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## **Bioengineering and biophysics of viral hemorrhagic fever**

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## Propositions

### Stellingen

Behorende bij het proefschrift

Bioengineering and Biophysics of Viral Hemorrhagic Fever

1. Microfluidic Organ Chip culture devices are a promising strategy for reproducing various viral disease phenotypes, including viral hemorrhagic fever. (Chapter 2)
2. The microvessels-on-a-chip platform is robust in mimicking the viral hemorrhagic fever-associated vasculopathy, and helps in understanding the effect and mechanism of experimental compounds on Ebola and Lassa. (Chapters 3 & 4)
3. Dengue NS1-mediated mechanical alterations of endothelial cells is a key element of Dengue virus disease, revealed by microvessels-on-a-chip and acoustic force spectroscopy. (Chapter 5)
4. Ebola virus-like particles induced specific cellular metabolic reprogramming to endothelial cells, M1 and M2 macrophages, in a cell specific manner. (Chapter 6)
5. Conventional *in vitro* culture and animal models cannot faithfully reflect human physiology and pathophysiology in response to pathogens, highlighting the importance of complex human-derived systems. – Adapted from Widerspick, L., et al., *Viruses*, 2023
6. The involvement of vascular endothelium and the perturbation of vascular barrier integrity as well as coagulation abnormalities, has been recognized as common pathological signature of viral hemorrhagic fevers. – Adapted from Srikiatkachorn, A., et al., *Cell and Tissue Research*, 2014
7. Dengue NS1 can directly trigger systemic vascular leakage *in vivo* and endothelial hyperpermeability *in vitro* in the absence of infection, however, until this PhD thesis, direct measurement of endothelial cell mechanics in Dengue disease has been lacking. – Adapted from Puerta-Guardo H., et al., *PLOS Pathogens*, 2016

8. Macrophages play a central role in viral hemorrhagic fever as initial viral targets and targets throughout the course, its M1 polarization shows the ability to inhibit Ebola infection while M2 can promote infection. – Adapted from Rogers, K., et al., *Journal of Leukocyte Biology*, 2018
9. What I cannot engineer, I do not understand.
10. Engineer every organ as simple as possible, but not simpler.

Huaqi Tang

Leiden, 19 September 2023