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Objective
The circadian rhythm, which is controlled by the central clock in the suprachiasmatic nucleus of the hypothalamus and the peripheral clock in other tissue, regulates physiological functions such as fluctuations of body temperature, blood pressure and hormone secretion. It has been reported that women having shift work increase the prevalence of ovulation disorders, infertility and recurrent pregnancy loss. Thus, it is warned that disturbing circadian rhythms may impair female reproductive functions. In fact, deletion of one of the core clock genes, brain and muscle aryl hydrocarbon receptor nuclear translocator-like protein 1 (Bmal1), in mouse whole body (Bmal1 KO) show female infertility due to suppression of progesterone biosynthesis in ovaries. However, Bmal1 functions in uterus have not known yet.

Methods
To study Bmal1 functions in uterus during pregnancy, we generated uterine-specific Bmal1 deletion (Bmal1 cKO) mice by crossing progesterone receptor (PR) Cre and brain and muscle aryl hydrocarbon receptor nuclear translocator-like protein 1 (Bmal1) floxed mice.

Results
Despite normal ovarian function, Bmal1 cKO mice did not deliver any pups due to the impairment of maternal neovasculogenesis in decidua on day 8 and in placenta on day 12 of pregnancy.

Conclusion
Deletion of Bmal1, the core clock gene, in the uterus decreased reproductive function in mice. The circadian clocks, especially within the reproductive organs, will provide new therapeutic interventions for treating reproductive dysfunction.

11. THE ANALYSIS OF THE ASSOCIATION BETWEEN FETAL VASCULAR MALPERFUSION AND THE PERINATAL / NEONATAL CLINICAL COURSE
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Objective
Fetal vascular malperfusion (FVM) is the recommended new terminology for fetal thrombotic vasculopathy by the Amsterdam Placental Workshop Consensus Statement. The present study aimed to investigate relationship between FVM and the perinatal and neonatal clinical course in our hospital.

Methods
The placentas were obtained from January 2015 to December 2020 in Hamamatsu university hospital. We selected the case that were examined pathologically and have positive findings of FMV. Clinical course was referred retrospectively from patient chart, we investigated the association between FMV and clinical course of perinatal course or neonatal outcome.

Result
We compared with and without FMV cases by clinical findings. 587 placentas were submitted pathological examination among 4091 cases, and 51 (8.6%) placentas were diagnosed as FVM. ‘Intrauterine fetal death’, ‘abnormality cord insertion’, ‘small for dates infant’ were significantly higher than the cases without findings of FMV. There were no significant differences of oligohydramnios, hypertensive disorders of pregnancy, non-reassuring fetal status, emergency cesarean section, coiling of cord, hyper coiled of cord, thin cord (<8 mm), neonatal asphyxia, respectively.

Conclusion
FVM is related to IUFD, abnormal cord insertion. Further study is needed to examine about the risk factors of FVM that can detected in daily prenatal checkup.
Objective
To date, the low probability of COVID-19 vertical transmission must be attributed to local immune responses, though we do not have enough information in placenae obtained from SARS-CoV-2 infected mothers. Here, we investigated the immunopathological characters of placenta associated with SARS-CoV-2 infection.

Methods
This study was approved by the ethical committees of each institution. Sixteen placental samples from COVID-19 patients and 3 control samples were investigated. Immunohistochemical detections of the viral spike protein, CD3 (T cell), CD20 (B cell), and CD163 (Hoebbauer cells) were performed in formalin-fixed paraffin-embedded tissue sections.

Results
The viral spike protein was detected in all samples. Some cases showed fibrin depositions and infarctions. In one case, the spike protein was still found in syncytiotrophoblast, although approximately 30 days had passed after the first confirmation of SARS-CoV-2 infection, even after the disappearance of the antigen and PCR testing of the respiratory specimen. In the 6 cases examined, the number of CD3+, and CD20+ cells were significantly increased in fetal vessels (7.67±1.86 vs 2.33±0.67/10 HPFs, 3.67±0.80 vs 0.67±0.33/10 HPFs). The number of CD3+ cells in intervillous space also tended to increase.

Conclusion
In spite of the detection of viral spike protein in syncytiotrophoblast, no evidence of vertical transmission was found in all cases, indicating that the placentical barrier may inhibit vertical transmission. Some chemokines from maternal blood might come across the placentical barrier and recruit fetal lymphocytes. Further investigations are required to confirm the subsets of lymphocytes and their immunological roles in maternal-fetal interactions.

14. THREE CASES OF PLACENTA ACCRETA THAT WERE TREATED DIFFERENTLY IN OUR HOSPITAL

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Introduction
In this article, we report three cases of placenta accreta, each of which had a different course, and discuss how to deal with placenta accreta.

Case 1: 30 years old.
After vaginal delivery, she did not deliver the placenta and was brought to our hospital, where an MRI revealed placenta accreta. After discharge from the hospital, she visited our outpatient department with complaints of genital bleeding and fever, and was readmitted. Because of persistent active bleeding and SI >1, we attempted manual dissection under general anesthesia in the operating room, but the bleeding continued, so we performed a suprapubic amputation.

Case 2: A 33-year-old.
The fetus died in utero at 38 weeks’ gestation, and she was admitted to our hospital. Subsequently, labor occurred and the baby was delivered. Manual abruption of the placenta was attempted, but it could not be delivered, and persistent bleeding was observed. Subsequently, SI >1.5, and a partial hysterectomy was performed.

Case 3: A 32-year-old.
Induced labor was performed at her previous doctor’s office due to an overdue delivery. The mother was transported to our hospital for delivery arrest, and delivered vaginally at our hospital. Because the placenta was not delivered and the blood loss was small, we decided to wait for spontaneous delivery without performing manual placental abruption. On the 78th day after childbirth, genital bleeding was observed, and the patient was admitted to our hospital, where the placenta was delivered spontaneously.

Conclusion
The management of placenta accreta has not been clearly defined, and it is necessary to decide the management and treatment plan for each individual case, taking into consideration various factors such as the state of bleeding, signs of infection, and whether the patient wishes to preserve the uterus.

15. EXPRESSION ANALYSIS OF THE ALTERNATIVE SPlicing OF DROSHA IN THE TROPHOBLAST CELL LINE BeWO

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Objective
The RNAS III enzyme DROSHA cleaves pri-miRNA into pre-miRNA in miRNA biosynthesis in the nucleus. However, the function of DROSHA in the cytoplasm remains unclear. It has been reported that DROSHA gene has a region (exon 7) with a signal to keep it in the cytoplasm, and its expression is regulated by alternative splicing. In this study, we investigated the expression of DROSHA splicing variants in the trophoblast cell line BeWo.

Methods
We analyzed the mRNA expression of four splicing variants [exon 6/7 (+/+), exon 6/7 (+/-), exon 6/7 (-/+), exon 6/7 (-/-)] in the exon 6 and 7 regions of DROSHA in non-syncytialized (wild type) and syncytialized BeWo cells by real-time PCR. Syncytial fusion of BeWo cells was induced by stimulation of forskolin.

Results
Real-time PCR analysis showed that in wild type BeWo cells, the percentage of variants with exon 7 was about 78%, while the percentage of exon 7-deficient variants was about 22%. After syncytial fusion, the percentage of variants with exon 7 was about 71%.

Conclusion
Regardless of syncytialization of BeWo cells, DROSHA may not only translocate to the nucleus but also retain in the cytoplasm.

16. TWO CASES OF MONOCHORIONIC-DIAMNIOTIC TWINS WITH DIFFERENT PHENOTYPES

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Introduction
Here we report two cases of monochorionic-diamniotic twin (MD twin) pregnancies with morphological abnormalities for only one of fetuses.

Case1
The patient is a 29-year-old primipara. After spontaneous pregnancy, she was diagnosed MD twin pregnancy at first trimester. She was referred to our hospital at 15weeks’ gestation due to cystic hygroma of fetus A. She didn’t wish to have chromosome analysis. Fetus A presented selective FGR (-1.6→-3.0SD) and single umbilical artery. Fetus B showed neither anomalies nor FGR. She delivered by elective C/S at 37weeks’ gestation. Infant A was a 1,560g female, Apgar score 8/9. Infant B was a 2,154g female, Apgar score 8/9. Infant A was admitted to NICU and noted ASD, VSD, and PDA. This infant is still in NICU.

Case2
The patient is a 33-year-old one-parity woman. After spontaneous pregnancy, she was diagnosed MD twin pregnancy at first trimester. She was referred to our hospital at 17weeks’ gestation due to abdominal cyst of fetus A. Fetus A presented omphalocele, spina bifida, left renal aplasia, lung hypoplasia, and single umbilical artery. The bladder and external genitalia were unclear, suggesting OEIS complex. She didn’t wish to have chromosome analysis. Fetus B showed FGR (-1.6→-3.0SD) after 30weeks’ gestation, without any anomalies. She delivered by elective C/S at 35weeks’ gestation. Infant A was 2,378g, Apgar score 3/3. External genitalia was immature and sex was indeterminate. Infant B was a 1,690g female, Apgar score 8/9.