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**ISP-32-8** Leukemia inhibitory factor in the cervical epithelium is a possible biomarker of uterine receptivity

## The University of Tokyo

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[Objective] The uterus acquires the capacity to receive the embryo successfully in the periimplantation period, and this capacity called uterine receptivity is critical for embryo implantation. Although several endometrial biomarkers of uterine receptivity such as leukemia inhibitory factor (LIF) have been studied, there are no reports about cervical biomarkers of uterine receptivity. The aim of this study is to examine whether cervical LIF can be a biomarker for uterine receptivity. [Methods] Mouse models of implantation and ovariectomy using C57/BL/6 wild-type mice were used. Uteri and cervices were obtained from pregnant and ovariectomized mice to assess LIF expression. [Results] Cervical LIF mRNA was expressed primarily in the epithelium, and was upregulated in the receptive phase compared to the pre-receptive phase. Two different mouse models of implantation failure induced by a progesterone (P<sub>4</sub>) receptor antagonist RU486 or an oxidative stress inducer paraquat revealed downregulation of cervical LIF mRNA. However, RU486 injection did not suppress cervical LIF mRNA levels in the ovariectomized mice treated with estradiol-17 $\beta$  and P<sub>4</sub>. [Conclusion] These findings indicate that cervical LIF is expressed in a manner depending on uterine receptivity rather than P<sub>4</sub> signaling, and LIF expression in the cervical epithelium can be a novel biomarker of uterine receptivity.

**ISP-32-9** Role of Versican V1 in an Embryo Implantation Model

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[Objective] Versican, a component of an extracellular matrix, can regulate cell-to-cell adhesion mediated by integrin $\beta$ 1 or CD44. We have shown that versican expression in endometrial epithelial cells was most prominent in the mid-secretory phase. The aim of this study was to investigate a possible role of versican in embryo implantation. [Methods] Endometrial carcinoma cell lines (Ishikawa) and spheroids of choriocarcinoma cell lines (BeWo) were used as a model for endometrial epithelium and embryo, respectively. We established versican V1-overexpressing Ishikawa cells (ISKW). First, the numbers of BeWo cells or BeWo spheroids that attached to ISKW and control Ishikawa were compared in attachment assay. Next, expressions of CD44 and integrin $\beta$ 1 on Ishikawa and BeWo cells were examined by immunocytochemistry. Finally, versican expression in Ishikawa cells treated with TGF- $\beta$ 1 was evaluated through RT-PCR and immunocytochemistry. [Results] The number of BeWo spheroids that attached to ISKW were significantly higher than that attached to control Ishikawa. This difference was not observed when solitary BeWo cells were used. Integrin $\beta$ 1 but not CD44 was strongly expressed in BeWo spheroids. TGF- $\beta$ 1 treatment significantly enhanced mRNA as well as protein expression of versican V1 in Ishikawa cells. [Conclusion] Versican may facilitate embryo implantation.

**ISP-33-1** Infertility problems after abdominal radical trachelectomy

## Kyushu University

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[Objective] In our facility, oncologic surgeons performed over 140 radical trachelectomy (RT) for the patients of uterine cervical cancer. We cannot estimate accurate conception rate because we do not recognize the number of patients who attempted to conceive. [Methods] We investigated 18 patients who visited our facility for infertility treatment after RT between 2012 to 2015 by medical record. Written informed consent was obtained from all participants of trachelectomy. [Results] Till now there have been a total of 19 pregnancies in 15 patients. Four pregnancies were achieved naturally. Pregnancies after IUIs were 3, and after IVFs or ICSIs were 12. The infertility rate after RT is reported to be high. Some patients complained about oligomenorrhea and had adhesion of endometrium for unknown reason. Thin endometrium despite the sufficient estrogen replacement is also seen. We also experienced some cases of premature ovarian insufficiency. [Conclusion] In our experience, 78% of patients who got pregnant were under infertility treatment. RT is meaningful for young cervical cancer patents. But it is difficult to get pregnant naturally after RT. We must be taken care of uterine body and blood flow from ovarian arteries, and pay attention to condition of endometrial cavity. We think that early application of the artificial reproductive technology is recommended.