

## ABSTRACT OF DISSERTATION

Title	Dentin-Pulp Complex Tissue Regeneration via Three-Dimensional Cell Sheet Layering (積層細胞シート化技術を用いた象牙質-歯髄複合組織の再生-)
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<p><b>[Background]</b> Dentin-pulp complex could be destroyed by deep caries and trauma which will lead to irreversible pulpitis, pulp necrosis and even tooth loss. Cell sheet technology is a promising tissue engineering approach that can easily produce transplantable regenerative tissues. Previously, we successfully fabricated a complex cell sheet that enabled to reproduce the bone-ligament structure equivalent to natural periodontal tissue. Similarly, dentin-pulp complex tissue contains characteristic hard and soft tissue, a single type of cell or applying monolayer cell sheet is not sufficient to regenerate the natural tissue architecture.</p> <p><b>[Objective]</b> Fabricate a layered cell sheet composed of rat dental pulp (DP) cells and odontogenic differentiation of pulp (OD) cells and to investigate the ability to regenerate the dentin-pulp complex in a scaffold tooth.</p> <p><b>[Methodology]</b> Fabricated two single cell sheets composed of DP cells (DP cell sheet) or OD cells (OD cell sheet) and a layered cell sheet made by layering both cells. The characteristics of the fabricated cell sheets were analyzed using light microscopy, scanning electron microscopy (SEM), hematoxylin-eosin (HE) staining, and immunohistochemistry (IHC). Furthermore, the cell sheets covered onto a scaffold tooth and transplanted into the subrenal capsule of immunocompromised mice for 8 weeks. Following this, the regenerative capacity to form dentin-like tissue was evaluated using micro-computed tomography (Micro-CT), HE staining, and IHC.</p> <p><b>[Results]</b> The findings of HE staining, SEM and IHC confirmed that layered cell sheets fabricated by stacking OD cells and DP cells maintained their cytological characteristics. Micro-CT of layered cell sheet transplants revealed a mineralized capping of the access cavity in the crown area. The bone volume/tissue volume (BV/TV) showed a significant increase in hard tissue formation of layered cell sheet group compared to that of control group (<math>p &lt; 0.05</math>). HE staining and IHC also showed a combination of soft and hard tissue formation in the layered cell sheet group and the dentin-like tissue generated from the layered cell sheet expressed characteristic markers of dentin but not bone equivalent to that of a natural tooth.</p> <p><b>[Conclusion]</b> Our data suggests that the layered cell sheet could regenerate dentin-pulp</p>	

complex-like tissue in a three-dimensional structure.

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