rhAPC reduces the endothelial cell permeability via a decrease of cellular mechanical contractile tensions

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Abstract - **All cells generate contractile tension. Mechanical strain is crucial for controlling the cell shape, function and survival. In this study, the CellDrum technology quantifying cellular mechanical tension on a pico-scale was used to investigate the effect of LPS (lipopolysaccharide) on HAoEC (Human Aortic Endothelial Cell) tension. The LPS effect during gram-negative sepsis on endothelial cells is due to cell contraction causing an endothelium permeability increase. The aim was to finding out whether rhAPC (Recombinant Activated Protein C) would reverse the endothelial cell response to LPS in an in-vitro sepsis model. In this study, the established in-vitro sepsis model was confirmed by IL-6 (interleukin 6) levels at the proteomic and genomic levels by ELISA, real time-PCR and ROS (reactive oxygen species) activation by florescence staining. The thrombin induced cellular contraction of endothelial cells was used as a positive control when the CellDrum technology was applied. Additionally, the Ras homolog gene family, member A (RhoA) mRNA expression level was checked by real time-PCR to support contractile tension results. According to contractile tension results, the mechanical predominance of actin stress fibers was a reason of the increased endothelial contractile tension leading to enhanced endothelium contractility and thus permeability enhancement. The originality of this data supports firstly the basic measurement principles of the CellDrum technology and secondly that rhAPC has a beneficial effect on sepsis induced cell tension enhancement. The technology presented here is promising for future high-throughput cellular-tension analysis that will help identify pathological contractile tension responses of cells and prove further cell in-vitro models.**