Department of Chemical and Environmental Engineering

2013—2014 Seminar Series

Friday, April 11, 2014
9:30—10:30 AM
WCH 205/206

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Mimicking the Blood-Brain Barrier In Vitro and Overcoming it In Vivo.

Millions of people worldwide are afflicted with neurological diseases such as Parkinson's disease, Alzheimer's disease, brain cancer, and cerebral AIDS. Although many new drugs are being developed to combat these and other brain diseases, few new treatments have made it to the clinic. The impermeable nature of the brain vasculature, also known as the blood-brain barrier (BBB), is at least partially responsible for the paucity of new brain therapeutics. As examples, approximately 98% of small molecule pharmaceuticals do not enter the brain after intravenous administration, and the BBB prevents nearly all protein and gene medicines from entering the brain. Our research group is therefore focused on developing tools for the analysis of the brain drug delivery process and identifying novel strategies for circumventing this transport barrier. This presentation will detail our recent work regarding the development of cell-based in vitro experimental models that accurately mimic the BBB characteristics observed in vivo. Such models are amenable to drug permeability screening and a priori prediction of brain uptake. In addition, I will discuss our efforts to overcome BBB restrictions on brain drug delivery. To this end, we are mining large antibody libraries to identify antibodies that can target and act as artificial substrates for endogenous receptor-mediated BBB nutrient transport systems. After conjugation to drug payloads that can include small molecules, proteins, or DNA therapeutics, these antibodies have the potential to deliver medicines across the BBB noninvasively.

Dr. Shusta received his Ph.D. in 1999 from the University of Illinois where, under the guidance of Dr. Dane Wittrup, he studied the production and engineering of antibodies and T-cell receptors using yeast. He followed this with postdoctoral training at the University of California-Los Angeles in the laboratory of Dr. William Pardridge where he helped pioneer molecular level analyses of the blood-brain barrier. Currently, Dr. Shusta is a Professor and H.I. Romnes Faculty Fellow in the Department of Chemical and Biological Engineering at the University of Wisconsin. His research focuses on antibody-based brain drug delivery and the development of molecular, cellular and protein engineering tools that can help gain a better understanding of blood-brain barrier transport and function. He has been recognized by the Dreyfus New Faculty Award, an NSF Career award, the ACS BIOT division young investigator award, among others, and was recently elected fellow in the American Institute for Medical and Biological Engineering.