Reconstituting brain-vascular microenvironment

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Abstract— Neural stem cells (NSCs) are located in specialized microenvironment that is called brain-vascular microenvironment [1]. The mutual relationship of endothelial cells (ECs), neurons, glia and NSCs in the microenvironment plays an important role for a balance between NSC self-renewal and differentiation [2][3]. Understanding the influence of the microenvironment on NSC will therefore help developing potential therapies for degenerative CNS injuries and disorders [3].

Here, we describe a 3D in vitro co-culture assay that reconstitutes brain-vascular microenvironment in NSC niche. This assay may therefore expand capacity of drug testing and toxicological studies.

I. BRIEF DESCRIPTION OF THE WORK

NSC is a self-renewing multipotent progenitor cell, being able to develop major cell types including neuron, astrocyte and oligodendrocyte [4]. NSC is one of the promising subjects for neuroscience, especially for CNS neurodegenerative disorders [3]. NSC resides in the functionally specialized brain-vascular niche [fig 1(a)]. The brain-vascular niche provides maintenance of the NSC pools in quiescence with self-renewal and proliferation, under various conditions of cell-cell, cell-ECM interactions and other microenvironmental cues [2][3]. The brain-vascular microenvironment within the NSC niche is integrated by endothelium-derived angiocrine factors and paracrine signaling molecules to regulate NSC fates [5][6]. Therefore understanding the relationship between NSCs and environments may guide efforts toward effective cellular therapies.

In the past decades most in vitro studies of the interaction of NSCs with ECs have been established in a two-dimensional (2D) macro culture systems [7], which have not be able to mimic complex brain-vascular microenvironments. Here, we co-cultured NSCs and brain endothelial cells in 3D microfluidic assays by incorporating hydrogel with visualization and quantification metrics [fig. 1(b)].

We confirmed the effects of the brain vasculature on NSC viability, self-renewal and differentiation. NSCs in the presence of the brain vasculature maintained higher viability and self-renewal that were confirmed by live/dead assay and quantified qRT-PCR analysis. A tendency to differentiation affected by the brain vasculature was also precisely monitored.

REFERENCES


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