2750
Topic Category: 4150-ASIP Stroke/vascular diseases

First Author: Shyanne Page
TTUHSC 1300 S. Coulter St. Amarillo, TX 79106
United States
Phone: 806-477-9074
shyanne.page@ttuhsc.edu

First Author is a: Graduate Student
First Author is a member of: American Society for Investigative Pathology, The American Physiological Society
First Author Degree: BA, BS, or equivalent

Presentation Preference: Indifferent

Sponsor: Shyanne Page
Sponsor Phone: 806-477-9074
shyanne.page@ttuhsc.edu
Sponsor's Society: Association of Pathology Chairs (APC) - ASIP Guest Society
Keywords: 1. Ischemic Stroke 2. Stem Cells 3. WNT pathway
Awards: ASIP Trainee Travel Award, ASIP Promoting Diversity in Science Trainee Travel Award, HCS-Sponsored Trainee Travel Award

Determining the effect of the WNT/b-catenin pathway on the ischemic blood-brain barrier using induced pluripotent stem cells

Shyanne Page, Abraham Al-Ahmad. TTUHSC, Amarillo, TX

The blood-brain barrier (BBB) is a selectively permeable barrier made up of tight junctions formed by endothelial cells that separates the circulating blood from the brain extracellular fluid. The primary function of this barrier is to keep toxins, bacteria, viruses, and drugs from entering the brain. In the event of an ischemic stroke, the BBB becomes leaky due to the activation of hypoxia inducible factor 1-alpha (HIF1-a) and neurons become apoptotic. It is known that activation of the WNT pathway results in the production of B-catenin, which has been shown to enhance HIF1-a mediated transcription, which promotes the survival of cells and their adaptation to hypoxia. Currently, there are no drugs that have been formulated to restore the BBB function as well as neuron survival following ischemic stress. The purpose of our study was to determine the effect of small molecules on the BBB/WNT pathway during ischemia/re-oxygenation. Brain microvascular endothelial cells (BMECs) derived from iPSCs and the immortalized human brain endothelial cell line, HCMEC/D3, were cultured and placed in ischemic stress for 6hrs, followed by a 24 hour period of re-oxygenation. At the time of re-oxygenation, cells were treated with small molecules CHIR99021, TWS (WNT activators), IWP-4, IWR, and XAV (WNT inhibitors) in order to determine the effect of the WNT pathway on cell survival. Transendothelial Electrical Resistance (TEER) and permeability were performed to assess the effect that the WNT pathway has barrier integrity following re-oxygenation. Further, MTT and ICC were performed to determine cell viability and tight junction expression, respectively. Preliminary results of this study have shown that inhibition of the WNT pathway during re-oxygenation results in up-regulation of tight junction proteins and an increase in cell viability as well as an increase in barrier function.

Support or Funding Information
Laura W. Bush Institute for Women's Health