



Pharmaceutical Sciences Seminar Series
Hybrid

Wednesday, November 30, 2022
4:00pm
NCRC Building 10 - South Atrium
[Zoom Link](#)

**“Bispecific antibodies for efficient and long-lived
brain delivery of off-the-shelf IgGs”**

Presented by:



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Abstract: The blood-brain barrier (BBB) is often considered the main obstacle preventing delivery of antibodies and other biologics to the brain. One promising strategy is to deliver IgGs using a bispecific BBB shuttle, which involves fusing an IgG to a second affinity ligand that engages a cerebrovascular endothelial target and facilitates transport across the BBB. Nearly all prior efforts have focused on engaging the transferrin receptor (TfR-1) as the prototypical endothelial target despite inherent delivery and safety challenges. Here we report a bispecific antibody shuttle that engages CD98hc, the heavy chain of the large neutral amino acid transporter (LAT1), and efficiently transports IgGs into the brain parenchyma. Notably, CD98hc-mediated shuttles leads to much longer-lived brain retention of IgGs than TfR-1 shuttles while enabling more specific brain targeting due to the apparent lack of CD98hc target engagement in the brain parenchyma. We demonstrate the broad utility of the CD98hc shuttles by delivering three existing IgGs to the mouse brain parenchyma that either agonize a neuronal receptor (TrkB) or target other endogenous antigens on specific types of brain cells (neurons and astrocytes).