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caused by maternal blood flow, on trophoblast development in early pregnancy.

**Methods**

We generated trophectoderm-like cells from human naive induced pluripotent stem cells (iPSCs). After differentiation to trophoblast-like cells, they were seeded to the micro chamber slide. The cells were placed under shear stress (10 dyn/cm², or static condition: 0 dyn/cm²) by computer-controlled flow culture system (Ibidi pump system) with treatment of forskolin. The quantitative polymerase chain reaction of mRNA and immunofluorescence staining of E-cadherin and hCG was performed.

**Results**

The mRNA expressions of placental growth factor, and ERVW-1, (which can serve as marker of trophoblastic invasion and formation of the syncytiotrophoblasts) were higher in the trophoblasts under the shear stress compared to those under static condition (5.98 and 3.15-fold higher, respectively, p<0.05). Concomitantly, the fusion index was significantly increased by flow condition compared to static condition (3.0 fold higher, p<0.05). In immunofluorescence, hCG positive cell area was increased (3.05 fold higher, p<0.05).

**Conclusion**

Our results indicated that the shear stress generated by maternal blood flow in the intervillous space is necessary for syncytialization of trophoblasts.

### 41. PATHOLOGICAL FINDINGS IN PLACENTAS OF PREGNANT WOMEN WITH COVID-19

Hikari Nembashi 1,2,3, Ken Takahashi 1, Yukari Kobayashi 1, Mariko Sato 1, Satoru Funaki 1, Yuki Ito 1, Masami Iwamoto 1, Hiroyuki Takahashi 1, Hirotaka Kanuka 2, Osamu Samura 1, Aikou Okamoto 1. 1 Department of Obstetrics and Gynecology, The Jikei University School of Medicine; 2 Department of Pathology, The Jikei University School of Medicine; 3 Department of Tropical Medicine, The Jikei University School of Medicine

**Purpose**

The effects of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection on the fetus and placenta of women who develop coronavirus disease (COVID-19) during pregnancy have not been determined. Therefore, we evaluated placental histopathological findings in pregnant women with COVID-19, as well as the status of SARS-CoV-2 infection in the placenta.

**Methods**

We examined placental histopathological findings in pregnant women with COVID-19 who underwent delivery management at our hospital between April 2020 and April 2021. In addition, quantitative reverse transcription polymerase chain reaction (RT-qPCR) was performed on a section of the placental tissue to evaluate SARS-CoV-2 infection. This study was approved by the Jikei University Hospital Ethics Committee (approval number: 32-478).

**Result**

A total of 11 patients were included: two, three, and six patients were diagnosed during the 1st, 2nd, and 3rd trimesters, respectively. Acute presentation was seen in one patient with severe pneumonia, while the others had mild COVID-19-related symptoms, such as fever and cough; RT-qPCR of the placenta was negative in all cases. Histopathological findings suggestive of circulatory disturbances, such as infarction, intervillous thrombus, and subchorionic hematoma, were found in 7 of 11 cases (63.6%), but all were mild, involving less than 10% of the total placenta. Peri-and intervillous fibrin deposition and calcified deposits were frequently observed. Choriocarcinoma edema and histiocyte infiltration of the intervillous spaces were partially prominent in two cases. In the case with severe pneumonia, subchorionic hematoma was found in less than 5% of the total placenta, but this was not significantly different from that in non-severe cases. Furthermore, there were no findings suggestive of impaired fetal vascular reflex, such as thrombi or recanalization in the vessels of the stem villi.

**Conclusion**

In this study, we found no SARS-CoV-2 infection in the placenta. The observed placental histopathological findings are non-specific to COVID-19 cases.

### 42. PLACENTAL PATHOLOGY PREDICTS INFANTILE NEURODEVELOPMENT DURING 10-40 MONTHS: HAMAMATSU BIRTH COHORT FOR MOTHERS AND CHILDREN (HBC STUDY)

Megumi Ueda 1, Chizuko Yaguchi 1, Masako Matsumoto 1, Naomi Isomura 1, Hiroaki Ito 1. 1 Department of Obstetrics and Gynecology, Hamamatsu University School of Medicine

**Objective**

The present study aimed to investigate relationship between placental pathological findings and neurodevelopment in infants during 10 to 40 months.

**Methods**

Study participants were 258 cases from singleton pregnancies enrolled in HBC Study. Neurodevelopment was assessed by Mullen Scales of Early Learning (gross motor, visual reception, fine motor, receptive language, expressive language) at 10-40 months. Placental pathological findings were reviewed based on the Amsterdam placental workshop group consensus statement, including Maternal vascular malperfusion (MVM: Accelerated villous maturation and Decidual vasculopathy), Fetal vascular malperfusion (FVM: Avascular villi and Thrombosis or Intramural fibrin deposition), Delayed villous maturation, Maternal inflammatory response (MIR), Fetal inflammatory response (FIR), Deciduitis, and Villitis of unknown etiology (VUE). Mixed model analysis was performed for neurodevelopment and placental pathology.

**Results**

Of the 258 cases, 120 cases were MVM (67 cases of Accelerated villous maturation and 92 cases of Decidual vasculopathy), 86 cases were FVM (26 cases of Avascular villi and 76 cases of Thrombosis or Intramural fibrin deposition), 50 cases of Delayed villous maturation, 103 cases of MIR, 55 cases of FIR, 14 cases of Deciduitis and 15 cases of VUE. The analyses identified ‘Accelerated villous maturation’, ‘Delayed villous maturation’, and ‘MVM’ as significant predictors of relatively delayed achievement of neurodevelopmental milestones. On the other hands, ‘Avascular villi’, ‘Thrombosis or Intramural fibrin deposition’, ‘Fetal inflammatory response’, and ‘FVM’ were identified as significant predictors of relatively faster achievement of neurodevelopmental milestones.

**Conclusion**

The present study is the first to report that some placental pathological findings are bidirectionally associated with the progress of infantile neurodevelopment during 10-40 months of age.

### 43. FROM NAIVE IPS CELLS TOWARD HUMAN PLACENTAL TISSUE VIA TROPHECTODERM

Shingo Ito 1,2,3, Eiji Kondoh 3, Yasuhiro Takashima 4, Masaki Mandai 1. 1 Department of Gynecology and Obstetrics, Kyoto University; 2 Department of Obstetrics and Gynecology, Kosaka Women’s Hospital; 3 Department of Obstetrics and Gynecology, Kumamoto University; 4 Department of Life Science Frontiers, Center for iPS Cell Research & Application, Kyoto University

**Objective**

Abnormal differentiation of trophoblasts during early pregnancy is supposed to cause placenta-related complications. To elucidate the