 (37.3% v.s. 55.8%, p=0.02). And, blastocyst formation rate in group 2 were also significantly lower than group 3 (43.6% v.s. 55.8%, p=0.03). The blastocyst euploidy rates were 26.5% in group 1, 37.6% in group 2 and 35.7% in group 3. The blastocyst mosaic rate were 58.8% in group 1, 40.6% in group 2 and 47.6% in group 3. The blastocyst aneuploidy rate was 14.7% in group 1, 21.8% in group 2 and 16.7% in group 3. Pregnancy rates were 60.0% in group 1, 61.5% in group 2 and 66.7% in group 3.

Conclusions: This study showed that high levels of sperm DNA fragmentation impacts on blastocyst formation rate. But it seems that DFI does not correlate with blastocyst aneuploidy or pregnancy outcomes.

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論文摘要

稿件編號：OF9

臨時稿件編號：
0667

胚胎非整倍體基因檢測後的冷凍囊胚在植入時放置的子宮深度位置對於臨床懷孕率的影響

The influence of the depth of frozen blastocyst replacement into the uterine cavity on clinical pregnancy rate after preimplantation genetic testing for aneuploidy

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論文發表方式：
口頭報告

論文歸類：
生殖內分泌

Background: The influence of the depth of embryo replacement into the uterine cavity has been postulated as being one of the most important factors to the success of an IVF treatment cycle. The ASRM guideline suggested that placement of the catheter tip in the upper or middle (central) area of the uterine cavity, greater than 10 mm from the fundus for embryo expulsion, optimizes pregnancy rates. However, there was no study to evaluate the effect of the depth of frozen blastocyst transfer (FET) replacement on clinical pregnancy rate after preimplantation genetic testing for aneuploidy (PGT-A). This study investigates the influence of the depth of embryo replacement less than 10 mm on the clinical outcomes when controlled embryo quality in PGT-A cycles.

Methods: Data from a total of 114 FET cycles (patients) were collected for this study from 2021 Mar. to 2021 Aug. in Lee Women's Hospital. All patients underwent blastocyst biopsy for PGT-A. Only qualified and expanded blastocyst was selected for trophectoderm biopsy. A hormone replacement treatment (HRT) protocol was used for the endometrium preparation. The procedure of embryo transfer is utilized ultrasound guidance to direct the placement of the catheter tip, allowing for more accurate placement. The patients were matched in three groups according to the distance between the tip of the catheter and the uterine fundus at transfer undergoing ultrasound guided (group A < 5 mm (n=33), group B ≥ 5 and < 10 mm (n=71) and group C ≥10 mm (n=11)). The same method of loading embryos into the embryo transfer catheter was used. All FET cycles have least one euploidy or low mosaicism (30%) blastocyst for transfer.

Results: Average of women age was 37.7±5.9 years. The overall clinical pregnancy and implantation rates were 73.7% (84/114) and 62.7% (138/220), respectively. the average distance of embryo transfer into the uterine cavity was 6±2 mm (range: 2-13 mm). The mean number of embryos transferred no significant difference between the groups (A-C groups: 2.0±0.4, 1.9±0.5, 1.9±0.3). The clinical pregnancy rates between all groups (75.8%, 73.2% and 70.0%, respectively) were no significant difference. The implantation rates between all groups (60.6%, 64.4% and 57.9%, respectively) were no significantly different. Furthermore, in a multivariate regression analysis adjusted for women age and patient characteristics, no significant differences in clinical pregnancy rates between different depths of embryo replacement.

Conclusions: The results suggest that the depth of embryo replacement undergoing ultrasound guided, even less than 10 mm, may not impact the clinical pregnancy and implantation rates after blastocyst FET with PGT-A.

稿件編號：OF10

臨時稿件編號：
0478

利用小鼠囊胚研究冷凍解凍過程對於微型核糖核酸及基因表現的影響

Study on the effect of frozen-thawed process on microRNA and gene expression profiles by blastocyst stage mouse embryos

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論文發表方式：
口頭報告

論文歸類：
生殖內分泌

Objective:
The frozen-thawed embryo is frequently applied in the assisted reproductive technology. The advantage of delayed embryo transfer obtains enough time to wait genetic test results and prepare accepted uterine environment to avoid the risk of ovarian hyperstimulation syndrome. So far, whether the frozen-thawed process would affect embryo development remains to be clarified. The aim of this study is to investigate the effect of frozen-thawed process on embryo development and clarify the underlying regulatory mechanism.
Material and methods:
We explored the effect of frozen-thawed process on embryo development after the embryo transferred. Briefly, the fresh and frozen-thawed blastocysts were separately transferred into different sides of the uteri of 2.5-day pseudo-pregnant female mice. After 5 days, mice were sacrificed and collected tissue of visualized implantation sites. In addition, we collected 100 fresh and frozen-thawed blastocysts and analyzed by microRNA (miRNA) and gene expression profiles using the miRCURY LNA miRNA miRNome PCR Panels and next-generation sequencing (NGS) system, respectively.
Results:
The results of implantation rate in frozen-thawed blastocysts embryo transferred group showed higher than fresh blastocysts transferred group. Compared with the control fresh blastocysts, we found that 36 miRNAs were down-regulated (≤2 fold) and 6 miRNA were up-regulated (≥2 fold) in frozen-thawed blastocysts. In addition, 1606 genes were down-regulated (≤2 fold) and 1215 genes up-regulated (≥2 fold) in frozen-thawed blastocysts. The data indicated that the frozen-thawed process affected the miRNA and gene expression profiles of blastocysts.
Conclusions:
The results showed that embryo implantation rate was slightly improved by the frozen-thawed process but there was no significant effect on embryo development. In addition, we suggested that the miRNA and gene expression profiles of blastocysts were changed during the frozen-thawed process. In the future, we will further elucidate the underlying regulatory mechanism of frozen-thawed process on embryo development. A more detailed understanding of embryo cryopreservation should help improving the clinical use of this technology in reproductive medicine.

台灣婦產科醫學會 111 年度年會暨學術研討會

論文摘要

稿件編號：OF11

臨時稿件編號：
0466

以非侵入性胚胎染色體篩檢預測染色體套數並探討臨床預後

The ploidy prediction by Non-invasive preimplantation genetic testing for aneuploidy in IVF prognosis.

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論文發表方式：
口頭報告

論文歸類：
生殖內分泌

Study Question:
To investigate the concordance of ploidy results between TE biopsy samples and spent culture medium from the same blastocyst by high-resolution NGS platform.

Study Design, Size and Duration:
The study was conducted from March 2021 to Nov 2021 in Lee Womens' Hospital. A total of 97 TE biopsy samples and their spent culture medium (SCM) from 44 couples underwent PGT-A cycles were performed. DNA extracted from the spent culture medium and from TE biopsy samples were analyzed for chromosome abnormalities. This study was approved by the Institutional Review Board of Chung Shan Medical University Hospital (IRB No. CS1-21005). All patients signed an informed written consent.

Materials and Methods:
Ninety-seven freshly cultured day-5/6 blastocysts and their surrounding culture media from couples undergoing in vitro fertilization were included. Embryos were fertilized by intracytoplasmic sperm injection (ICSI) and cultured until the blastocyst stage. The culture medium was changed on Day 3, and assisted hatching was performed on Day 4. On Day 5-6, a trophectoderm biopsy was performed for PGT-A analysis as part of the clinical routine, and SBM was collected from each embryo for niPGTA analysis. TE biopsy samples and SBM cells were lysed and the cell's genomic DNA was amplified using the SurePlex DNA Amplification System. The NGS libraries were prepared using a VeriSeq PGS-MiSeq kit from quantified WGA products. The resulting library pools were sequenced by synthesis on a MiSeq instrument using the VeriSeq PGS recipe. The amplification rate and its affecting factors, the concordance rate between niPGT-A and TE biopsy results were analyzed, and clinical outcomes were also evaluated.

Main Results:
A total of 97 TE biopsy samples and their spent culture medium (SCM) from 44 couples underwent PGT-A cycles were performed. Informatively NGS result of SCM was significantly increased on day 6 compared with day 5 sample collection (75% vs. 100%; P=0.0005). The concordance rate for ploidy of TE biopsy and SCM was 78.3%. 100% concordance rate of sex chromosome means there are no DNA contamination in spent culture medium. There are 11 blastocysts that underwent single embryo transfer (SET), guided by PGT-A results of the TE biopsy. Clinical outcomes were retrospectively calculated in two different scenarios: when euploid TE was concordant with euploid SCM and when euploid TE was discordant with aneuploid SCM. The clinical pregnancy rate for euploid TE/ euploid SCM and euploidy TE/aneuploidy SBM are 50% vs. 100%, respectively. Because of the low number of SETs performed, differences were not significant.

Conclusion:
Spent culture medium is an alternative approach to obtaining embryo DNA. Non-invasive preimplantation genetic testing for aneuploidy (niPGTA) has the potential of applicability in clinical IVF to provide another selection to predict the ploidy status of a blastocyst.

台灣婦產科醫學會 111 年度年會暨學術研討會

論文摘要

稿件編號：OF12

臨時稿件編號：
0666

分裂早期發生多核化之胚胎較易形成高度染色體嵌合狀態

An increased incidence of high-level mosaicism in embryos with the occurrence of multinucleation at early cleavage stages

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論文發表方式：
口頭報告

論文歸類：
生殖內分泌

Background:
In the mouse model, the multinucleation (MN) occurrence at the 2-cell stage (MN2) or the 4-cellstage (MN4) appears to affect blastomere ploidy and compromises blastocyst developmental potential. However, the pregnancy loss rate was not significantly increased by transferring MN-derived blastocysts to surrogate mothers. The effects of MN on embryo ploidy in humans are still under debate and worth further investigation.

Methods:
The current retrospective study was aimed to evaluate the effects of MN on ploidy status of biopsied blastocysts derived from IVF patients using time-lapse (TL) monitoring and next-generation sequencing (NGS)-based preimplantation genetic tests for aneuploidy (PGT-A) and enrolled 178couplesfrom January 2017 to August 2018.The embryonicmorphokintics and morphologywere evaluated by all of the recorded images at118hours post insemination (hpi). The blastocysts with morphology >4CC on day 5 or day 6 were selected for TE biopsy andPGT-A (n = 918).The statistical analysis was performed by generalized estimating equations (GEE), Pearson's chi-squared test, or Fisher's exact test.

Results:
This study revealed that the rates of MN2 (36%) and MN4 (18.9%) in high-level mosaic embryos were higher thanthose of euploid (21.6% and 12.1%), low-level mosaic (22.7% and 11.6%) and aneuploid (20% and 8.2%) embryos. In consideration of confounding variables, i.e.female age, matureoocyte numbers, oocyte sources, the timingof the blastocyst with a full-filled blastocoel (tB), and blastocyst morphology, the GEE analysisdemonstrated the occurrences ofMN2 (odds ratio [OR] = 1.57, 95% confidence interval [CI] = 1.039–2.372, p

Conclusion:
This study demonstrates that multinucleated blastocysts with MN have similar rates of euploidy and low-level mosaicism but a higher rate of high-level mosaicism as compared with non-multinucleated blastocysts. In order to reduce the possibility of selecting blastocysts with high-level mosaicism, this study thus suggests to lower the priority of good morphology blastocysts with MN4 for embryoselection.

稿件編號：OF13

臨時稿件編號：
0473

IL-33 在人類子宮內膜異位症所扮演的角色
Role of IL-33 in human ovarian endometriosis

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論文發表方式：
口頭報告

論文歸類：
生殖內分泌

Introduction
Endometriosis is a leading cause of infertility in women of reproductive age. Currently, various theories on the pathogenesis of endometriosis have been proposed; however, the underlying mechanisms are not clearly elucidated. Among these theories, the most commonly accepted mechanism of endometriosis is Sampson's theory. The theory indicates that viable endometrial cells are shed from the endometrium to the pelvic peritoneum or ovaries, possibly through menstrual retrograde. These cells subsequently attach, invade, and injure other tissues. According to this theory, cytokines that can regulate the growth and angiogenesis of these endometrial cells play a vital role in the progression of endometriosis. Interleukin-33 (IL-33) is expressed in the nucleus of various cell types including endometrial stromal cells. Previous studies showed that IL-33 is a key regulator of many processes including inflammation, angiogenesis, and lesion proliferation, and speculated that IL-33 expression may also have a potential role in the pathogenesis of endometriosis. Therefore, the present study aimed to evaluate the possible role of IL-33 in the pathogenesis of endometriosis.

Materials and methods
The study used human endometriotic stromal cells derived from ovarian endometrioma (hOVEN-SCs) as the experimental cell. Proliferation potential was measured by cumulative population doubling level and colony-forming efficiency. Gene expression was confirmed by RT-PCR analysis.

Results
Previously, our study revealed that 17β-estradiol could increase IL-33 expression through the estrogen receptor pathway in hOVEN-SCs. Moreover, IL-33 upregulated MMP-9 expression in and enhanced the invasion ability of hOVEN-SCs through the MAPK signaling pathway. This study aimed to investigate the effects of IL-33 on the cell adhesion and angiogenesis of hOVEN-SCs. We examined the expression of the cell adhesion molecule (vascular cell adhesion molecule-1, VCAM-1) and angiogenesis molecule (vascular endothelial growth factor, VEGF) in hOVEN-SCs/IL-33 and hOVEN-SCs by RT-PCR analysis. The results found that treatment of hOVEN-SCs with IL-33 significantly increased VCAM-1 and VEGF expression in a dose-dependent manner (0, 1, 2, 3, 4, and 5 ng/ml). Moreover, we observed that IL-33 up-regulated the expression of VCAM-1 and VEGF in hOVEN-SCs through the ST2 (an IL-33 specific receptor)/MAPK signaling pathway. Furthermore, the cell adhesion results showed that 73% and 51% of cells detached from hOVEN-SCs and IL-33-treated hOVEN-SCs monolayer cultures respectively after 12 minutes of trypsinization, indicating that IL-33 can increase hOVEN-SCs adhesion.

Conclusion
These findings indicate that IL-33 may play a key role in the pathogenesis of endometriosis by increasing the adhesion, inflammation, angiogenesis and invasion of endometriotic stromal cells. Further investigation on the IL-33 signaling pathway contributes to developing more effective treatments for endometriosis.

台灣婦產科醫學會 111 年度年會暨學術研討會

論文摘要

稿件編號：OF14

臨時稿件編號：0472

褪黑激素透過降低 COX-2 表現對 BPA 刺激而減少 Cx43 間隙連接蛋白表現之顆粒細胞產生保護作用

Protective effect of melatonin on BPA-reduced Cx43 gap junction protein expression in human granulosa cells by down-regulation of COX-2 expression

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論文發表方式：口頭報告

論文歸類：生殖內分泌

Introduction
Female infertility may be closely related to endocrine-disrupting chemicals (EDCs) such as bisphenol A (BPA), which are widely used in the production of epoxy resins and polycarbonate plastics. Many studies have shown that important signaling pathways involved in folliculogenesis and oocyte maturation are mediated by gap junctions. BPA may cause reproductive toxicity by inducing apoptosis of granulosa cells (GCs), altering oocyte maturation by prematurely closing gap junctions in the GCs-oocyte complex. Connexin43 (Cx43) is an important gap junction protein required for communication between GCs and GCs or oocytes, which is present at every stage of folliculogenesis. Studies have shown that increased expression of cyclooxygenase-2 (COX-2) contributes to aberrant expression of connexin in many cell types. Melatonin, well-known for its anti-inflammatory and antioxidant effects, can participate in the regulation of reproductive processes. Former studies have shown that melatonin has therapeutic effects on steroidogenesis, folliculogenesis and oocyte maturation in PCOS. The aim of this study is to investigate whether melatonin has protective effects on BPA-treated GCs reproductive toxicity.

Materials and methods
The human GCs were collected from patients undergoing IVF procedures after controlled ovarian stimulation. To explore the effect of melatonin on BPA-induced Cx43 and COX-2 expression of GCs, we used RT-PCR and western blotting assays in this study.

Results
Previously, we reported that BPA (10-7 M) could down-regulate Cx43 expression through the estrogen receptor-dependent signaling pathway in GCs. In this study, we found that BPA treatment of GCs significantly increased COX-2 gene expression. Next, we analyzed the dose-dependent effect of melatonin (concentration: 10-5 to 10-8 M) on the expression of Cx43 and COX-2 in BPA-treated GCs. The results showed that GCs treated with melatonin (concentrations: 10-5, 10-6, and 10-7 M) significantly inhibited the expression of the COX-2 gene increased by BPA. In addition, melatonin (concentration: 10-5 M) significantly restored Cx43 gene expression in GCs with reduced BPA. We also conducted experiments to clarify the effects of melatonin on the expression of Cx43 and COX-2 in BPA-treated GCs, and further explained the underlying mechanisms of these effects. The results showed that the expression of COX-2 was essential for BPA-reduced Cx43 expression of GCs, as the effect can be negated by NS398 (a selective COX-2 inhibitor).

Conclusion
Our current results speculate that melatonin restores the expression of Cx43 in BPA-treated GCs by reducing the expression of COX-2. However, this mechanism needs more evidence to further clarify this hypothesis.

稿件編號：OF16 臨時稿件編號： 0630	chromosome inv(9)(p12q13) 在不明原因男性不孕的角色 Role of chromosome inv(9)(p12q13) in unexplained male infertility 停寧萱[1] 陳寶珠[1] 花蓮慈濟醫院[1]
論文發表方式： 口頭報告 論文歸類： 生殖內分泌	Objective Chromosome inv(9)(p12q13) is a common normal variant polymorphism in humans. However, poor reproductive outcomes related to de novo or familial inv(9)(p12q13) were reported. We found a man with chromosome inv(9)(p12q13) presented with 80% of embryos being chromosomal multiploidy. The gene manipulations among this inversion region were explored. Methods At the region of the breakpoint, 5 genes (PRKACG, DCTN3, C9orf24, SPATA3 and TESK1) related to G2M transition were tested for the effect on cell division. Knockdown (siRNA) and overexpression (adenovirus) of the Dynactin subunit 3 (DCTN3) gene for testing its function. Three cell lines including embryonic carcinoma (NCCIT), trophoblast cell (NTERA-2) and fibroblast were used for the above experiments. Results Knockdown of DCTN3, TESK1, C9orf24 genes showed polyploidy and DCTN3 was known as microtubule related genes. Knockdown of DCTN3 led to cell multiploidy in above cell lines. But overexpression of DCTN3 did not show any chromosome abnormality in above cell lines. Interestingly, both knockdown and overexpression of DCTN3 led to an increase in the expression of stem cell markers (LGR5, SOX-2). Conclusion DCTN3 is found to play an important role in cell division, especially in the G2M phase of the cell cycle. Further exploration of the role of DCTN3 in male reproductive medicine can be anticipated.