Ouch, There Goes My Blood-Brain Barrier:
How Inflammatory Pain in the Periphery Modulates Drug Delivery to the CNS

Conducted by Patrick T. Ronaldson, Ph.D., University of Arizona

Moderated by Douglas H. Sweet, Ph.D., Virginia Commonwealth University

Wednesday, November 10, 2010 from 12:30 – 2:00 pm EST

Description:

The blood-brain barrier (BBB) constitutes a physical and biochemical barrier between the brain and the systemic circulation. This dynamic structure regulates critical processes of nutrient uptake and waste removal, thus enabling the BBB to maintain homeostasis of the brain. However, characteristics of the BBB involved in homeostatic control (i.e., tight junction complexes, functional expression of membrane drug transporters) are also significant obstacles to effective CNS drug delivery. As paracellular permeability is limited by tight junctions between adjacent endothelial cells, drug development is often focused on improving affinity for specific uptake transporters while circumventing drug efflux mechanisms. In fact, the utility of endogenous BBB uptake transporters as facilitators of CNS drug delivery has been a subject of considerable controversy. Furthermore, the complexity of CNS drug delivery is underscored by the fact that the BBB may be compromised in response to pathophysiological stressors. Recently, our laboratory has shown that pain/inflammation in the periphery can dramatically affect BBB drug transport mechanisms. In particular, we identified Organic Anion Transporting Polypeptide 1a4 as a transporter target that may be exploited to optimize delivery of therapeutic agents to the brain. Overall, results from these studies may profoundly impact drug development and/or design as well as treatment of CNS disease. This webinar will present highlights of our recent studies and how these data may translate to optimization of CNS drug delivery.

Outline:

- Brief background on the Blood-Brain Barrier.
  • Structure and function of the tight junction.
  • Localization and functional expression of ABC and SLC transporters at the BBB.
- Effect of peripheral inflammatory pain on tight junction integrity.
  • Paracellular transport of drugs.
- Effect of peripheral inflammatory pain on putative membrane transporters.
  • P-glycoprotein
  • Organic Anion Transporting Polypeptide 1a4
- Potential impact of studies on drug development and treatment of CNS diseases.
- Conclusions and Future Directions

About the Presenter

Dr. Patrick T. Ronaldson is a Research Assistant Professor in the Department of Medical Pharmacology at the University of Arizona College of Medicine. His research interests encompass effects of pathophysiological conditions on drug transporter expression at the blood-brain barrier and in glial cells (i.e., microglia, astrocytes) as well as pharmacological targeting of intracellular signaling systems as a means of optimizing CNS drug delivery. He holds an Honours B.Sc. in Pharmacology and a Ph.D. in Pharmaceutical Sciences, both conferred by the University of Toronto. He has presented his research as an invited speaker at several national and international meetings. He has 11 peer-reviewed publications on drug transport and blood-brain barrier biology. He has also co-authored 2 book chapters, including "Drug Transport in the Brain" in "Drug Transporters: Molecular Characterization and Role in Drug Disposition" (G. You & M.E. Morris, eds). Hoboken: John Wiley & Sons, 2007.