

Supplementary Figure 1 - Fabrication process of COC-gratings. **A)** Molds were obtained starting from a commercial p-doped silicon wafer. Two examples are shown with ridge and groove width of 1 μm and ridge height of 1 μm (A-10), and with ridge and groove width of 5 μm and ridge height of 1 μm (B-10), respectively. **B)** COC foils were placed on top of the silicon mold and softened by increasing the temperature up to 160 $^{\circ}\text{C}$. 50 bar pressure was applied for 10 min before cooling down to 40 $^{\circ}\text{C}$. The pressure was finally released and mold and COC detached. **C)** High-magnification SEM image of an A-10 grating.

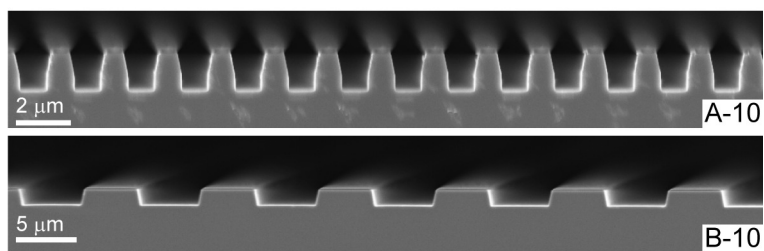
Supplementary Figure 2 – Generation of differentiated endothelial monolayers on COC substrates. Formation of well differentiated adherens junctions in endothelial monolayers generated on flat (FLAT, upper row) and grating (A-10, lower row) substrates. Cell nuclei are revealed by blue staining with DAPI (Nuclei, left column) while VE-Cadherin distribution is depicted in green (middle column). The two channels are merged in the right column. Scale bar corresponds to 10 μm .

Supplementary Figure 3 - Time to onset of spreading and cell alignment to gratings with deep grooves **A)** The histogram bars reports the time to onset of spreading normalized by the value measured for the flat substrate. The number of analyzed events is reported in the upper right corner. Significant differences between the population means are reported (* indicates $p < 0.05$, ** indicate $p < 0.01$). Error bars represent the measured standard error of the mean. **B)** The histogram reports the average angle in degrees between cell orientation and the direction of the gratings. The graph shows a significant difference for all structured substrates compared with the flat surface substrate. The number of analyzed events is reported in the upper right corner. Significant differences between the population means are reported (** indicate $p < 0.01$). Error bars represent the measured standard error of the mean.

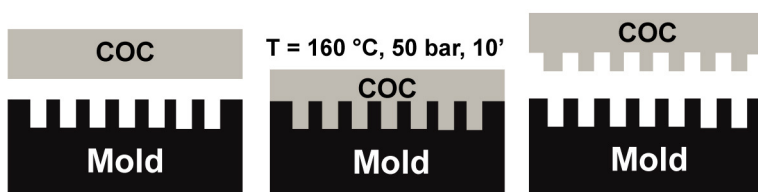
Supplementary Figure 4 – Groove bridging efficiency on gratings with increasing groove depth. The histogram reports the ratio between the number of grooves showing membrane bridging and the total number of grooves encompassed by cells spreading on gratings with groove depth of 0.2 nm (A-2), 0.4 nm (A-4), 0.6 nm (A-6), 0.8 (A-8), and 1 μm (A-10). Significant differences between the population means are reported (** indicate $p < 0.01$, * indicates $p < 0.05$). Error bars represent the measured standard error of the mean. The number of analyzed events is reported in the upper left corner.

Supplementary Fig. 1

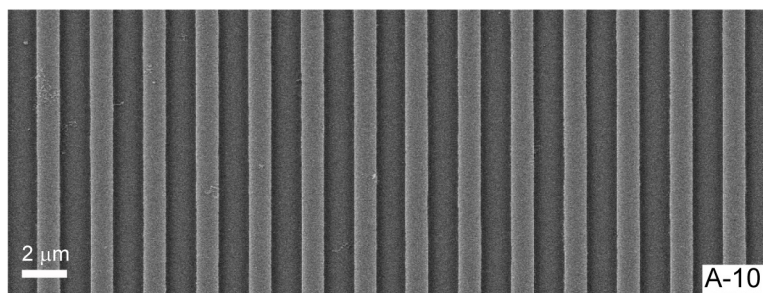
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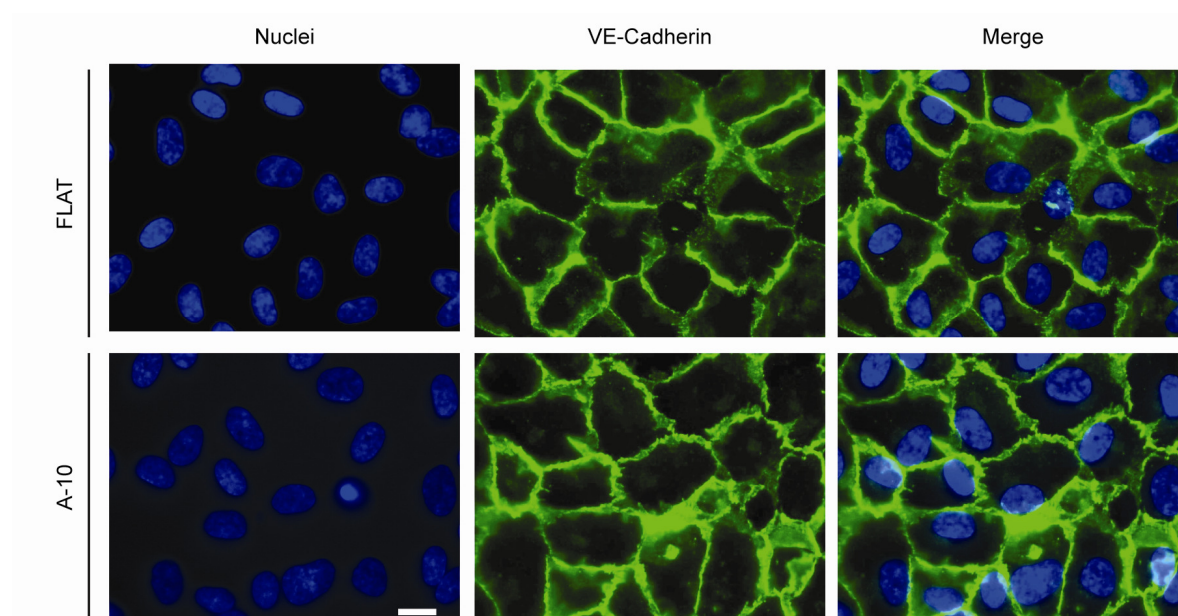
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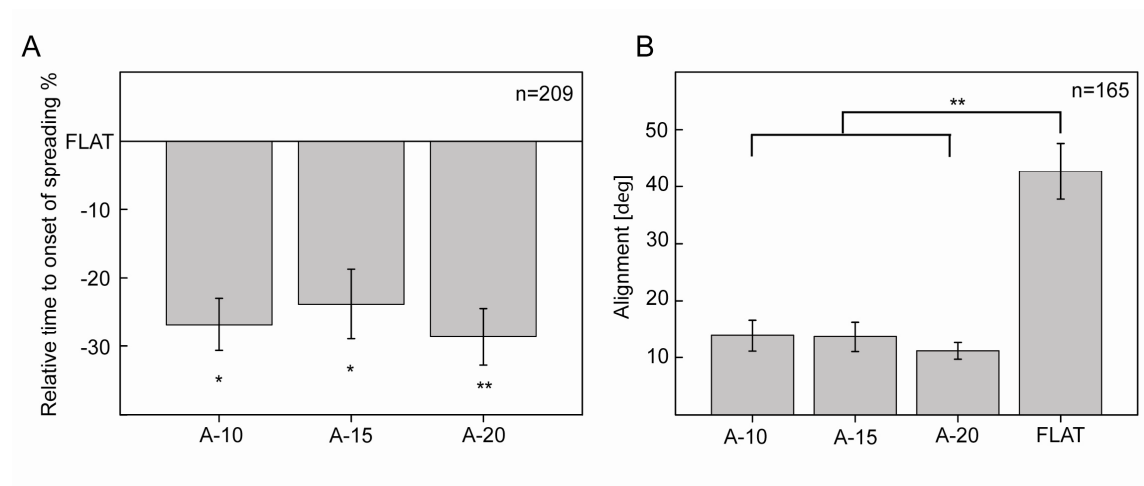
C



Supplementary Fig. 2



Supplementary Fig. 3



Supplementary Fig. 4

