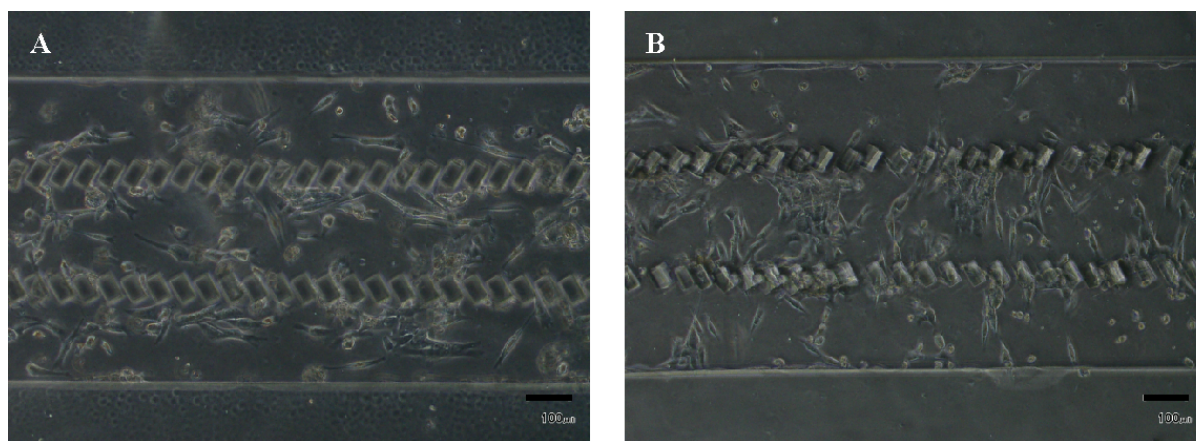
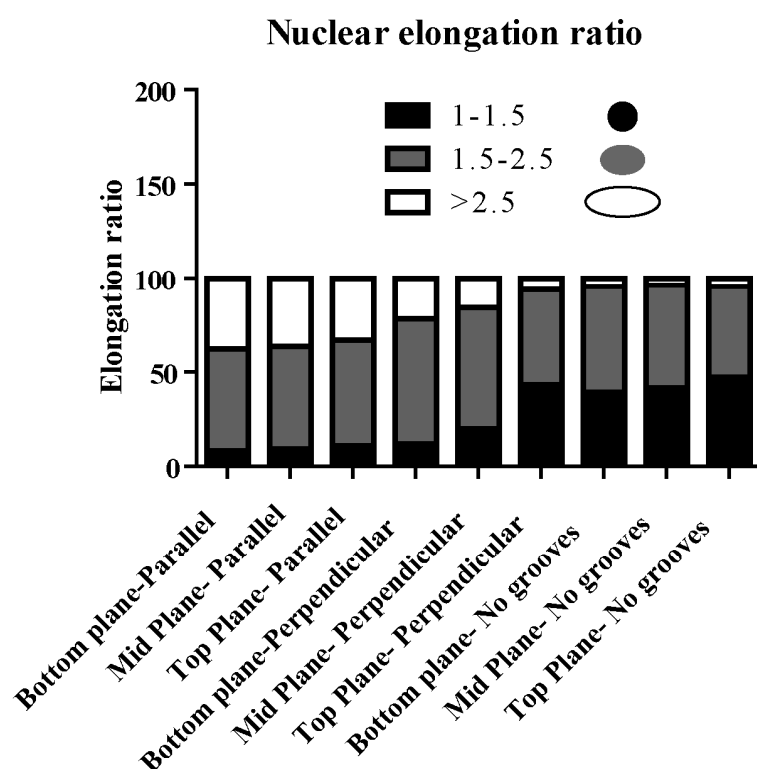
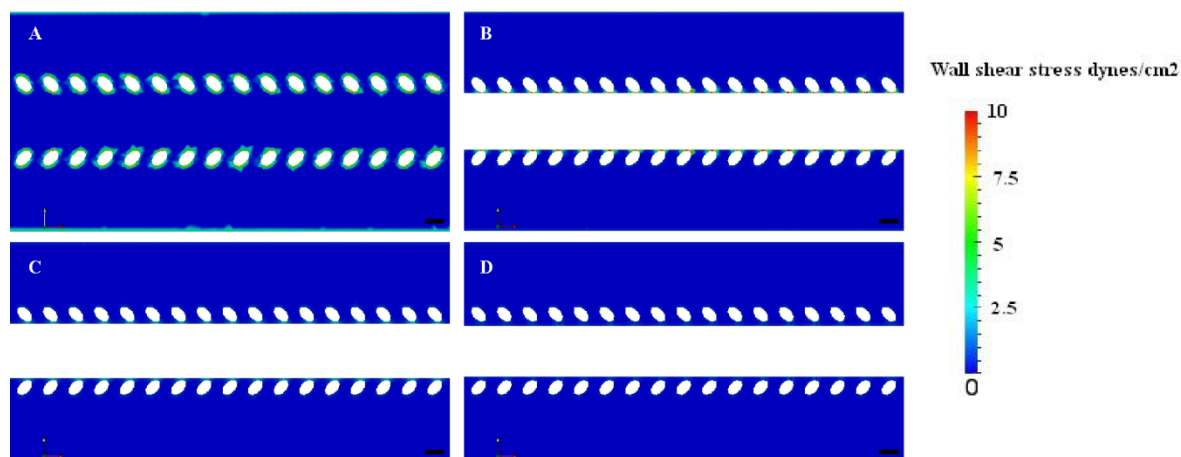




Supplementary Figure 1: Monolayer culture of C2C12 cells in the chip 8 hours after cell seeding. 1A) Cells cultured with grooves parallel to the flow direction. 1B) Cells cultured with grooves perpendicular to the flow direction



Supplementary figure 2: Nuclear elongation ratio by plane. The cells nearest to the grooves had a higher elongation ratio for both the cells cultured on the parallel (38% with >2.5 and 54% with 1.5-2.5) and perpendicular grooves (22% with >2.5 and 66% with 1.5-2.5). This ratio reduced in the top layer especially for the cells in the perpendicular chip (6% with >2.5 and 51% with 1.5-2.5) while the parallel grooves reduced but at a lower rate (33% with >2.5 and 56% with 1.5-2.5). The cells cultured on the chips with no grooves had similar orientation. The slight increase in the bottom layer may be due to the effect of the flow on the cells.



Supplementary figure 3: Shear stress simulation. Shear stress simulation of the chip without cells (A) and with cells at 1 μm (B), 5 μm (C) and 10 μm (D). The cells at the edge experience a range of “0.3 dynes to 15 dynes/cm²” depending on the distance to the pillars. The flow in this study was modeled as the incompressible viscous fluid and governed by Navier-Stokes (NS) equations. The governing equations were discretized in space using finite volume method where a finite set of discrete equations was constructed on unstructured hybrid grids to approximate the NS equations. The computational domain is subdivided into a set of non-overlapping tetrahedral elements. The 3D micro-tissue was modeled as a rectangular block situated at different distances (i.e., 1 μm , 5 μm and 10 μm) from the micropillar array. We used a modified computational fluid dynamic laminar flow solver in OpenFOAM to simulate the flow. The resultant wall shear stress is then calculated. Scale bar 50 μm