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Endothelial cell mechanics as marker for cellular function and dysfunction

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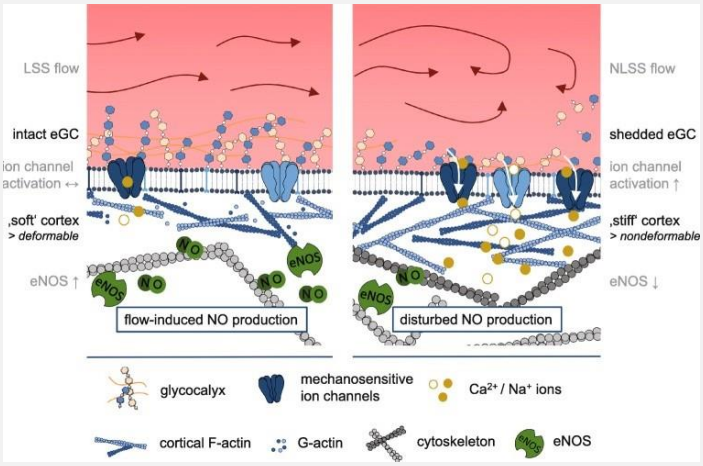
Short summary:

Endothelial cells form the innermost layer of blood vessels and are therefore exposed to the haemodynamic forces of the blood flow. This ‘strategic position’ enables the vascular endothelium to control vascular functions. Endothelial cells change their mechanical properties and thus react flexibly to different shear forces. The ability to switch between soft and stiff endothelial cell surfaces is of great physiological importance and regulates the release and bioavailability of vasodilatory substances, such as the vasodilatory nitric oxide: soft endothelial cells are more strongly deformed by the blood flow and release more NO than stiff cells. The ‘stiffness’ is therefore a mechanical property that reflects the physiological state of (endothelial) cells. We have shown that a chronically stiffened endothelium leads to endothelial dysfunction and contributes to the development of cardiovascular diseases such as atherosclerosis and hypertension. We have identified mechanosensitive structures, ion channels, vasoactive factors and signaling pathways which are mediators for the mechanical surface properties of endothelial cells. Major focus is hereby the endothelial glycocalyx on top of endothelial cells. This negatively charged, brush-like structure is known as the uppermost surface layer of the

endothelial cells. It consists mainly of glycoproteins and proteoglycans and covers the luminal surface of the endothelium along the entire vascular tree. Together with the underlying actin-rich endothelial cortex, 50-150 nm below the plasma membrane, the endothelial glycocalyx is recognized as a vasoprotective nanobarrier and reactive hub. Importantly, both eGC and cortex are highly dynamic and can adapt their nanomechanical properties (i.e. stiffness and height) to changes in the environment.

By using the atomic force microscope (AFM.) as a nanoindentation tool and for single cell force spectroscopy, we are interested in both the basic mechanical properties of the endothelial surface and the dysfunction associated with inflammatory diseases of the vasculature. The main goal of our work is therefore to build a translational bridge between cell mechanics and clinical aspects. (1-6)



1. Cosgun ZC et al. Rapid shear stress-dependent ENaC membrane insertion is mediated by the endothelial glycocalyx and the mineralocorticoid receptor. Cell Mol Life Sci. 2022;79(5):235.
2. Fels B et al. Effects of Chronic Kidney Disease on Nanomechanics of the Endothelial Glycocalyx Are Mediated by the Mineralocorticoid Receptor. Int J Mol Sci. 2022;23(18).
3. Achner L et al. AFM-based nanoindentation indicates an impaired cortical stiffness in the AAV-PCSK9(DY) atherosclerosis mouse model. Pflugers Arch. 2022;474(9):993-1002.
4. Pacia MZ et al. Rac1 regulates lipid droplets formation, nanomechanical, and nanostructural changes induced by TNF in vascular endothelium in the isolated murine aorta. Cell Mol Life Sci. 2022;79(6):317.
5. Fels B, Kusche-Vihrog K. It takes more than two to tango: mechanosignaling of the endothelial surface. Pflugers Arch. 2020;472(4):419-33.
6. Cosgun ZC, Fels B, Kusche-Vihrog K. Nanomechanics of the Endothelial Glycocalyx: From Structure to Function. Am J Pathol. 2020;190(4):732-41.

Biosketch:

Education / Training	
1993-1999	Studies of biology, Universities of Mainz (Germany) and Umeå (Sweden)
1999	Diploma in biology, University of Mainz, Germany
2001	PhD thesis (Dr. rer. nat.), University of Mainz, Germany
Research Experience / Academic Appointments	
2001 - 2002	Postdoc at the Institute of Animal Physiology, University of Mainz, Germany
2002 – 2008	Research Assistent (C1) at the Institute of Animal Physiology, University of Münster (WWU), Germany
2005	Postdoc at the Laboratory of Lung Cellular Physiology and Biophysics, (CRCHUM), Université de Montréal (Kanada)

2008 – 2018	Group leader at the Institute of Physiology, University of Münster (UKM), Germany
2013	Post-doctoral lecture qualification and university teaching credentials (Habilitation) in Physiology, University of Münster (UKM), Germany
Since 2018	W3 Professor and Director of the Institute of Physiology, University of Lübeck, Germany
Fields of interest	1. Endothelial function and dysfunction 2. Ion channels 3. Mechanomedicine 4. Vascular inflammation 5. Vascular barrier function
Important Scientific Awards / Functions	
2011	Dieter-Klaus Award, German Society for Hypertension
2018	Hypertension Award, German Society for Nephrology (DGfN)
Since 2017	Board member, German Society of Hypertension
Since 2017	Editorial Board Member, Scientific Reports
Since 2019	Editorial Board Member, PLOS ONE
Since 2021	Editorial Board Member, IJMS

Relevant publications:

1. Roy-Chowdhury E, Brauns N, Helmke A, Nordlohne J, Bräsen JH, Schmitz J, Volkmann J, Fleig SV, **Kusche-Vihrog K**, Haller H, von Vietinghoff S. Human CD16+ monocytes promote a pro-atherosclerotic endothelial cell phenotype via CX3CR1-CX3CL1 interaction. Cardiovasc Res. (2021) 117:1510-1522. doi: 10.1093/cvr/cvaa234.

2. Bartolomaeus H, Balogh A, Yakoub M, Homann S, Markó L, Höges S, Tsvetkov D, Krannich A, Wundersitz S, Avery EG, Haase N, Kräker K, Hering L, Maase M, **Kusche-Vihrog K**, Grandoch M, Fielitz J, Kempa S, Gollasch M, Zhumadilov Z, Kozhakhmetov S, Kushugulova A, Eckardt KU, Dechend R, Rump LC, Forslund SK, Müller DN, Stegbauer J, Wilck N. Short-Chain Fatty Acid Propionate Protects From Hypertensive Cardiovascular Damage. Circulation (2019) 139:1407-1421. doi: 10.1161/CIRCULATIONAHA.118.036652.

3. Maase M, Rygula A, Pacia MZ, Proniewski B, Mateuszuk L, Sternak M, Kaczor A, Chlopicki S, **Kusche-Vihrog K.** Combined Raman- and AFM-based detection of biochemical and nanomechanical features of endothelial dysfunction in aorta isolated from ApoE/LDLR-/- mice. Nanomedicine. (2019) 16:97-105. doi: 10.1016/j.nano.2018.11.014

4. Tarjus A, Maase M, Jeggle P, Martinez-Martinez E, Fassot C, Loufrani L, Henrion D, Hansen PBL, **Kusche-Vihrog K***, Jaisser F*. The endothelial αENaC contributes to vascular endothelial function in vivo. PLoS One. (2017) 12:e0185319. doi: 10.1371/journal.pone.0185319. eCollection 2017. *equal contributors

5. Schierke F, Wyrwoll MJ, Wisdorf M, Niedzielski L, Maase M, Ruck T, Meuth SG, **Kusche-Vihrog K.** Nanomechanics of the endothelial glycocalyx contribute to Na+-induced vascular inflammation. Sci Rep. (2017) 7:46476. doi: 10.1038/srep46476