



THE CHINESE UNIVERSITY OF HONG KONG  
School of Life Sciences & School of Pharmacy  
Polyglutamine Disease Collaborative Research Group  
Seminar Series

# Challenges in Brain Drug Delivery - Pharmacokinetic and Methodological Aspects

*by*



**Professor Margareta Hammarlund-Udenaes**  
Professor of Pharmacokinetics and Pharmacodynamics  
Department of Pharmaceutical Biosciences  
Head, Translational PKPD Research Group  
Uppsala University, Sweden

*on*

September 8, 2015  
(Tuesday)

*at*

11:00 am

*in*

Room G02  
Lo Kwee-Seong Integrated Biomedical Sciences Bldg.  
Area 39, The Chinese University of Hong Kong

*ALL ARE WELCOME*

## **Abstracts on “Challenges in Brain Drug Delivery - Pharmacokinetic and Methodological Aspects”**

*Margareta Hammarlund-Udenaes*

*Ph.D., Professor, Translational PKPD, Department of Pharmaceutical Biosciences,*

*Uppsala University*

[mhu@farmbio.uu.se](mailto:mhu@farmbio.uu.se)

The blood-brain barrier (BBB) and binding to brain parenchyma are the two most important aspects when evaluating new drugs for action within the CNS. The free drug hypothesis states that it is the unbound-drug molecules that can interact with the receptor, be it in the brain interstitial fluid or intracellularly. There are two aspects of brain drug delivery, the rate and the extent of transport across the BBB, of which the extent measure has the closest relationship to clinical success.

Methods for measuring delivery of drugs across the blood-brain barrier (BBB) are now available to accommodate the unbound, active moiety, thereby providing important information on success rate of compounds for CNS action. The methods, united into the Combinatory Mapping Approach (CMA), include measurements of brain tissue binding through the brain slice and the brain homogenate methods and in vivo measurement of the partition coefficient between brain and blood, to find the unbound partition coefficient across the BBB,  $K_{p,uu,brain}$ . The method has been further developed into CMA-ROI, where ROI is used for the region of interest, with which regional drug uptake and BBB transport can be estimated. With CMA and CMA-ROI, it is also possible to estimate intracellular accumulation of drugs.

The seminar will discuss the pharmacokinetic basis of BBB drug transport, as well as methods and results regarding drug distribution to and in the brain as a whole and also regarding regional distribution.