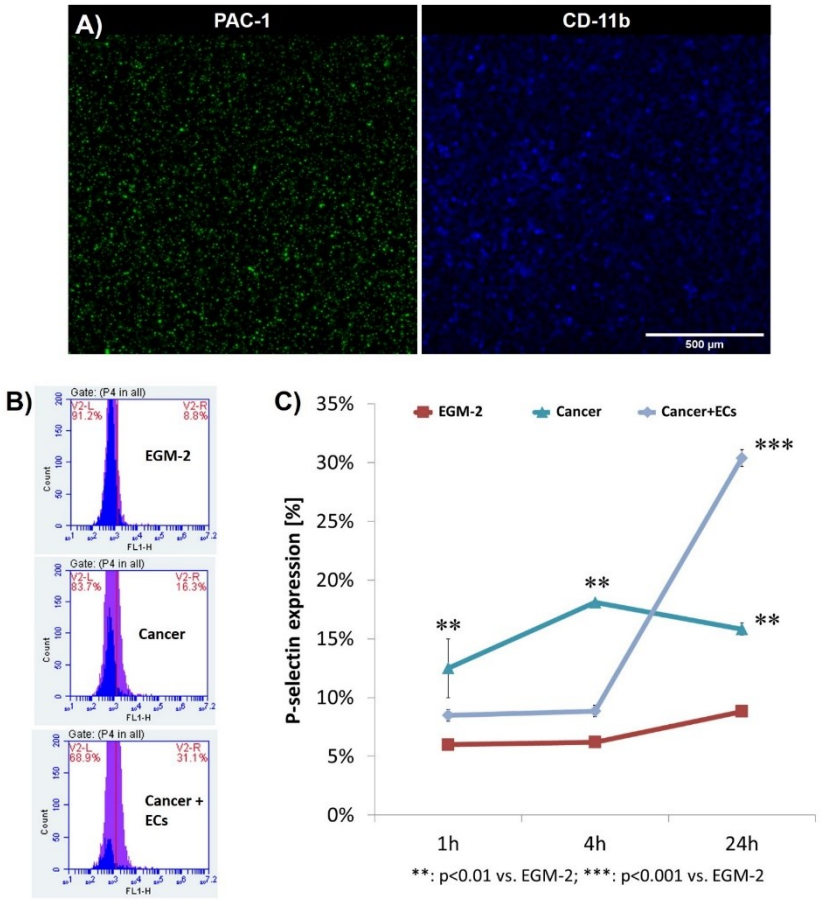
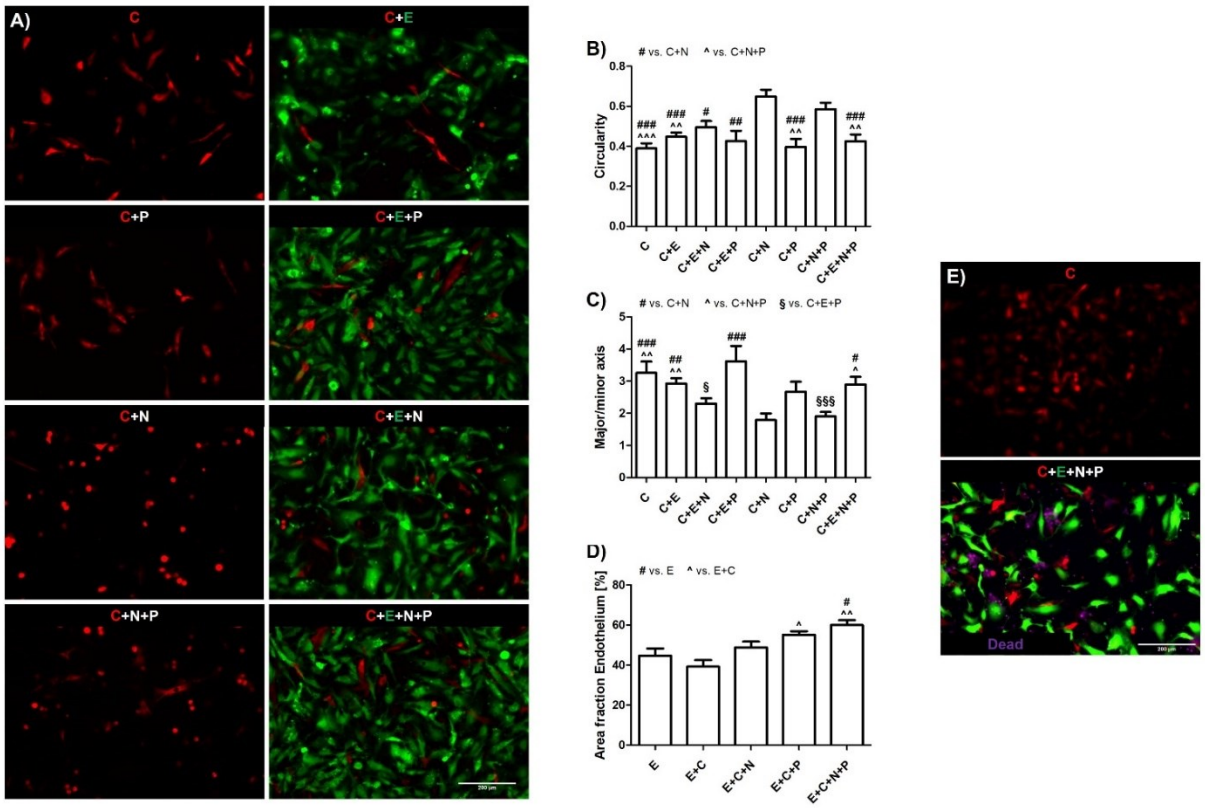
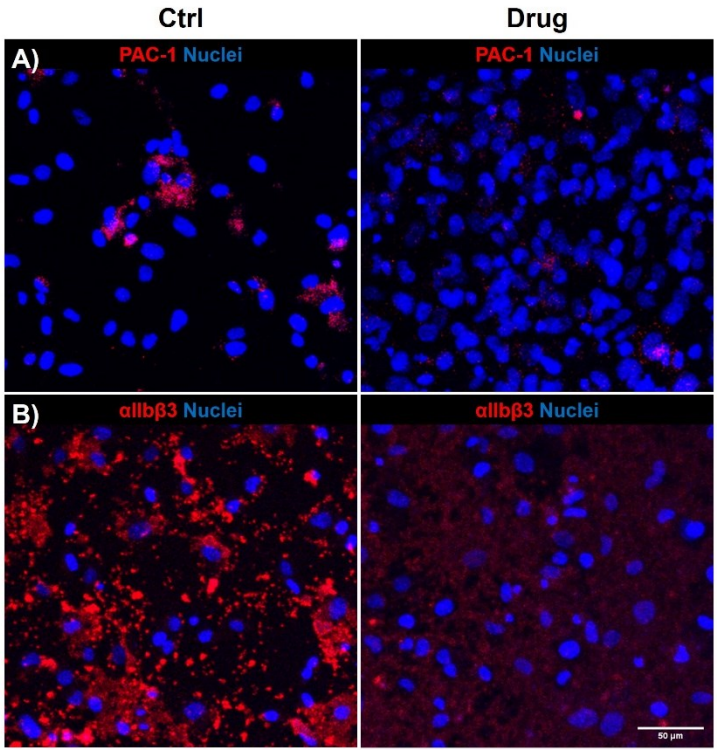
Electronic Supplementary Material (ESI) for Lab on a Chip.



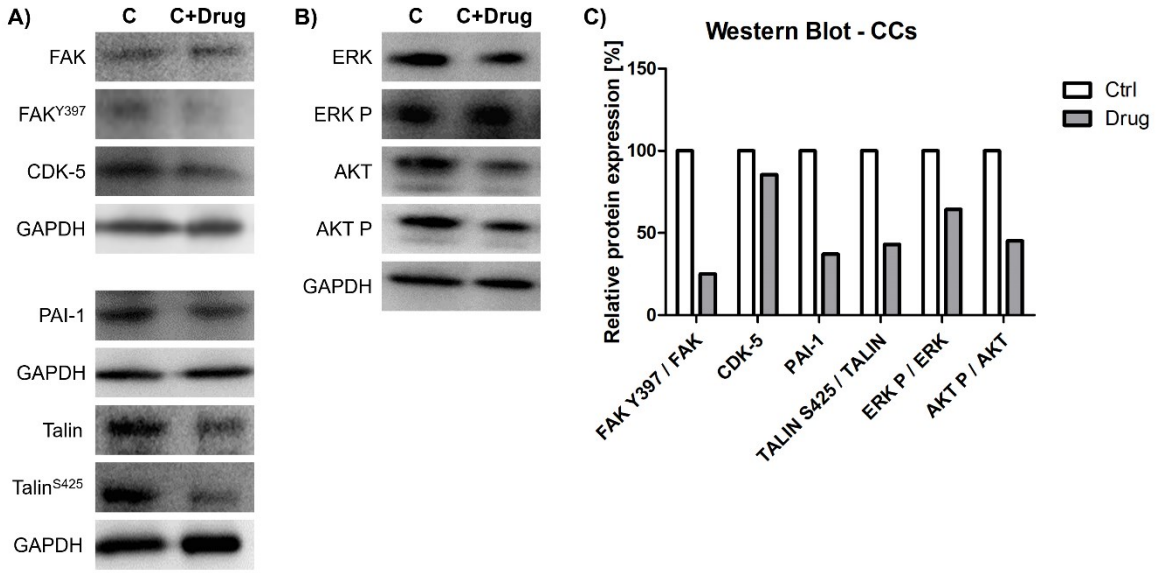
Supplementary Figure 1: *Analysis of platelet activation. Isolated platelets (PAC-1, green) and neutrophils (CD11b, blue) after sorting from whole blood (A, original magnification 4X). Histograms showing the percentage of activated platelets (P-selectin expression above a selected threshold) after 24 h incubation in different experimental conditions (CCs or CCs+ECs) or without cells (incubation with endothelial growth medium) (B). Time-dependent analysis of platelet activation (P-selectin positive platelets) in different experimental conditions (n=3, **: p<0.01; ***: p<0.001) (C).*



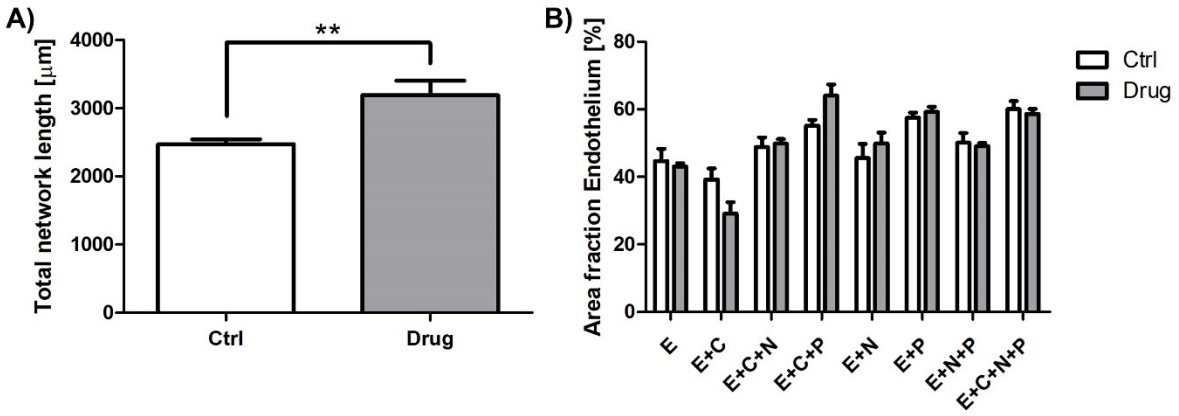
Supplementary Figure 2: *The EMN affects CC morphology. Morphological analysis of CCs (red) co-cultured with combinations of platelets and neutrophils (A). CC morphology was analyzed in terms of circularity index (at least n=27 measurements in 3 biological replicates, #: p<0.05 as compared to the group cancer cells+neutrophils C+N; ^: p<0.05 as compared to the group cancer cells+neutrophils+platelets, C+N+P) (B) and major to minor axis ratio (at least n=27 measurements in 3 biological replicates, #: p<0.05 as compared to the group cancer cells+neutrophils, C+N; ^: p<0.05 as compared to the group cancer cells+neutrophils+platelets, C+N+P; §: p<0.05 as compared to the group cancer cells+endothelial cells+platelets, C+E+P) (C). Quantification of the area fraction covered by ECs alone or when co-cultured with combinations of CCs, platelets and neutrophils (n=4, #: p<0.05 as compared to the group ECs (E); ^: p<0.05 as compared to the group endothelial cells+cancer cells (E+C) (D). Staining of dead cells with DRAQ7 dye (purple) in CC monoculture (red) or co-culture of CCs (red), neutrophils, platelets and ECs (green) (E). All fluorescence images were taken with a 10X original magnification. Legend: C (cancer cells), P (platelets), N (neutrophils), E (endothelial cells). Statistical differences were quantified using ANOVA test with Bonferroni correction.*



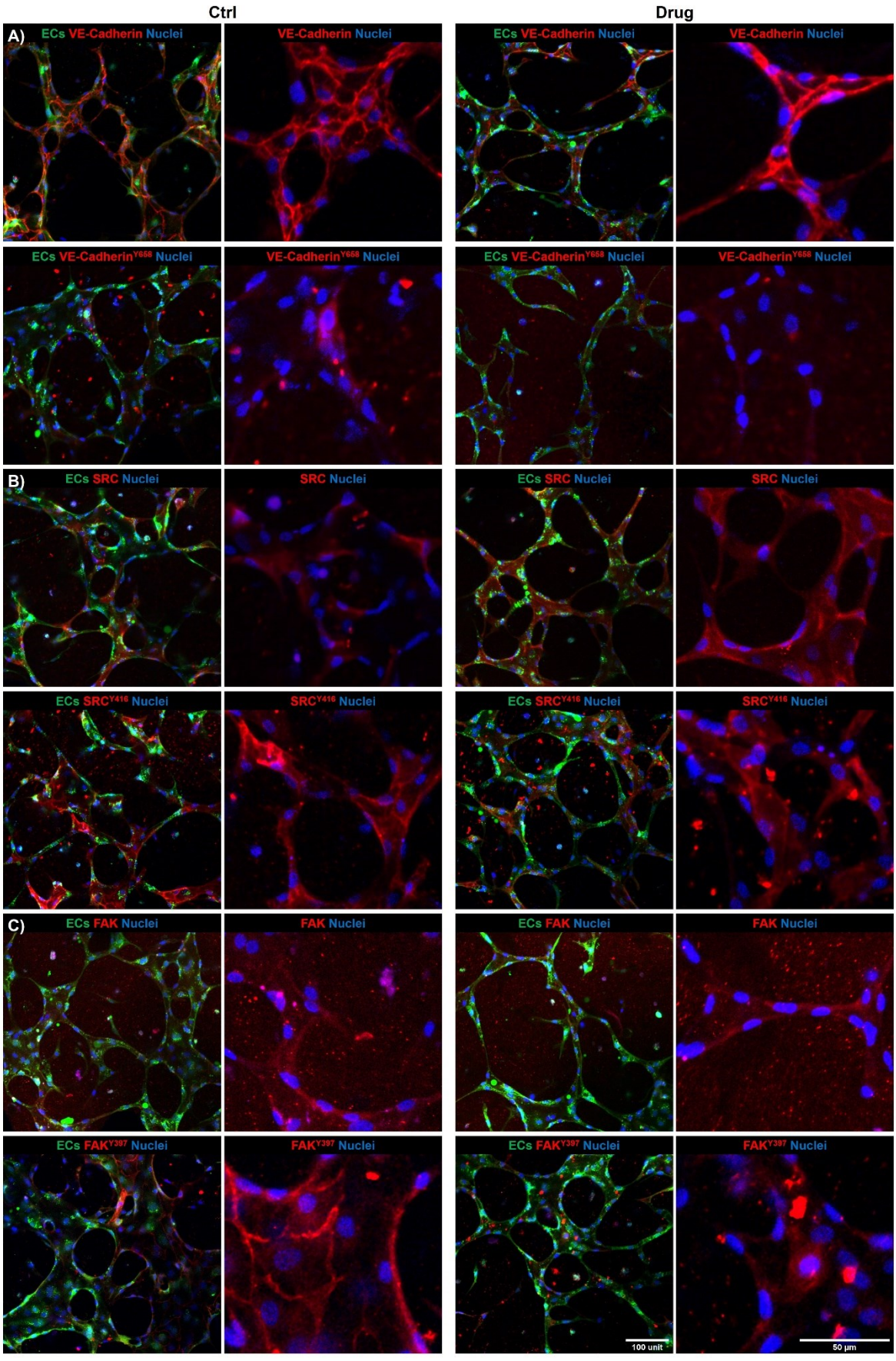
Supplementary Figure 3: *Effect of eptifibatide on platelet activation and integrin $\alpha_{IIb}\beta_3$ expression. PAC-1 and $\alpha_{IIb}\beta_3$: red. Nuclei: blue. Fluorescence images were taken with a 4X original magnification and then magnified 4X. Legend: C (cancer cells), P (platelets), N (neutrophils).*



Supplementary Figure S4. *Western Blot showing CC expression of AKT, phosphorylated AKT, ERK and phosphorylated ERK in co-cultures with ECs, neutrophils and platelets (A). Quantification of Western Blot data regarding CCs. Data reported are normalized to GAPDH. The data show the percentage of protein expression of drug treated samples compared to non-treated samples, which are arbitrarily normalized to 100% (B).*



Supplementary Figure S5. *Effect of Eptifibatide on the endothelium in 2D and 3D experiments. Total network length (n=6 in 6 biological replicates, p=0.0088) (A). Area fraction covered by ECs in different co-culture conditions with or w/o eptifibatide (B).*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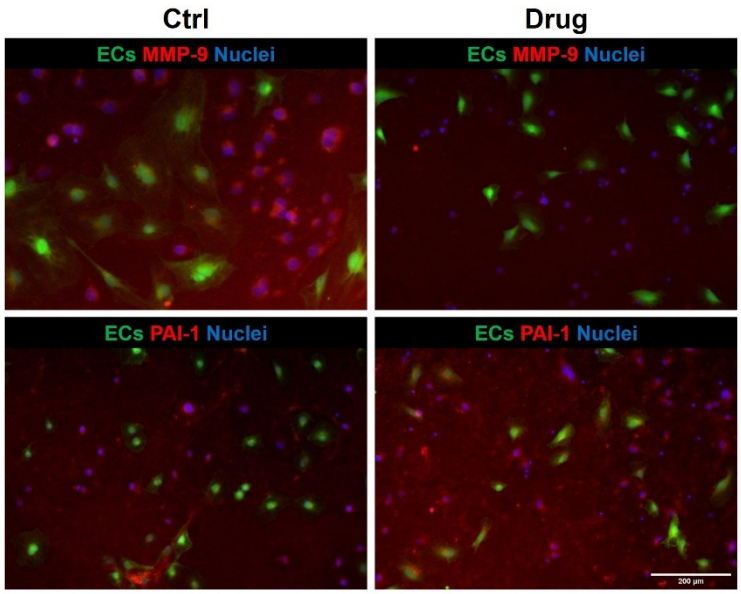
Supplementary Figure S6. *Immunofluorescence images of the microvascular network showing EC expression of VE-cadherin, phosphorylated VE-cadherin (Y658), FAK and phosphorylated FAK (Y397) cultured w/ and w/o eptifibatide. Fluorescence images of endothelial cells (ECs, green), nuclei (blue) and VE-cadherin, Y658 VE-cadherin, FAK and Y397 FAK (red) were taken with a 10X original magnification.*



Supplementary Figure S7*. CC expression of MMP9 and PAI-1 in co-cultures w/ ECs and platelets but w/o neutrophils, in presence or absence of eptifibatide.*