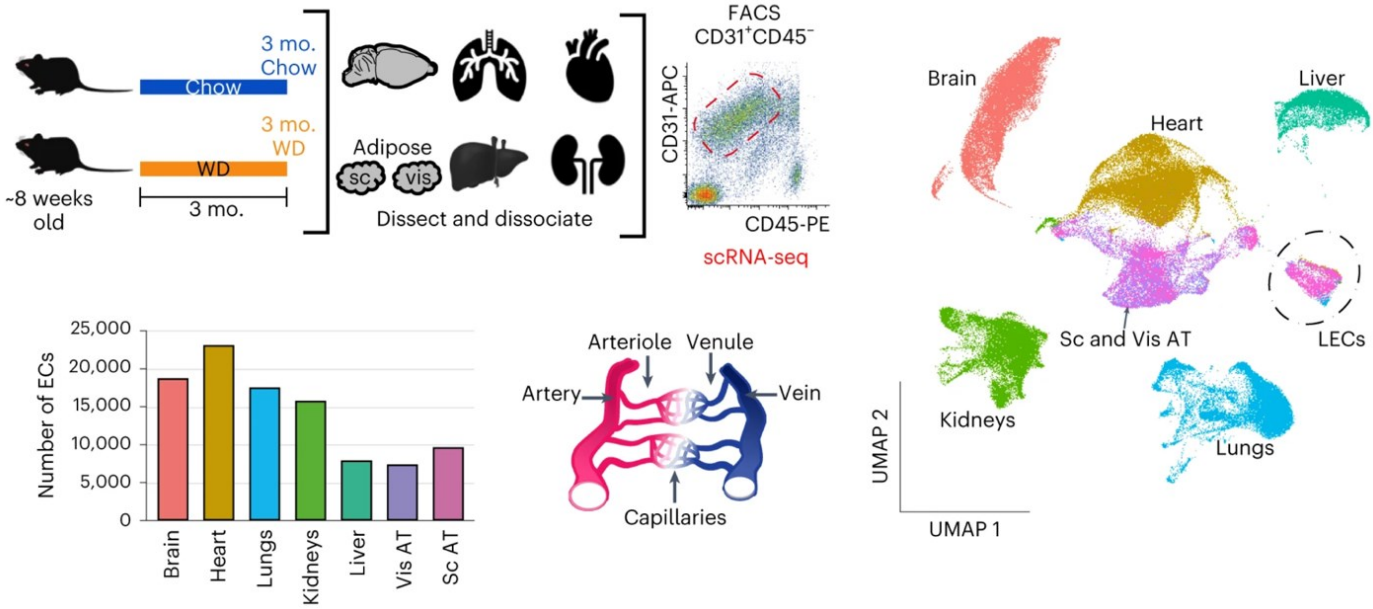
Single-cell profiling of vascular endothelial cells reveals progressive organ-specific vulnerabilities during obesity. Bondareva, O., Rodríguez-Aguilera, J.R., Oliveira, F. Liao L, Rose A, Gupta A, Singh K, Geier F, Schuster J, Boeckel JN, Buescher JM, Kohli S, Klöting N, Isermann B, Blüher M, & Sheikh BN. Nat Metab. 2022; 4:1591–1610. doi.org/10.1038/s42255-022-00674-x



Obesity can promote diverse pathologies, including atherosclerosis and dementia, which frequently involve vascular defects and endothelial cell (EC) dysfunction. Each organ has distinct EC subtypes, but whether ECs are differentially affected by obesity is unknown.

In this current study, the authors have used used single-cell RNA sequencing to analyze transcriptomes of ~375,000 ECs from seven organs in male mice at progressive stages of obesity to identify organ-specific vulnerabilities. They discovered that obesity deregulates gene expression networks, including lipid handling, metabolic pathways and AP1 transcription factor and inflammatory signaling, in an organ- and EC-subtype-specific manner. The transcriptomic aberrations did worsen with sustained obesity and were only partially mitigated by dietary intervention and weight loss. Dietary intervention attenuated dysregulation of liver, but not kidney, EC transcriptomes.

Through integration with human genome-wide association study data, the authors further identified a subset of vascular disease risk genes being induced by obesity. Their work catalogues the impact of obesity on the murine endothelium, constitutes a useful resource and reveals leads for investigation as potential therapeutic targets in human disease.