Cardiovascular Diseases

VASOGENIC EDEMA

Background

Vasogenic edema is characterized by an increase in extracellular fluid volume due to increased permeability of brain capillary endothelial cells to macromolecular serum proteins (e.g., albumin). The key mechanism of endothelial dysfunction is the imbalance of endothelium-derived nitric oxide (NO) production and reactive oxygen species (ROS) generation, resulting in a decline in the bioavailability of NO and excessive accumulation of ROS. This finally leads to oxidative stress and cellular injuries.

Normally, the entry of plasma protein-containing fluid into the extracellular space is limited by tight endothelial cell junctions, but in the presence of massive injury, there is increased permeability of brain capillary endothelial cells to large molecules. Vasogenic edema can displace the brain hemisphere and, when severe, lead to cerebral herniation.

Pathology Model

Endothelial cells will be exposed to metabolic stress (i.e. oxygen glucose deprivation) in the presence/absence of the CLIENT's compounds.

Readouts

The following parameters will be taken into consideration:

- Total ROS production (i.e. DCF-DA fluorescent assay)
- Cell viability and toxicity: (i.e. MTT assay)
- Mitochondrial damage (i.e HCS Mitochondrial Health assay)
- Inflammatory profile. A detailed analysis of pro inflammatory and angiogenic factor production will be characterized (i.e. IL-1a , IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, VEGF, TNF-a, IFN-γ, EGF, MCP-1 etc)