**Supplementary Video Legends:** All videos are representative of at least three biological replicates.

**Supplementary Video 1:** CTRL-EC and R-VEC in 3D gel matrices and in large-volume perfusable microfluidic devices.

**Video 1a.** GFP-labeled CTRL-ECs and GFP-labeled stage 1 induction R-VECs, suspended in the defined Laminin, Entactin, Collagen IV (LEC) three-dimensional (3D) matrix, were cultured in various established defined pro-angiogenic medium formulations: commercialized EC medium (MV2, PromoCell), and serum free StemSpan tube formation medium. Either CTRL-ECs or R-VECs (each 5 million cells/ml) were embedded inside LEC. The 3D rendering of the CTRL-ECs and R-VEC in StemSpan medium displayed here demonstrates that R-VECs without the support of bioprinted scaffolds spontaneously self-organize in 3D into a durable continuous lumenized and branching vascular network throughout the entire Z-stack, while CTRL-ECs fail to do so. Time-lapse videos were acquired at 40-minute time interval over 3 days using a 20x objective with a confocal spinning disk microscope.

**Video 1b:** Stage 1 induction R-VECs were seeded into the device with dimension of 5x3x1 millimeter (mm) (15 microliters capacity) at 3 million cells/ml cell density as shown by the schematic. The entire device was captured by stitching several overlapping bright field images. At Day 5 after culture, the GFP-labeled R-VECs (in green) with the need of restrictive scaffolds had already self-assembled and established interconnected multilayered lumenized 3D patterned vascular networks over the entire device, connecting the two microfluidic channels that are 3 mm apart. On the same day, we pipetted human whole blood collected in a BD Vacutainer heparinized tube and gently pipetted 100µL of the whole human blood to the inlet of the device. Time-lapse video was then recorded. A still image of the time-lapse video was displayed to show that the hematopoietic cells, plasma, WBCs, platelets and red blood cells were fully contained within the R-VEC vessels without any major leakiness or vascular disruption, thrombosis or collapse. The haematopoietic cells quickly entered the fluidic channels and readily traversed from one fluidic channel to the other fluidic channels through the lumenized R-VEC vessels and finally exited to the outlet of the device.

**Video 1c:** At the end of the time-lapse video, we also captured the entire device to show that whole blood was present at the inlet, outlet and inside the device. Time-lapse video was acquired with a 10x objective.
Video 1d: R-VEC vessels in one of the scalable microfluidic devices with larger dimension of 10x5x1 mm (50 microliters capacity) were captured with higher magnification and rendered to display the 3D multi-layered patterned organization of R-VEC vessels. Before image acquisition, R-VEC vessels were stained by perfusion of fluorescent dye-conjugated antibody against human VE-cadherin (in red) into the inlet of the device. The device was fixed and imaged with confocal spinning microscope using a 20x objective.

Supplementary Video 2: Interaction of R-VECs with human pancreatic islets

Video 2a: GFP-labeled CTRL-ECs (in green) or stage 1 induction R-VECs (in green) were intermingled with human pancreatic islets pre-stained with CellTracker (in red). Physically malleable R-VECs form 3D vascular networks that avidly co-opt the human pancreatic islets, while CTRL-ECs fail to do so. Time-lapse videos were acquired with a 20x air objective every 40mins over 3 days using a confocal spinning disk microscope.

Video 2b: R-VEC and human pancreatic islets (unlabeled) were seeded into the 5x3x1 mm (15 microliters fibrin gel volume) device. After 4 days in co-culture, the R-VECs self-assembled into extensive interconnected branching vascular 3D networks arborizing intimately the human pancreatic islets over the entire device. Approximately 100µL of freshly phlebotomized whole human peripheral blood collected in a BD Vacutainer heparinized tube and was pipetted into the inlet of the device. This time-lapse video was zoomed in area of the device with perfused whole human blood. Red circle shows an islet in this field of view. In this zoom-in time-lapse, haematopoietic cells most prominently discoid shape red blood cells, WBCs, and platelets were shown to flow through R-VEC vessels arborizing and transversing through microcapillaries within the islets. Despite prolonged perfusion and washing of the whole blood multiple times, the R-VEC vessels maintain their vascular integrity without haematopoietic cell leakiness, thrombosis or vascular regression or collapse. The time-lapse video was captured using a 10x objective.

Video 2c: R-VEC and human pancreatic islets were seeded into the 5x3x1 mm device. After 4 days in co-culture, the R-VEC formed extensive vessel networks perfusing the human pancreatic islets over the entire device. We pipetted diluted human blood collected in a heparinized tube and pipetted 100 µL of diluted (10 fold) human blood into the inlet of the
device. This time-lapse video captured a larger area of the device with 10x objective with several human pancreatic islets in the field of view. During the time-lapse video acquisition, we adjusted the focal plane of the image in Z direction to demonstrate the multiple layers of perfusing R-VECs throughout the depth of the device. Haematopoietic cells, in particular red blood cells, occasional WBCs and platelets were captured tunneling and crisscrossing through the R-VEC vessels at different depths of the device.

**Video 2d:** GFP-labeled R-VECs and human pancreatic islets were seeded into the 5x3x1 mm microfluidic device. After 4 days in co-culture, the R-VECs self-organized into extensive 3D vascular networks surrounding and arborizing the human pancreatic islets over the entire device. We gently pipetted diluted human peripheral blood collected in a heparinized tube and dropped 100µL of diluted human heparinized whole peripheral blood into the inlet of the device. This time-lapse video captured in one focal Z plane. First, the video was captured in bright field mode. Then, we acquired both GFP images and bright field images simultaneously to display the GFP-labeled R-VEC vessels and the diluted human blood cells. In the portion of the video where both GFP and brightfield were captured, the haematopoietic and red blood cells were shown to travel through the GFP-labeled R-VEC vessels. Please note, despite prolonged perfusion and washing of the blood multiple times, the R-VEC vessels maintained their vascular integrity without hematopoietic cell leakiness, thrombosis or vascular regression or collapse.

**Video 2e:** GFP-labeled R-VECs (in green) and human pancreatic islets were seeded into the 5x3x1 mm (15 microliters fibrin gel volume) device. After 4 days in co-culture, the R-VEC self-organized into an extensive lumenized vascular networks of patterned branching 3D vessels surrounding the human pancreatic islets over the entire device. We pipetted diluted (1:10) human whole peripheral blood collected in a heparinized tube and injected 100µL of diluted human blood into the inlet of the device. This time-lapse video captured another area of a device where human pancreatic islets were not present in this field of view. We acquired both GFP images and bright field images simultaneously to display the GFP-labeled R-VEC vessels and the 10-fold diluted human blood cells. Haematopoietic cells traveled through the GFP-labeled R-VEC vessels, without impairing the integrity of the vessels. This video further demonstrates that R-VEC vessels are haemodynamically stable during the full perfusion of the haematopoietic cells regardless whether the R-VECs were further away or in proximity to human pancreatic islets. Blood perfused vessels showed very low leakiness, thrombosis or collapse.
**Video 2f:** R-VECs and human pancreatic islets were seeded into a 5x3x1 mm (15 microliters fibrin gel volume) device. After 4 days in co-culture, the device was fixed and stained for human VEcad (R-VECs) (in green), human EpCAM (in red) and human insulin (in blue). This video displays several focal z planes of a confocal Z-stack image. The R-VEC vessels, without the need of bioimprinted scaffolds or synthetic semipermeable membranes, formed extensive lumenized 3D vascular networks connecting the two islets, while also delving deep within the islets, establishing Islet-On-VascularNet platform. This Video demonstrates the direct cellular interaction of islet cells with the R-VECs.

**Supplementary Video 3:** Time-lapse videos of R-VEC or CTRL-EC in co-culture with either normal human colon organoids (hCO) or human colorectal cancer organoids (hCRCO) in 3D matrix.

**Video 3a:** Stage 1 induction R-VEC (in green) were intermingled with normal human colon organoids (in red) in defined 3D laminin-entactin-collagenIV (LEC) matrix for 7 days. The co-culture was fixed and colon organoids were identified by staining with fluorescent-conjugated antibody to human EpCAM (in red), and R-VECs were identified by staining with fluorescent conjugated-antibody human VE-cadherin (in green). Several focal z planes of a Z-stack confocal image, which was acquired at 10x objective, are displayed in both brightfield, red, and green channels. R-VEC vessels formed extensive lumenized network that without the support of artificial scaffolds directly arborized and inter-connected different normal human colon organoids. This model establishes an Organ-On-VascularNet platform.

**Video 3b:** GFP-labeled CTRL-ECs (in green) or stage 1 induction R-VECs (in green) were intermingled with normal human colon organoids (live-stained with fluorescent-dye conjugated human EpCAM antibody, in red). The first video with top and bottom panels shows two examples of dynamic interactions of R-VEC vessels (in green) with human normal colon organoids (in red). R-VECs (in green) avidly tap and wrap the human normal colon organoids (in red).

The second video contains simultaneous time-lapse videos from 5 different organoids in co-culture with either CTRL-EC (top 5 video panels) or with R-VEC (bottom 5 video panels). R-VECs avidly self-assembled into 3D interconnected vessels and interacted with normal human colon organoids, while CTRL-EC displayed very minimal interactions with human normal colon organoids. All time-lapse videos were acquired with 20x objective every 40 minutes over 3 days using a confocal spinning disk microscope.
**Video 3c**: GFP-labeled CTRL-EC (in green) or stage 1 induction R-VECs (in green) were intermingled with human colon tumor organoids (in red) in LEC 3D matrix. First video represents several examples of R-VECs (in green) in co-culture with human colon tumor organoids (in red, either stained with red cell-tracker dye or labeled with mCherry). R-VECs self-assemble into continuous 3D vascular network and avidly engage the human colon tumor organoids, as well as interconnect to other vascularized clusters of organoids.

The second video displays examples of CTRL-ECs and R-VECs in co-culture with colorectal tumor organoids. Top 2 video panels show CTRL-ECs (in green) with very minimal interaction with colorectal tumor organoids (in red, mCherry-labeled). Bottom 2 video panels show intimate cellular interaction of R-VECs (in green) with each other and with colorectal tumor organoids (in red, mCherry-labeled). The third video is a 3D rendering of one example from the CTRL-ECs with colorectal tumor organoids and one of examples from R-VEC with colorectal tumor organoids. The 3D rendering demonstrates that R-VECs arborize the colorectal tumor organoids by tapping and wrapping the colorectal tumor organoids at different angles and locations, while CTRL-EC fail to interact with colorectal tumor organoids. These models lay the foundation of Tumor-on-VascularNet platforms. All time-lapse videos were acquired with 20x objective every 40 minutes over 3 days using a confocal spinning disk microscope.