2024 WMS PGR Symposium Poster Abstract

Title: "Extracellular vesicles: the messengers of the clock in the blood-brain barrier."

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The blood-brain barrier (BBB) is a neurovascular structure vital for the regulation of nutrient transportation to the brain as well as providing protection against harmful substances for the brain. Composed of brain endothelial cells, pericytes and astrocyte end-feet, the BBB is one of the tightest junctions in the human body, posing an issue for neurotherapeutics to reach their targets. It has recently been shown that the permeability of the BBB follows 24-hour circadian rhythmicity. Most importantly, this rhythm is independent of the clock in endothelial cells, and astrocytes and pericytes can restore this rhythmicity in endothelial cells when in tri-culture BBB models *in vitro*. Interestingly, extracellular vesicles (EVs) have been shown to modulate BBB permeability and core clock gene expression in peripheral cells. Thus, as it is known astrocytes and pericytes produce EVs, we hypothesise that EVs are involved in communication between astrocytes, pericytes and endothelial cells of the BBB. To this end, we treat a well-developed tri-culture or endothelial cell model of the BBB with EVs isolated from these cells to determine changes in permeability. Furthermore, the use of bioluminescence reporter assays will allow us to determine whether EVs can alter the expression of key structural proteins in the BBB and core clock gene expression in peripheral cells. In addition, we will analyse the contents of EVs to understand how the signals produced lead to changes in BBB integrity and circadian gene expression. Our work will allow us to further understand the role of EVs in cell-to-cell communication and how this plays a role in diseases such as Alzheimer's where BBB integrity is compromised, and robustness of the internal clock is reduced.