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Curcumin modulates vascular endothelial permeability and monocyte transendothelial migration by affecting endothelial cell dynamics

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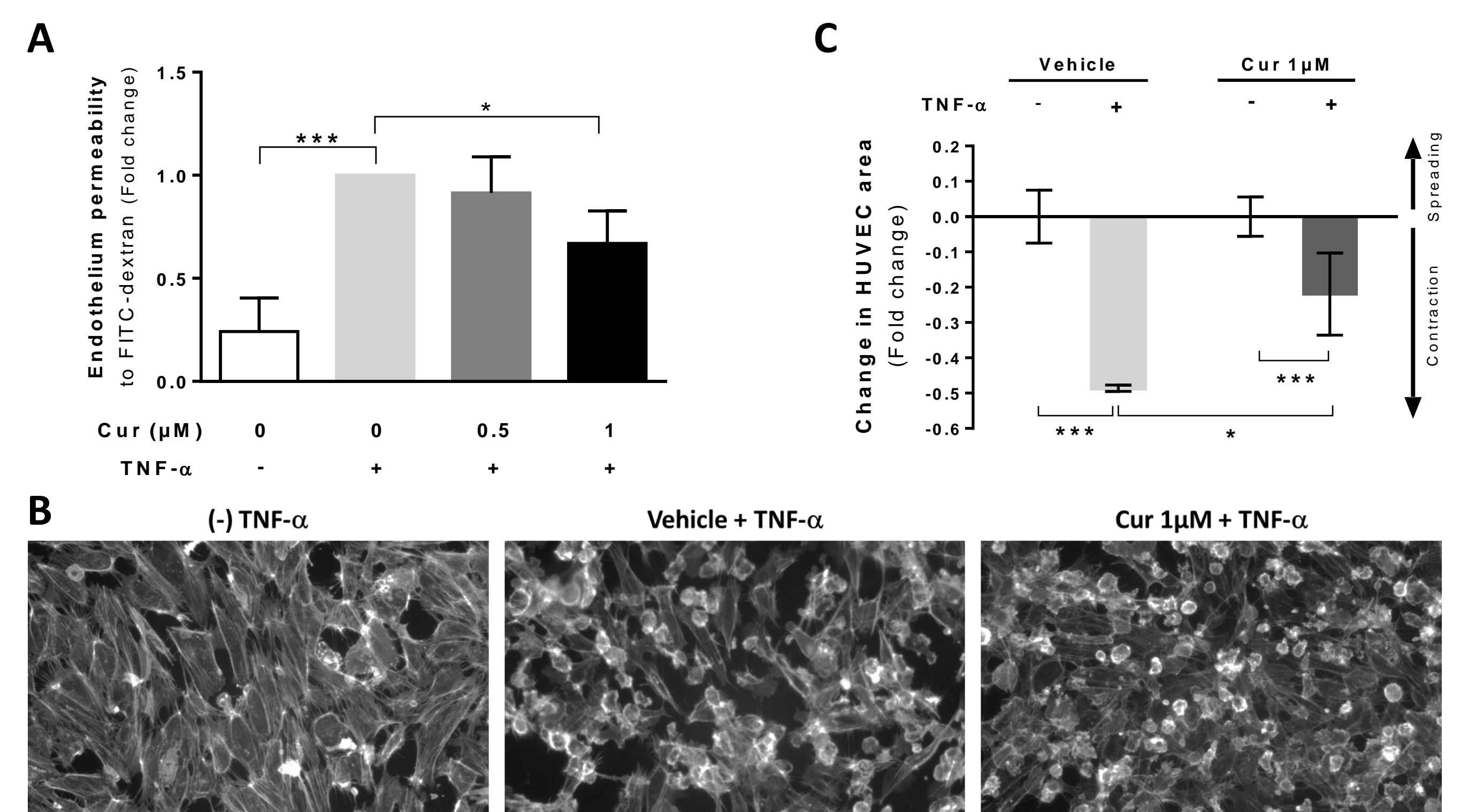
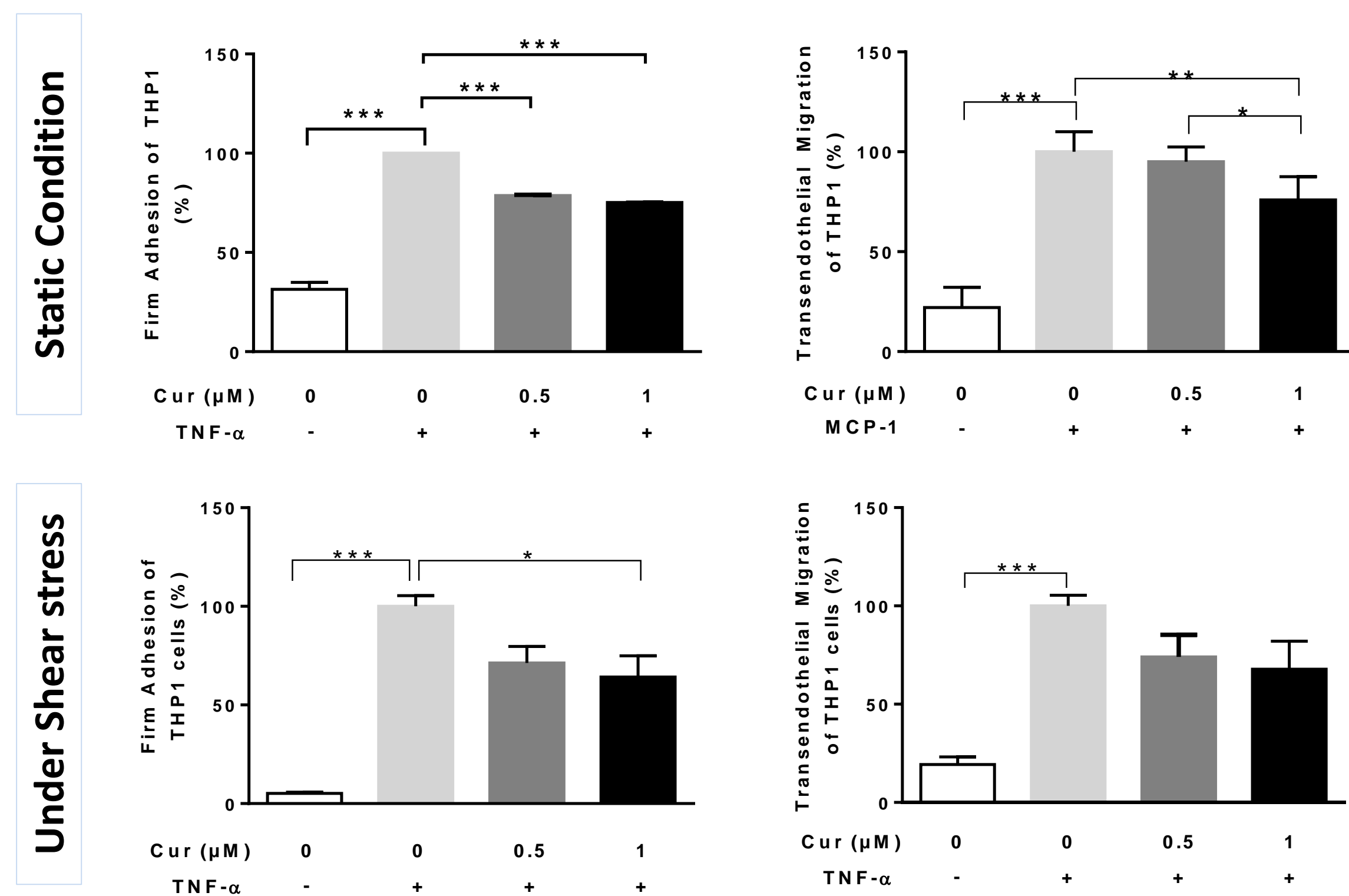
Curcumin is a phenolic compound that exhibits beneficial properties for cardiometabolic health. We previously showed that curcumin reduces the infiltration of immune cells into the vascular wall and prevented atherosclerosis development in mice.

This study aimed to investigate the effect of curcumin on monocyte adhesion and transendothelial migration (TEM) and to decipher the underlying mechanisms of these actions.

Study Design: Human umbilical vein endothelial cells (HUVECs) were exposed to curcumin (0.5-1 μ M) for 3 hours prior to their activation by Tumor Necrosis Factor alpha (TNF- α).

Effect of curcumin on monocyte adhesion to endothelial cells and their transendothelial migration (TEM)

Effect of curcumin on endothelium integrity



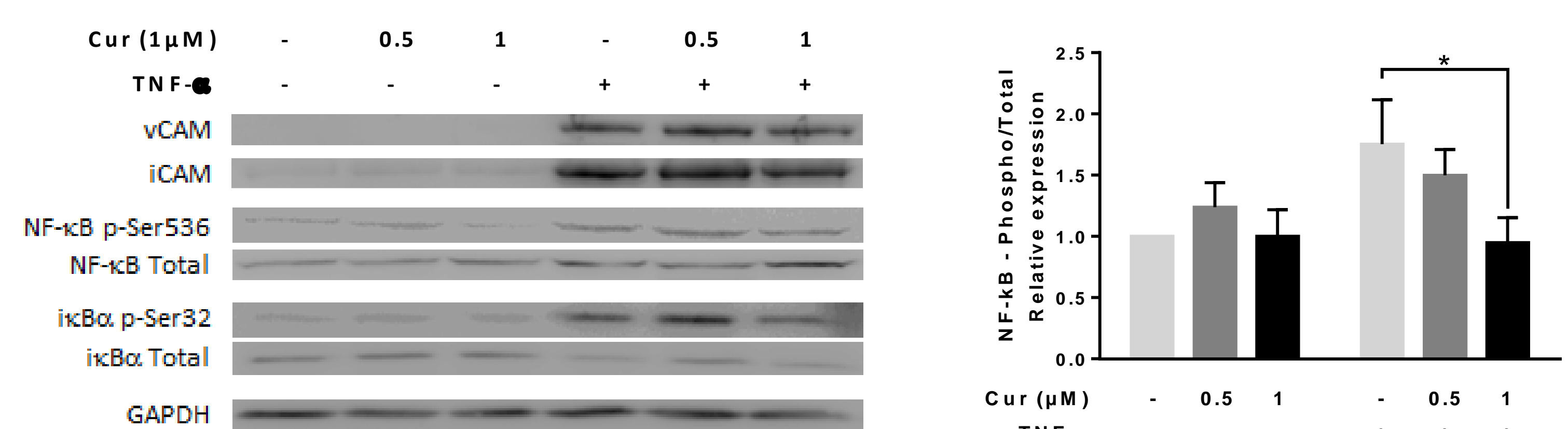
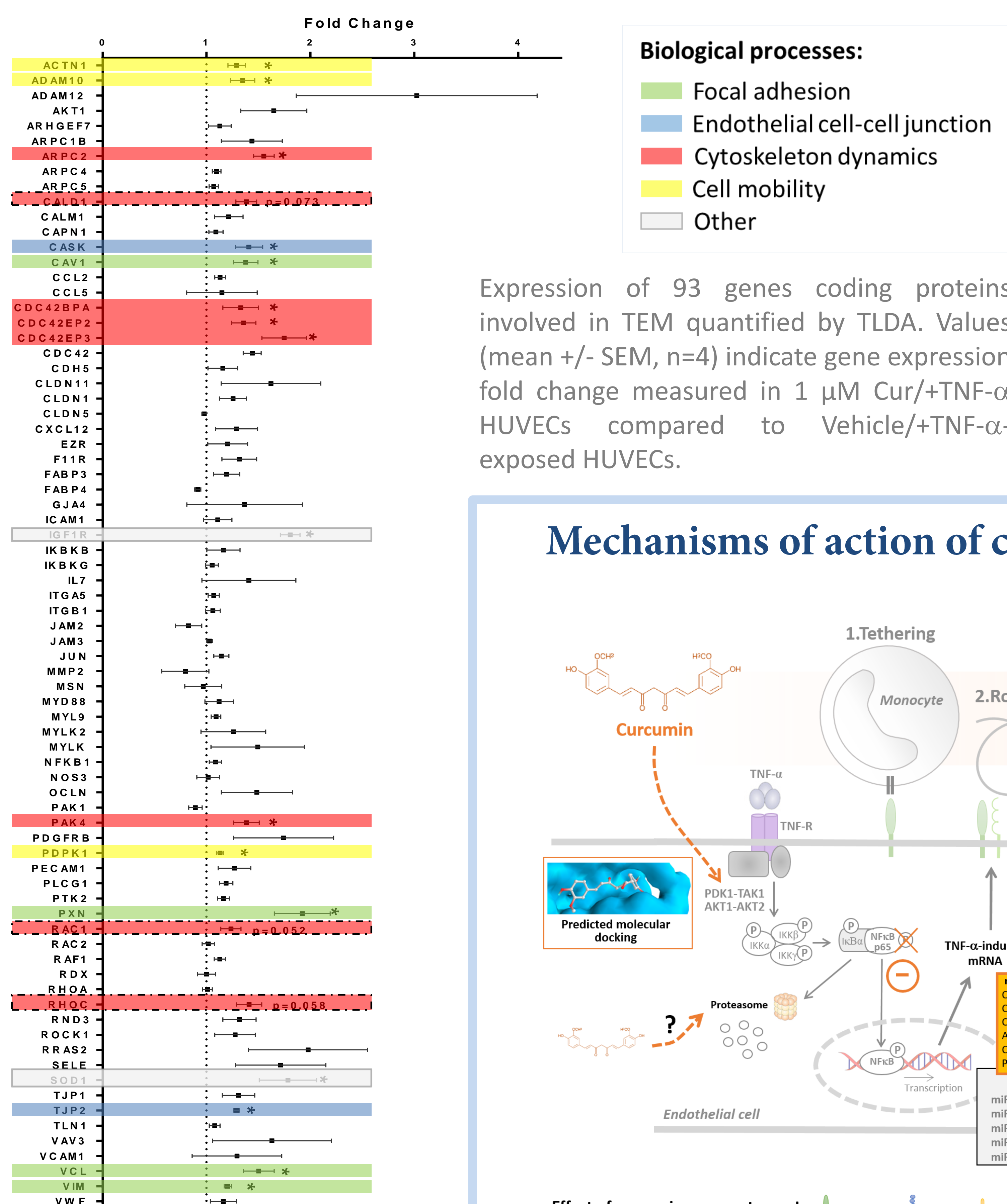
In vitro assays showed that a pre-exposure of HUVECs to curcumin reduced the firm adhesion of monocytes to the endothelial surface induced by TNF- α stimulated (-25%), and their transmigration (-24%).

Cell permeability assays, performed using Transwell system, revealed that a pre-incubation of endothelial cells with 1 μ M curcumin reduced by 34% the increase of endothelial permeability to FITC-dextran induced by TNF- α (A). In addition, exposure of endothelial cells to 1 μ M curcumin reduced by 50% the TNF- α -induced contraction of HUVECs (B-C) ($p < 0.05$).

Time-lapse microscopy assessing monocyte adhesion and transendothelial migration under shear stress (~ 7 dyne/cm²) showed that the pretreatment of HUVECs with 0.5 μ M or 1 μ M curcumin tended to decrease the number of adherent and the number of migrated monocytes.

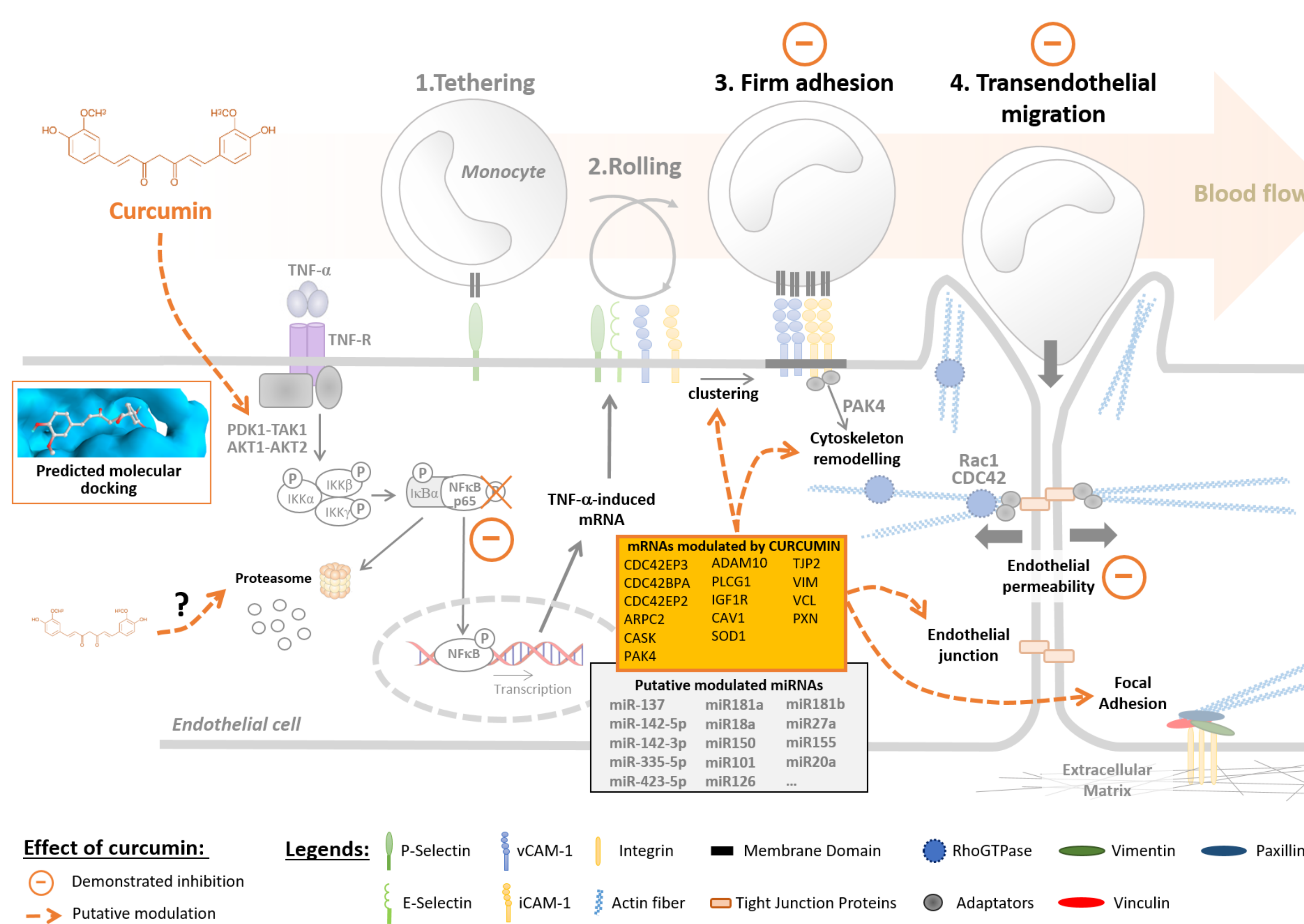
Impact of curcumin on endothelial adhesion molecules and on NF- κ B signaling pathway proteins in HUVECs.

Gene expression in curcumin-exposed HUVECs

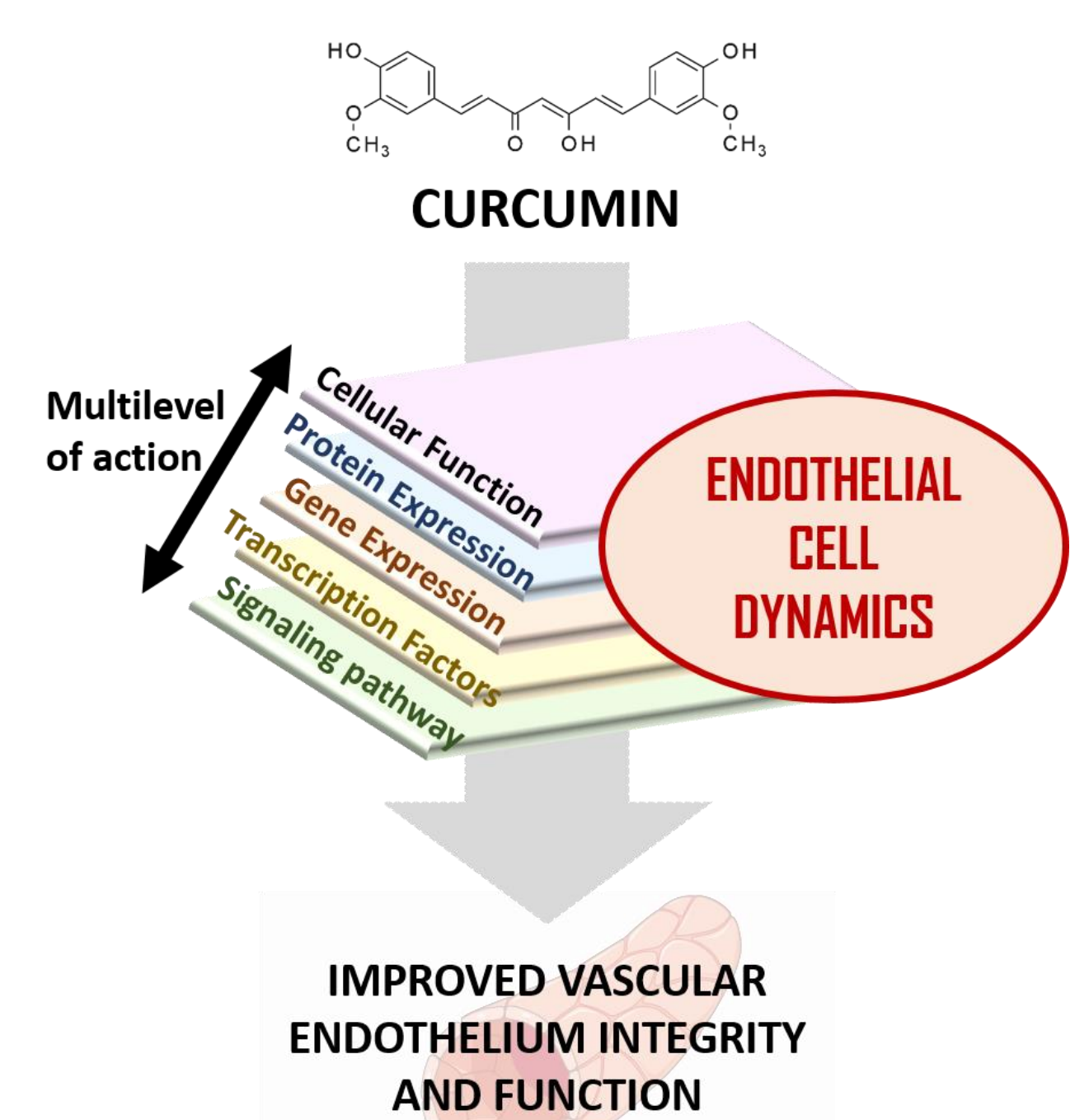


The exposure of HUVECs to 1 μ M curcumin prior to TNF- α -activation did not affect the expression of adhesion molecules (vCAM, iCAM) highly induced by TNF- α . However, it significantly reduced the level of phosphorylation of NF- κ B p65 without affecting that of κ B α .

Mechanisms of action of curcumin in endothelial cells



Conclusion



Our findings demonstrate the ability of curcumin to reduce monocyte TEM through a multimodal regulation of the endothelial cell dynamics with a potential benefit on the vascular endothelial function barrier.