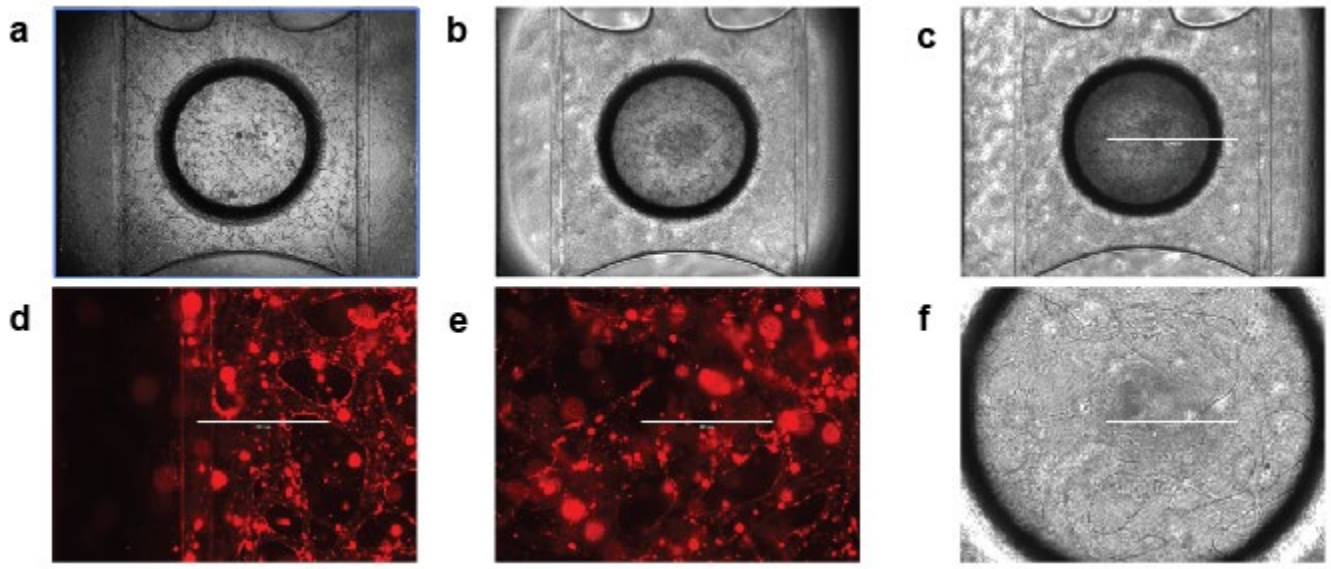
Supplemental Information



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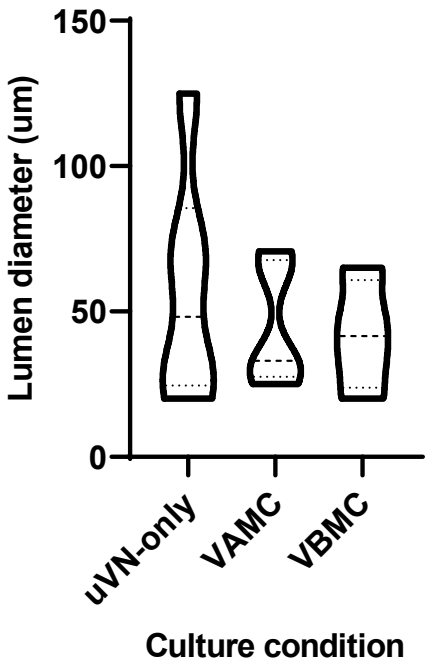
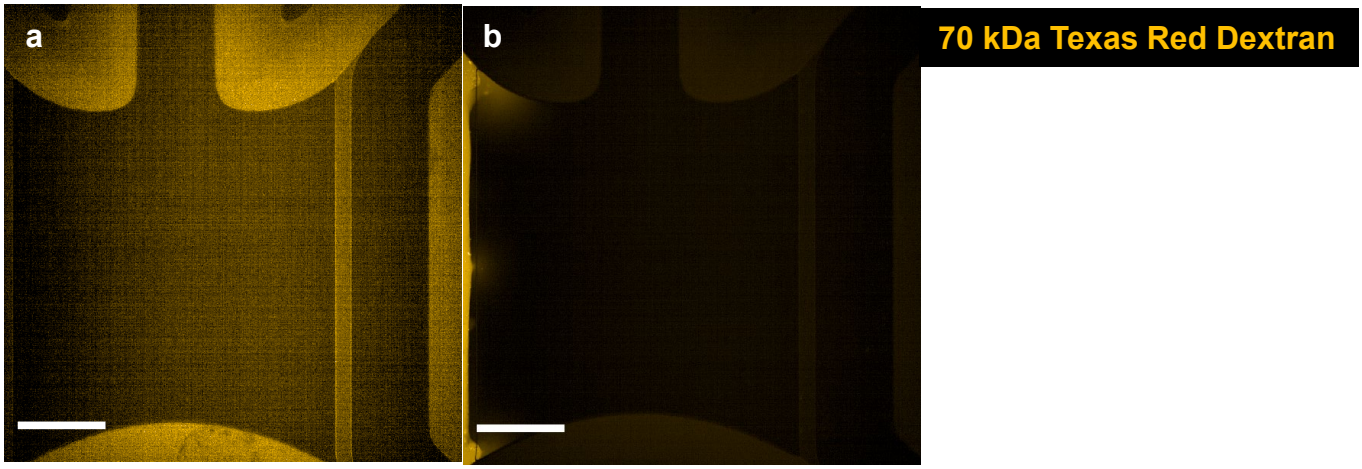
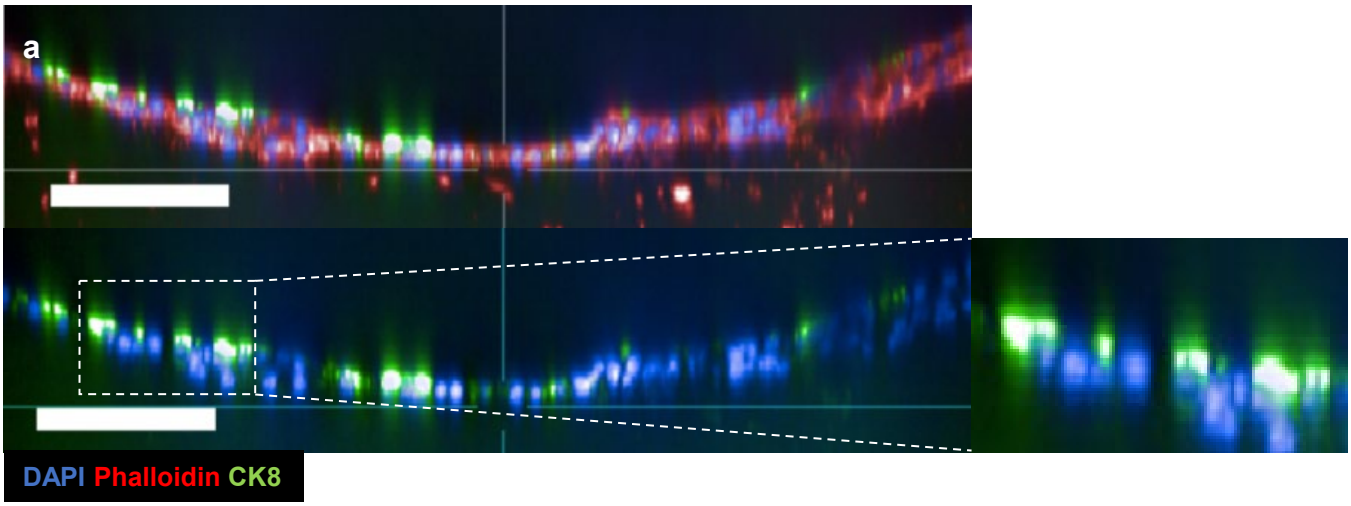


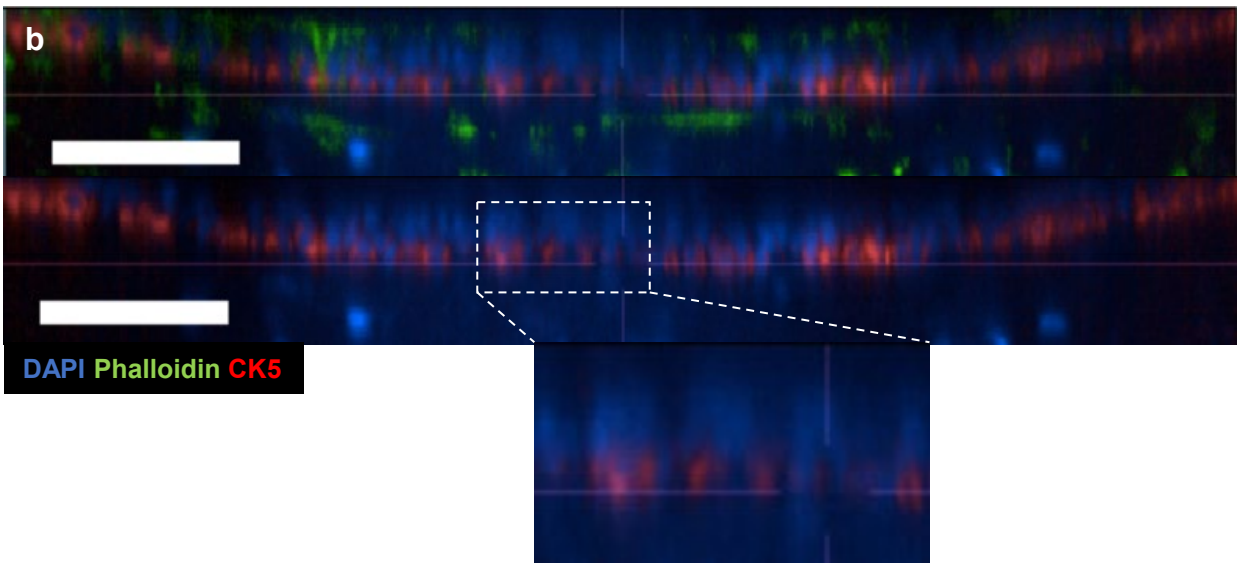
Parameters	uVN-only	VAMC	VBMC
Minimum	20.02	25.00	20.00
25% Percentile	24.51	27.50	23.75
Median	48.23	33.02	41.51
75% Percentile	85.57	67.68	60.76
Maximum	125.0	70.71	65.01
Mean	56.65	44.67	42.01
Std. Deviation	39.84	21.30	19.13
Std. Error of Mean	16.27	9.526	9.567

Supplemental figure 1. Co-culture of respiratory epithelial cells and vascular bed. (**a**) DIV0 of seeding (Dil-stained HPMEC and fibroblasts, pericytes in the gel chamber; non-Dil-stained HPMEC in the side channels). (**b**) DIV7 pre-ALI epithelial layer over open access of gel chamber. (**c**) 48h post-ALI induction on epithelial layer on top of the vasculature. (**a**)-(**c**) taken on EVOS at 4x objective. (**d**) RFP channel at the side lane-gel chamber interface; only Dil-stained cells that were seeded in the gel are making up the vasculature, not the unstained cells from the side lanes. (**e**) RFP channel on the open access in the gel chamber, showing vascularization by the Dil-stained endothelial cells. (**f**) brightfield image of (**e**). (**g**) Comparison of lumen diameters from **figure 2e-g** (vessels with asterisk). Statistics table provided adjacent to violin plot. (**a**)-(**c**) taken on EVOS at 4x objective, 1000 µm scale bar. (**d**)-(**f**) taken on EVOS at 10x objective 400 µm scale bar.

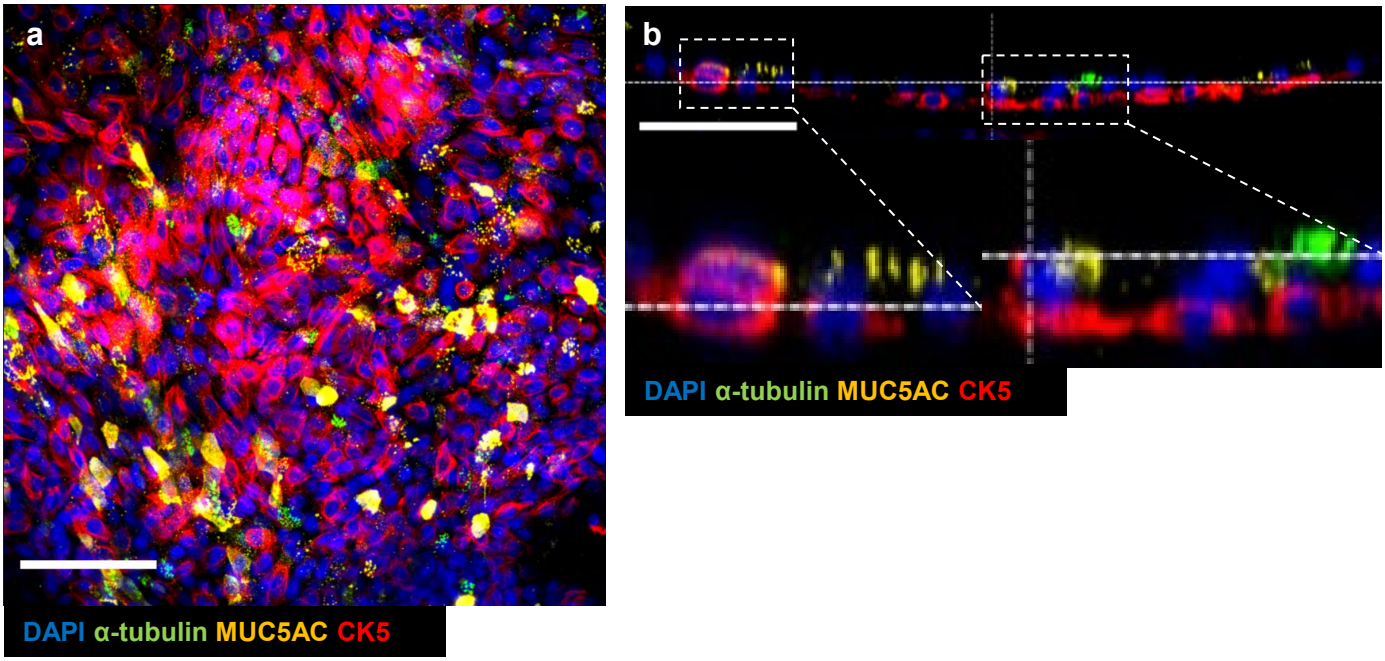


Supplemental figure 2. Cell-free control and side lanes with empty gel controls for perfusion assay. (**a**) cell-free control, only fibrin gel in the gel chamber; no cells. (**b**) vasculature control, only endothelial cells in the side lanes, no cells in the gel chamber, only fibrin gel. Scale bar = 500 µm





Supplemental figure 3. (**a**) *z*-stack of CK8 localization in alveolar cells against phalloidin. It can be observed that CK8 lies closely near the nuclei localization indicating, most cells are non-columnar, and those expressing CK8 may be more like type-2 cells (since they are more cuboidal shaped/less flat morphologically. (**b**) *z*-stack of CK5 localization in small airway epithelial cells against phalloidin. Compared to alveolar cells, the nuclei/DAPI extends much more upwards than the CK5 localization, indicating that there is polarity in CK5 expression and that the elongated nuclei indicate columnar-like cells. Taken with Opera Phenix. Scale bar = 100 µm.



Supplemental figure 4. (**a**) Vascularized bronchiolar-multi chip model along the surface of open access (a-tubulin green, ACE2 magenta). At maximum projection, the small green puncta is most likely the protruding α -tubulin forming cilia. Taken with Leica confocal for better resolution. (b) *z*-stack of stratified columnar epithelium. The cilia can be clearly seen in the magnification box(es) for region(s) of interest. It can also be noted that CK5-positive cells are positioned basolaterally and the cells expressing either MUC5AC or α-tubulin are sitting superior to the CK5-positive cells. Taken with Leica confocal microscopy. Scale bar = 100 µm.

Supplemental video(s) captions

Supplemental video 1. 3D reconstruction of alveoli-capillary construct in **figure 1d**. Allows for spatial visualization and localization of CD31, CK8 for specific cell types. The vascular network perfuses and allows for support of alveolar epithelial layer on the top.

Supplemental video 2. 3D reconstruction of SAEC-capillary construct in **figure 1e**. Creates a more detailed 3-dimensional reconstruct of the vascular network that is essential to perfusing the small airway epithelial cells and for maturation of the epithelial population.

Supplemental video 3. Localization of extracellular matrix (ECM) proteins on vascular and epithelial layers in vascularized alveolar multi-chip (VAMC, top panel) and vascularized bronchiolar multi-chip models (VBMC, bottom panel). COL IV and/or III green; F-actin red; nuclei blue.

Supplemental video 4. Operation of World Precision Instrument trans-epithelial/endothelial electrical resistance (TEER) automation system, re-calibrated to measure on the 64-chip based microfluidic platform.