Introduction: Feto-maternal tolerance is essential for pregnancy maintenance. Seminal priming induces temporal inflammation and immature uterine DCs that would be related to tolerogenic DCs at the time of implantation. Additionally seminal plasma has been proposed to contribute to tolerance. We clarified dynamic changes of uterine DC phenotype related to sperm and seminal plasma.
Materials & Methods: Female C57BL/6 mice were mated with male intact, seminal vesicle-excised (SVX), or vasectomized (VAS) BALB/c mice. Non-mated control mice were prepared in the estrous stage. Uterine DCs were analyzed at days 1.5 and 3.5 post-coitus (pc) by using the flow cytometry.
Results & Discussion: Uterine $CD45^+F4/80^-CD11c^+$DCs were classified into $CD103^-$DCs, $CD103^+$DCs, and PDCA-1^+plasmacytoid DCs (pDCs). In addition, those were subdivided into immature and mature DCs based on their expressions of CD86 and MHC class II. At day1.5 mature DCs in $CD103^-$DCs and $CD103^+$DCs were increased in intact and SVX, but not changed in VAS. At Day3.5 immature DCs were increased in each mating. Then the level of PD-L2 expression on mature DCs were upregulated than immature DCs before implantation.
Conclusion: Seminal plasma might contribute to tolerogenic condition without maturation of DCs. Before implantation it might be two types of uterine DCs. One is the immature DCs as it used to be proposed, the other is mature DCs expressing PD-L2 which contribute to induction of feto-maternal tolerance by inhibiting effector T cells.

9.
LNCRNA H19-DERIVED MIR-675-5P IS INVOLVED IN THE REGULATORY MECHANISM OF TROPHOBLAST INVASION

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Objective: MicroRNA *miR-675-5p* is generated from long non-coding RNA (lncRNA) *H19* that is highly expressed in human trophoblasts, especially extravillous trophoblasts (EVTs). However, the role of *miR-675-5p* in EVTs is not established. In this study, we investigated the effect of *miR-675-5p* on EVT invasion; moreover, we compared the expression levels of *miR-675-5p* between normal and preeclampsia (PE) placentae.
Methods: For evaluation of the effect of *miR-675-5p* on EVT invasion, *miR-675-5p* was overexpressed in the HTR-8/SVneo EVT cell line. Cell invasion ability and gene expression were evaluated by Matrigel-coated Transwell assay and real-time PCR, respectively. For analysis of *miR-675-5p* expression in the human placenta, placental samples were obtained from the pregnant women who gave informed consent (normal: $n = 10$, early onset PE: $n = 7$, late onset PE: $n = 4$). The expression levels of placental *miR-675-5p* were evaluated by real-time PCR.
Results: Regarding evaluation of the effect of *miR-675-5p* on EVT invasion, cell invasion was significantly activated in *miR-675-5p*-overexpressing HTR-8/SVneo cells. Cell invasion-related genes (e.g., *CXCL12*) were significantly upregulated in the cells. As to *miR-675-5p* expression in the human placenta, its expression was significantly upregulated in early onset PE placentae (1.82-fold median increase) and late onset PE placentae (1.73) as compared with normal placentae.
Conclusion: Our findings suggest that *miR-675-5p* accelerates EVT invasion. Aberrant expression of *miR-675-5p* might be involved in the pathogenesis of PE.

10.
DAMAGE OF AMNIOTIC EPITHELIUM BY DNA OXIDATIVE STRESS IN DIFFUSE CHORIOAMNIOTIC HEMOSIDEROSIS

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Introduction: The amniotic membrane plays an important role in the physiological maintenance and protection of the embryo. Dysfunction of the amniotic membrane is thought to have an adverse effect on the continuation of pregnancy. Diffuse chorioamniotic hemosiderosis (DCH) occurs when marginal or sub-chorionic placental hemorrhage migrates into the amniotic fluid and diffusely deposited as hemosiderin in the chorionic plate or membrane. Amniotic epithelial necrosis is frequently identified in DCH. In this report, we examined the pathological changes in the amniotic epithelium in three cases of diffuse chorioamniotic hemosiderosis (DCH) and investigated the relationship with DNA oxidative stress.
Result: DCH was confirmed by berlin blue staining, and amniotic necrosis was severe depending on the deposition of hemosiderosis. Immunostaining of 8-OHdG (8-hydroxy-2'- deoxyguanosine) which is a marker of DNA oxidative stress showed that presence of 8-OHdG in amniotic epithelium was positive in the amniotic epithelial cells.
Discussion: In this report, we describe two new findings: (i) the severity of DCH is related to amniotic epithelial necrosis, and (ii) the amniotic epithelium sustains oxidative stress in association with DCH. We speculated that oxidative DNA damage of the amniotic epithelium occurs by decomposition products of blood cells in cases of sub-chorionic hematomas and pathological DCH. Disorders of the amniotic epithelium may also disrupt the balance of the amniotic fluid volume and cause oligohydramnios.

11.
THE PREDICTION OF ABNORMALLY INVASIVE PLACENTA IN SUBSEQUENT PREGNANCIES AFTER UTERINE ARTERY EMBOLIZATION FOR POSTPARTUM HEMORRHAGE

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Objective: It has been reported that pregnant women with histories of uterine artery embolization (UAE) are at high risk for abnormally invasive placenta (AIP). The aim of this study was to evaluate the predictive accuracy of imaging examinations for AIP in subsequent pregnancies after UAE for postpartum hemorrhage (PPH).
Methods: This retrospective study enrolled 14 pregnant women with histories of UAE for PPH who underwent both ultrasonography (US) and magnetic resonance imaging (MRI) during subsequent pregnancies from 2011 to 2019. US finding of grade 3 placental lacunae, bridging vessels, and loss of clear zone were evaluated, in addition to MRI findings. The predictive accuracy was evaluated.
Result: Six of the 14 women (43%) were diagnosed as having AIP. In three of the 6 pregnant women (50%) with both histories of UAE and AIP, AIP could be predicted by imaging examinations, two by both US and MRI, and one by MRI alone. On the other hand, two of the eight pregnant women (25%) who had US or MRI findings suggestive of AIP didn't have AIP. The sensitivity, specificity, PPV, and NPV were 60%, 67%, 50%, and 75%, respectively.
Conclusion: The predictive accuracy of US and MRI examinations for AIP was not so high. In subsequent pregnancies after UAE for PPH, we must consider the risk of AIP despite the results of prenatal imaging examinations.

12.
CLINICAL CHARACTERISTICS OF DECIDUITIS IN THE PLACENTA AT THE TIME OF THE MID-TRIMESTER MISCARRIAGE AND PRETERM DELIVERY

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Objective: Patients who had a miscarriage or preterm delivery in the mid-trimester are often found with deciduitis associated with severe inflammation in the decidua. The aim of this study is to investigate the presence or absence of deciduitis and its clinical background in the mid-trimester miscarriage and preterm delivery cases.
Methods: The subjects were 37 patients who had a miscarriage or preterm delivery in the mid-trimester due to labor pains or amniorrhexis between

January 2012 and December 2018. Deciduitis was defined as one with inflammatory cell infiltration including plasma cells and lymphocyte infiltration in the decidua or the one with inflammatory cells invading from the decidua to the villus and decidual necrosis. Chorioamnionitis (CAM; C) and deciduitis (D) were assessed microscopically. Then, the patients were classified into the following 4 groups to investigate maternal/clinical backgrounds: C(-)D(-), C(+)D(-), C(-)D(+), and C(+)D(+) group.
Result: CAM and deciduitis were observed in 29 patients (78%) and 21 patients (57%), respectively. There were 4 patients in the C(-)D(-) group, 12 in the C(+)D(-) group, 4 in the C(-)D(+) group, and 17 in the C(+)D(+) group. The average age in the D(+) group was lower than the other groups. The patients in the D(+) group were likely to repeat miscarriage and preterm delivery and get complicated with decidual polyp.
Conclusions: It was suggested that deciduitis is the important factor when taking precautions for the next pregnancy.

13.
RETROSPECTIVE ANALYSIS OF THE ASSOCIATION OF OPAQUE FETAL MEMBRANE WITH CHORIOAMNIONITS AND EARLY NEONATAL COMPLICATIONS

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Objective: Opaque fetal membrane is known as one of the abnormal findings of the placental gross screening which has been liked with histological chorioamnionitis (CAM). However, its sensitivity and specificity has not been established for predicting histological CAM or poor neonatal outcome. The aim of the present study is to retrospectively evaluate the association of the opaque fetal membrane with incidence of histological CAM and early neonatal complications.
Methods: Total 571 placentas were retrospectively enrolled to the study, because the records of both gross and histopathological findings were available, among 5201 deliveries at Hamamatsu University Hospital from April 2010 to March 2017. We evaluate the association of the presence of opaque fetal membrane with the incidence of CAM. Then, logistic regression analysis was performed to test if opaque fetal membrane could be a risk factor of neonatal respiratory disorder.
Results: Among 571 placentas, positive opaque fetal membrane was observed in 220 cases, but not in 351 cases. CAM was observed in 180 in the positive group and 97 cases in the negative group. Positive and negative predictive value of CAM were 81% (180/220) and 28% (97/351), respectively. Opaque fetal membrane was identified as the independent risk factor of neonatal complications that could cause breathing problems (OR: 1.81; 95% CI [1.05-3.12]).
Conclusion: Gross screening of opaque fetal membrane is clinically efficient to predict the presence of histological CAM as well as the predisposition to neonatal complications.

14.
IMPACT OF HUMAN CYTOMEGALOVIRUS INFECTION ON TROPHOBLAST TRANSCRIPTOME

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Objectives: Placental dysfunction is known as a pathological factor triggering fetal growth restriction in human cytomegalovirus(HCMV) infection. This study aimed to investigate the impact of HCMV infection on gene transcriptome in cytotrophoblasts(CTBs) associated with placenta dysfunction.
Methods: Human placentas were obtained from term deliveries. CTBs isolated from the placentas were infected with AD169rev, a HCMV strain. CTBs were collected at 72 hours after infection. The transcriptome profiles were compared between CTBs groups with and without infection by CAGE-seq. KEGG pathway analysis were utilized in the analysis of the gene expression data. The syncytialization of the CTBs with and without HCMV infection was assessed by hCG secretion and by immunostaining for cell surface desmoplakin.
Results: A total of 629 differentially expressed genes(DEGs) were identified. KEGG pathway analysis demonstrated that DEGs were enriched in the signaling pathways related to cell cycle, focal adhesion. Most of the genes known to be up-regulated with syncytialization were suppressed in the cultured CTBs with HCMV infection. Additionally, this gene suppression under HCMV infection was concurrent with the reduced hCG secretion. Immunostaining for cell surface desmoplakin revealed that HCMV reduced the cell fusion of cultured CTBs. These findings imply that HCMV infection has negative impact on the syncytializing process that is indispensable for the maintenance of virus function.
Conclusion: HCMV infection interferes with gene expression profile and functional differentiation in CTBs.

15.
A CASE OF PLACENTAL POLYP SAFELY REMOVED WITH HYSTEROSCOPIC OBSERVATION

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Introduction: Placental polyp is a rare disease occurring from placental tissue, which remain in the uterus after miscarriage or delivery. Spontaneous regression is possible. However, an abundant blood flow could lead to a severe hemorrhage by intrauterine manipulation. Here, we report the case with a placental polyp, which was safely removed with hysteroscopic observation.
Case: A 28-year-old G1P0 woman was diagnosed with miscarriage at 12 weeks of pregnancy. The patient underwent dilation and curettage at another hospital. Two months later, she visited the doctor due to missed period. A uterine mass was confirmed, and she was subsequently referred to our hospital. A transvaginal ultrasonography showed a mass measuring 18×11mm with abundant blood flow in the uterine cavity. Her serum hCG was 87.5 IU/ml. MRI revealed a remarkable contrast effect of the tumor and flow void by T2 weighted images. As a consequence, a placental polyp was suspected. Because of childbearing desire, we firstly performed a hysteroscopic observation. Hysteroscopy revealed a broad-sided polyp on the uterine anterior wall. Due to lack of blood flow evaluated by hysteroscopy and ultrasonography, the mass was removed using a curette. Intraoperative blood loss was small. Postoperatively, serum hCG levels became undetectable.
Histological examination was consistent with placental polyp.
Conclusion: Transvaginal ultrasonography and macroscopic observation by hysteroscopy confirmed that the placental polyp's blood flow spontaneously regressed, leading to a successful resection.

16.
TRANSCRIPTOMIC FEATURES OF HUMAN INDUCED PLURIPOTENT STEM CELL (HIPSC)-DERIVED TROPHOBLAST LINEAGE CELLS

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Objective: In the previous study, we established a culture system of human induced pluripotent stem cell (hiPSC)-derived trophoblast (TB) lineage cells. Although such differentiated cells are heterogeneous, it may be possible to elucidate novel genes expressed in TBs by analyzing their features. In this study, we isolated the cells that expressed the pan-TB marker KRT7, and performed comprehensive gene expression analysis.
Methods: Four types of hiPSCs were treated with 50 ng/mL of BMP4 for 10 days. KRT7-positive cells were purified using flow cytometry and analyzed by DNA microarray. Differences in gene expression profiles between KRT7-positive cells and hiPSCs were compared.