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## Abstract 626: RNA Interference To Knock Down Endothelial Von Willebrand Factor Protects Against Endothelial Infection By SARS-CoV-2

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### Abstract

**Background:** Long-Coronavirus Disease-19 (COVID19) endotheliopathy is related to high levels of endothelial von Willebrand Factor (vWF). However, the role of vWF in regulating the susceptibility of endothelial cells to severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) infection is still unknown. We hypothesized that targeting endothelial vWF with short interference RNA (siRNA) may prevent SARS CoV 2 entry into endothelial cells through angiotensin converting enzyme 2 (ACE2).

**Method:** Gene silencing of vWF or ACE2 was performed in Human Umbilical Vein Endothelial cells (HUVECs) by short interfering RNA (siRNA), while vWF overexpression was obtained by transient pcDNA3.1-WT-VWF plasmid transfection of endothelial cells. The expression of ACE2 and vWF in endothelial cells was measured by the aid of qRT-PCR. Fluorochrome-labeled antibodies were used as probes for surface detection of both endothelial proteins. Wild type and transfected HUVECs were incubated with SARS-CoV-2 for one hour, and the level of cell infection was assessed by qRT-PCR of viral RNA after 24-48 hours.

**Results:** Effective siRNA-mediated knockdown of vWF in viable HUVECs halved the susceptibility to infection by SARS-CoV-2 ( $p=0.0058$ ). Interestingly, endothelial vWF knockdown induced a downregulation of ACE2 expression on the same cell ( $p=0.0032$ ) and a significant localization on cell surface. Conversely, vWF overexpression led to significant upregulation of surface ACE2 ( $p=0.028$ ) and increased susceptibility of HUVECs to SARS-CoV-2 infection ( $p=0.0009$ ).

**Conclusions:** Our findings reveal a hitherto unsuspected role of vWF in susceptibility of endothelial cells to viral infection by modulating levels of ACE2. Our discovery might be helpful

to design new RNA-based therapeutics to prevent long-term viral persistence of SARS-CoV-2 in endothelial cells.

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## Footnotes

Author Disclosures: For author disclosure information, please visit the AHA Vascular Discovery: From Genes to Medicine 2023 Scientific Sessions [Online Program Planner](#) and search for the abstract title.



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