Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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of syncytiotrophoblast. These findings supported that the increased HMGB1 and TM levels in the peripheral blood of PE women originated from the placenta.

In conclusion, HMGB1 released from the dysfunctional placenta is deeply involved in the pathogenesis of PE and that inhibition of HMGB1 action by TM leads to improvement of placental function. Treatment strategy aiming to inhibit HMGB1 action, including TM, is a new therapeutic approach for PE.

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**Symposium 2-4**

Preventive effect of lactoferrin on late miscarriage and premature birth from the viewpoint of infection and immune control

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Prevention of preterm birth (PTB) is a global challenge and is one of the most important issues to be addressed in perinatal care. The hypothesis that ascending lower genital infection leads to PTB has been tested in numerous *in vitro* and *in vivo* studies. For patients with intractable vaginitis or high-risk patients with successive PTBs, mainly due to intra-uterine infection, the vaginal flora is enhanced to increase systemic immunity and locally propagate *Lactobacillus* species. It has been shown that the administration of lactoferrin, a prebiotic with minimum side effects, may be effective in suppressing PTB. This hypothesis has been evaluated in this presentation using various relevant test examples. The findings suggest that LF may play a role in inflammatory protection in human pregnant cervical tissue. It was clarified that LF suppresses PTB and improves the prognosis of pups in the inflammation-induced PTB animal models. Thus, we have identified the first ever clinical application of LF, a prebiotic contained in breast milk, for the purpose of suppressing PTB in humans. It can be used to prevent PTBs in high-risk pregnancies. In addition, we will introduce the possibility of improvement effect of LF for chronic endometritis before pregnancy, including recent findings and our own cases.

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**Symposium 2-5**

Clinical characteristics of pregnant women with COVID-19 in Japan from a nationwide questionnaire survey

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**Background:** We examined the clinical characteristics and outcomes of pregnant women with COVID-19 on a national scale in Japan.

**Methods:** A nationwide questionnaire-based survey for all maternity services in Japan by the Japan Association of Obstetricians and Gynaecologists was conducted in July 2020 and July 2021, respectively. Information regarding maternal characteristics and epidemiological, clinical, treatment, and perinatal outcomes of pregnant women with COVID-19 during the first wave and second to fourth wave were collected.

**Results:** Responses from 1,418 and 1,288 institutions were collected. Responses from 1,418 and 1,288 institutions were collected. Seventy-two and 1,474 pregnant women with COVID-19 were reported in the first wave and second to fourth wave, respectively. The most common route of infection was familial. Of the all patients, 80% were symptomatic, 7% had severe respiratory symptoms and one died (a tourist). The third trimester of pregnancy was the most common timing of diagnosis and severe cases were frequently reported in late pregnancy compared with in early pregnancy. Most pregnant women with COVID-19 had a cesarean section if delivery was necessary. In severe cases, preterm delivery due to infection was also common. There were no SARS-CoV-2 transmissions to newborns.

**Conclusions:** The importance of infection prevention should be emphasized, especially in women in late pregnancy, their families, and any cohabitants. The pregnant women in late pregnancy with COVID-19 need careful observation and follow-up.

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**OP-1**

IL-18 induces appropriate inflammatory responses contributing placental development and fetal growth

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IL-18 has pro- and anti-inflammatory effects. However, only a few studies have demonstrated its role in reproduction. Here, we developed the fetal growth restriction model mouse and examined the effect of IL-18 on fetal growth. The C57BL/6 female mice were mated with the BALB/c male mice, the anti-IL-18 neutralizing antibody was administered intraperitoneally, and the placenta and birth weight were measured. The pregnant uteri were analyzed using flow cytometry, western blotting, and immunofluorescence staining. The blockade of IL-18 significantly decreased in placenta and birth weight compared with control. The blockade of IL-18 also induced a decreased production of IFN-γ in the uterine T cells and NK cells, M2-polarization of uterine macrophages, and suppressed IL-12 production. Histologically, the vascular remodeling failure of the placental labyrinth was shown in mice with the blockade of IL-18. Importantly, we found that macrophages and smooth muscle cells are essential sources of IL-18. These findings indicate that IL-18 enhances an appropriate type 1 immune response leading to the proper placental development and fetal growth via the feedback between IFN-γ and IL-12.

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**OP-2**

HSPA4L and GIT1 as possible biomarkers in testicular autoimmunity

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Clinically, 60–75% of male infertility cases are categorized as idiopathic spermatogenic disturbance. In previous studies, lymphocytic infiltration and immune deposits were present in several testis biopsy specimens, indicating that immunological factors contribute to the occurrence of the idiopathic spermatogenic disturbance. We recently found that immunization of A/J male mice with heat shock