Optogenetic Modulation of Endothelial Cell Growth and Barrier Repair

Lin, Jayden (School: WP Davidson High School)

Vascular endothelial cells line blood vessels and are important in vascular health, growth, and repair, and pulsatile blood flow generated with each heartbeat sends mechanical signals to these cells. Indeed, the mechanically sensitive Ca2+ channels are activated when stretched, allowing Ca2+ influx into the endothelial cells. Thus, the physiological endothelial Ca2+ signal, activated by heartbeat and pulsatile blood flow, is thought to contribute to the health of these cells and blood vessels. Breakdowns of barrier integrity in the lung and in the brain can lead to numerous issues and diseases that can drastically affect overall health. To test the hypothesis that endothelial Ca2+ modulates cell growth and barrier integrity, we used blue light to activate channelrhodopsin to allow Ca2+ entry into the endothelial cells such as pulmonary or cerebral endothelium at various frequencies. Specifically, I tested whether the Ca2+ signal frequencies affect endothelial barrier integrity. After building a tunable device in order to control the frequency of channelrhodopsin stimulation, four experimental groups were created, each of them either with or without stimulation or channelrhodopsin. Three different stimulus frequencies were tested at 0.1, 1, and 6 Hz. Results from these studies showed an unexpected outcome–at 6 Hz which best mimics the physiological heart rate in rodents, the growth rate was significantly inhibited, most likely due to the excess Ca2+ influx into the cells. Therefore, the current conclusion is that high-frequency activation of channelrhodopsin impedes endothelial cell growth. Future studies are necessary to establish whether high-frequency stimulation causes cell death.

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