BACKGROUND/OBJECTIVE: The neurovascular unit is a complex, interdependent system composed of neurons, neural-supporter cells, namely astrocytes, and vascular cells, including endothelial cells (EC) and smooth muscle cells (SMC). Currently, our use of static culture conditions and limited cell types does not allow studies of vascular physiology, particularly under flow conditions that mimic blood circulation through the vessel lumen. Using tissue engineering technology, we have developed a 3D physiologically relevant model of human cerebral arteries composed of ECs, SMC and astrocytes. Our objective is to engineer human induced pluripotent stem cell (iPSC)-derived neurons within this innovative platform to generate the first human functional model of the neurovascular unit.

METHODS: Primary human EC, SMC, astrocytes and human iPSC-derived neurons is cultured on a polyglycosic acid/polycoprolactone scaffold under pulsatile flow conditions to generate bioengineered cerebral arterial neurovascular units that mimic human CNS arteries 2 mm or less in diameter. Using histology, we confirm the correct anatomical organization of our tissue and validate this model through studies of EC, SMC, astrocyte and neuron key cerebrovascular functions.

RESULTS/CONCLUSION: Using this model, we demonstrated that over a course of two weeks ECs of peripheral origin (HUVEC) acquire specific cerebral tight junctions and blood-brain barrier transporters when cultured in the presence of astrocytes with expression levels similar to native cerebral tissues. Immunofluorescent staining confirms that neurons form multilayers in close proximity to the astrocytes and that they are positive for synapsin. We measured beta-amyloid secretion in the media and the tissue, also supporting neuronal functionality.

Themes:

Check (highlight) the most applicable theme according to the abstract.

| Innovation and Technology | Health and Wellness | Culture and Society | Sustainability and Conservation |

Comments: The background is nicely written (well-defined acronyms, the need of a better model to allow us to study flow conditions is well-explained). Given the title mentions Alzheimer’s Disease (AD), I would recommend linking the Intro and Implication more explicitly to the disease (e.g., how your development fulfills the criteria of a good model of AD and what’s the potential use of the model to study AD). This will help a lay audience to understand what your results mean.