EVBO Paper of the month October 2023

Paloschi V, Pauli J, Winski G, Wu Z, Li Z, Botti L, Meucci S, Conti P, Rogowitz F, Glukha N, Hummel N, Busch A, Chernogubova E, Jin H, Sachs N, Eckstein HH, Dueck A, Boon RA, Bausch AR, Maegdefessel L. Utilization of an Artery-on-a-Chip to Unravel Novel Regulators and Therapeutic Targets in Vascular Diseases. *Adv Healthc Mater*. 2023 Oct 5:e2302907. doi: 10.1002/adhm.202302907.

In our EVBO paper of the month for October, Paloschi *et al.* utilize an organ-on-chip technology to develop an *in vitro* model of medium-to-large size arteries, the artery-on-a-chip (AoC). The objective is to recapitulate the structure of the arterial wall and the relevant hemodynamic forces affecting luminal cells. AoCs exposed either to *in vivo*-like shear stress values or kept in static conditions are assessed to generate a panel of novel genes modulated by shear stress. Considering the crucial role played by shear stress alterations in carotid arteries affected by atherosclerosis (CAD) and abdominal aortic aneurysms (AAA) disease development/progression, a patient cohort of hemodynamically relevant specimens was utilized, consisting of diseased and non-diseased (internal control) vessel regions from the same individual patient. Genes activated by shear stress follow the same expression pattern in non-diseased segments of human vessels. Single cell RNA sequencing (scRNA-seq) enables to discriminate the unique cell subpopulations between non-diseased and diseased vessel portions, revealing an enrichment of flow activated genes in structural cells originating from non-diseased specimens. Furthermore, the AoC served as a platform for drug-testing. It reproduced the effects of a therapeutic agent (lenvatinib) previously used in preclinical AAA studies, therefore extending the understanding of its therapeutic effect through a multicellular structure.