

Brain microvascular endothelial cell cytoskeletal reorganization in response to strain in a microvessel-on-chip

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Blood flow-derived forces are key regulators of microvascular structure and function. Although endothelial cells (ECs) from various vascular beds have been shown to exhibit humoral, metabolic, and structural responses to flow, much less is known about the flow responsiveness of brain microvascular ECs. Using a microvessel-on-chip, we are investigating how human brain microvascular ECs (HBMECs) respond to cerebral blood flow.

An HBMEC-lined microvessel is fabricated in a soft collagen hydrogel using the templating technique. Controlling luminal flow and intraluminal pressure allows subjecting the cells to different levels of circumferential stretch. Results to date indicate that in response to increased circumferential stretch, HBMEC actin filaments reorient in the stress direction and form prominent ventral stress fibers. In contrast, noticeable changes are observed in the organization of microtubules or intermediate filaments. Contrary to what has been reported in other EC types, HBMECs do not change shape or alignment in response to stretch despite the actin remodeling, and no change in nuclear shape is observed. Tension also induces a switch from linear to zig-zag cell-cell junctions, and sustained stresses provoke junctional rupture. These findings suggest that strain induces structural responses that are likely to profoundly influence HBMEC barrier function.