**Development of three-dimensional culture models for extrapolating the cell response *in vivo***

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To create new culture models for extrapolating the cell response *in vivo*, we attempted to devise culture substrata of anchorage-dependent cells. Two different substrata, TOSHI (tissue/organ sections for histopathology)-substratum conserving both microarchitecture and components *in vivo*[1] and collagen vitrigel membrane-substratum with excellent strength and transparency[2], were developed and utilized for the culture of various anchorage-dependent cells. TOSHI-substratum prepared from placenta induced unique cell behaviors to form a capillary network-like structure for CPAE cells, and a neuronal network-like structure for PC-12 cells. Also, the substratum from regenerating liver efficiently induced the differentiation of mouse ES cells into hepatocyte-like cells. These data suggests that the analysis of interactions between different cell types and various TOSHI-substrata will play an important role for a novel approach to study both cellomics and histomics. Meanwhile, the collagen vitrigel membrane-substratum enabled the double surface-culture of different cells by the manipulation of two-dimensional cultures, resulting in the reconstruction of a three-dimensional organoid. An intestinal epithelial-mesenchymal model was reconstructed by co-culturing fibroblasts on the opposite side of the monolayered Caco-2 cells on the substratum. Also, the substratum was useful for maintaining the function of rat primary hepatocytes. These data suggests the collagen vitrigel membrane-substratum has many advantages to reconstruct culture models.

1) Takezawa T, *et al.* FASEB J. 16: 1847-1849, 2002.
2) Takezawa T, *et al.* Cell Transplant. 13: 463-473, 2004.