Title: Piezo1: A missing piece to understand Microcirculation intrinsic control

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Structured Abstract:

Introduction: The complexity of the cardiovascular system can be reduced to a set of entities working dynamically to transport and distribute essential nutrients to all tissues, and remove the metabolic byproducts of the latter. The controling systems of the microvascular networks are indispensable to maintain, in achieving this fine –tuned machinery; providing all body tissues with blood flow & pressure at its optimal state.
Although the extrinsic control; primarily regulated by an extensive neural system, has been and still is broadly studied. Nevertheless, the lack of understanting of the intrinsic mechanisms regulation, has guide our research to other avenues, focusing primarily on Myogenic control and Shear stress mediated dilation.

Hypothesis: Piezo1 channel activation is indispensable for myogenic control and FID. Therefore, Blocking specifically Piezo1 channels, will generate disparities in myogenic control and FID.

Methods: Employing Sprague-Dawleys (n=6) as experimental subjects, we took Gracilis and Middle Cerebral Arteries for ex-vivo vessel preparations using Living Systems instrumentation. After confirming vascular viability, by setting the vessel to pharmacological challenges of Phenylephrine (Pe) and Acetilcholine (Ach) (Sigma-Aldrich). As control, the artery is subjected first to a set of pressure and then flow challenges, to measure its ability to adjust the diameter in relationship to the randomized pressure and flow rate changes. Then, the same set of pressure & flow changes is repeated after incubation of a spider toxin (GsMTx4), which blocks specifically Piezo1 protein receptors. For data analysis we used Student t-test and SD with SEM.

Results: After selective inhibition of Piezo1 proteins through GsMTx4, we see a correlation with increases in pressure and the incabability of the vessel to regulate its diameter. Also, with our flow experiments, we were surprised to see a decrease of about one third, in vascular variability, also, after GsMTx4 incubation, corresponding to a decrease of an effective flow induced changes in the diameter of the vessel.

Discussion: This reduction of vascular variability obtained by the specific blocking of the Piezo1 channels, impact the capacity of the vessels to adjust in phisiologycal settings where pressure and shear stress can increase do to normal and pathological scenarios, compromising their ability to provide proper regulation and damage the downstream tissues. We need further studies to actually measure the effect of Piezo1 in sex differences, and explain the loss of autoregulation in pathophysiological states, where the microcirculation seems to be the first system to be compromised.