

## Development of tissue-specific histamine-responsive vascular endothelial models using a collagen vitrigel membrane

Miaki Uzu, Toshiaki Takezawa

*National Agriculture and Food Research Organization*

The tightness of the endothelial barrier is tissue-dependent. We expect that tissue-specific barrier function can be induced in immature vascular endothelial cells by co-culturing with tissue-specific cells. The purpose of this study is to construct tissue-specific vascular endothelial models on a collagen vitrigel membrane (CVM) composed of high-density collagen fibrils equivalent to connective tissues *in vivo* and compare the responsivity to histamine. We used human microvascular endothelial cells (HMVECs) derived from a newborn foreskin. HMVECs were cultured in a CVM chamber with or without human dermal fibroblasts (HDFs), C6 cells (a rat glioma cell line) or HepG2-NIAS cells (a human hepatocellular carcinoma cell line) cultured on the reverse-side of CVM for up to 6 days. The endothelial barrier function was evaluated by transendothelial electric resistance (TEER). TEER values of a HMVEC monolayer were 15-20  $\Omega/\text{cm}^2$  during culture periods. It significantly increased up to 40-60  $\Omega/\text{cm}^2$  by co-culturing with HDFs, C6 cells and HepG2-NIAS cells. Also, TEER value was clearly decreased in the co-culture model composed of HMVECs and HDFs treated with 1  $\mu\text{M}$  histamine while HMVEC monolayer model showed slight response to 100  $\mu\text{M}$  histamine. Now we are investigating tissue-specific responses to histamine among the models.