審 査 の 結 果 の 要 旨

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The endometrium is subjected to a dynamic condition due to the contractile movement of the myometrium. Mechanical stimuli in the uterus are regarded as a significant factor for its physiological function on a par with biochemical stimuli induced by estradiol and progesterone. However, the effect of mechanical stimuli on the endometrium still remains unknown. The aim of the first study was to reveal the effect of cyclic strain onto human endometrial stromal cells (hESCs). Gene Expression and immunostaining results showed that applying cyclic strain for 7 days onto hESCs up-regulated smooth muscle cell markers via cAMP signaling pathway.

In the second study, he reconstructed engineered tissue constructs, scaffold-free tissue (SFT), using rat endometrial stromal cells (rESC). Since the SFT did not contain any artificial material, it was expected to become a great model for uterine regeneratoin. The rESC SFT had 100-125 μm of thickness with greater mechanical properties compared to the conventional cell sheet (25 μm). He transplanted this SFT to the endometrium in rats. Immunostaining results showed that the epithelial cells from the native tissue started covering the SFT after 1 day. The SFT was also successfully combined to the native tissue in as little as 3 days. After 14 days of transplantation, the SFT was spread out to the surrounding tissues in the endometrium without any negative interactions with transplanted cells. Application of rESC SFT promoted the partial uterine regeneration in murine model.

In the last study, he utilized the SFT reconstructed by hESC for early implantation of embryo. The novel method to fabricate SFT was established by using a ROCK inhibitor to weaken a strong cell-cell interaction in hESCs for retaining its three-dimensional (3D) shape. By coculturing rat embryos on the SFT, it provided a superior environment *in vitro* for the embryos to undergo early implantation with regard to development, hatching, and attachment. It implies a new *in vitro* application as embryo incubator to keep the embryo in a healthy condition and further to accelerate the development or hatching of the embryo during *in vitro* fertilization. Moreover, gene expression results showed that the hESC in the form of 3D structure exerted greater gene expressions related to uterine receptivity or blastocyst attachment, indicating the significance of hESCs in the form of 3D structure in the further study.

His works include novel original concepts, and enough data. Therefore, reviewing committee accepted his paper as a doctoral dissertation.