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学位論文の題名	<p>Role of cathepsin E in decidual macrophage of patients with recurrent miscarriage (反復流産病態における妊娠初期脱落膜中マクロファージのカテプシン E の役割)</p> <p>Molecular Human Reproduction. Accepted January 15, 2014</p>
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## Abstract

[Objectives] In our previous study, we reported that cathepsin-cystatin system cause endometrial dysfunction for early pregnancy. Cathepsin E plays an important role in cancer immunology, preventing tumor growth and metastasis *in vivo* through multiple machanisms. However, there are few reports about the possible correlation between cathepsin E and human reproduction. In this study, we investigated the existence and contribution of cathepsin E in early pregnancy of patients with recurrent miscarriage (RM).

[Methods] The fertility and the pathology of female reproductive organ of *CatE*<sup>-/-</sup> mice were analysed. With informed consent, cervical mucus were collected from RM patients with early pregnancy (4 to 6 gestational weeks, n = 21), and the pregnancy outcome was compared prospectively. The cathepsin E expression in decidua of RM patients (n = 49) and normal pregnant women undergoing elective surgical abortion (n = 24) was measured using SDS-PAGE, WB analysis. Decidual macrophages were isolated from RM patients (n = 6) and stimulated by lipopolysaccharide (LPS) and interferon gamma (IFN- $\gamma$ ).

[Results] *CatE*<sup>-/-</sup> mice were fertile, but the litter number was significantly smaller. The uterus of *CatE*<sup>-/-</sup> mice showed granulation tissue. A protease activity of cathepsin E measured with Fluorescence-Quenching Substrate (KYS-1) in cervical mucus of patients who developed miscarriage was markedly decreased. The expression of cathepsin E, semi-quantified by SDS-PAGE, W-B in decidua was significantly lower in RM patients compared to patients without RM. By double staining immuofluorescence, the staining of cathepsin E was observed in CD14 or CD68 positive cells in deciduas of both RM patients and patients without RM. Upon stimulation with LPS and IFN- $\gamma$ , the

expression of cathepsin E in cell lysate of decidual macrophages was markedly reduced.

[Conclusion] The results suggested that decreased activity of cathepsin E produced by decidual macrophages might be responsible for the induction of miscarriages in RM patients.