Featured Young Investigator's Recent Study in *Microcirculation* *

Involvement of the H1 Histamine Receptor, p38 MAP Kinase, Myosin Light Chains Kinase, and Rho/ROCK in Histamine-Induced Endothelial Barrier Dysfunction

Featuring: ***Shaquria Adderley, Postdoctoral Fellow, University of South Florida***

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Shaquria at her lab at the University of South Florida

The microvascular endothelial barrier is essential for maintaining circulatory homeostasis and organ function. Abnormally increased endothelial permeability can lead to excessive loss of plasma proteins, leading to edema and tissue dysfunction. Moreover, elevated permeability is a hallmark of inflammatory tissue injury and is associated with many pathologies. Currently no specific therapies are available to ameliorate excessive microvascular leakage. Histamine is a principal mediator of inflammation and blood histamine levels increase during insult or injury. While it has been known for nearly a century that histamine can cause tissue edema, understanding of the molecular signals in the endothelium leading to histamine-induced hyperpermeability remains less well understood. In our recent Microcirculation article, we report that endothelial cells (EC) derived from the heart, skin, and umbilical veins have different responsiveness to histamine. We also showed that the H1 histamine receptor consistently mediates histamine-induced endothelial hyperpermeability. In contrast, the involvement of the H2, H3, or H4 depends on the tissue source of the EC. We also observed that the p38 MAPK signaling pathway mediates the response in all three of the cell types tested, whereas PKC and PI3K only appear to be involved in human dermal microvascular endothelial cells. In addition, inhibition of RhoA, ROCK, or MLCK also prevented the histamine-induced decrease in transendothelial electrical resistance (TER) in these cells. These studies are a step toward comprehensive understanding of the complex signaling mechanisms in EC that control the microvascular barrier.

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