Introductory Remarks to Symposium 31

Transport mechanisms at the blood-brain barrier

Petra Henrich-Noack, Ingolf E. Blasig and Gert Fricker, Magdeburg, Berlin and Heidelberg

The blood-brain barrier (BBB), although protecting the delicate brain homeostasis, is an obstacle for drug delivery into CNS tissue. However, a silver bullet solution for this problem can be provided by colloidal carrier systems (G. Fricker): Delivery of drugs into the brain can be exploited including surface modified biodegradable polymeric nanoparticles using porcine brain capillary endothelial cells as well as in vivo rat models and confocal laser microscopy. By this therapeutic levels of otherwise not effective drugs can be reached inside the brain.

Importantly, it also has to be addressed whether the possibilities of nanoparticulate drug carriers is applicable and successful in pathological conditions. Here experiments with tumour models (glioblastoma) indicate that this is indeed the case (S. Gelperina). For example, preclinical studies demonstrated high efficacy of the nanoparticulate doxorubicin in the intracranial brain tumour model. A Phase 1 trial of the doxorubicin formulation based on the PLGA nanoparticles coated with poloxamer 188 demonstrated the safety of this delivery system.

However, it is important to know the molecular mechanisms determining the BBB function in health and disease (I.E. Blasig). The BBB-forming endothelium, paracellularly sealed by tight junction (TJ) proteins, ensures brain homeostasis and proper metabolite exchange. As far as known, claudin-5 dominates BBB's TJ function. Contribution of other TJ proteins is unclear. Therefore the structure and function of TJs upon stroke are investigated and the feasibility of Claudin mimetics to improve stroke recovery as well as cerebral drug delivery.

Last not least, it is important to understand the interaction and causal relationship of BBB damage and CNS diseases (A. Mahringer). A pathological breakdown of the BBB has been observed in many CNS diseases and results in edema, immune infiltration or neurodegeneration and CNS drug resistance. The characterization of molecular signaling pathways that modify physiological, vascular features in the presence of neurotoxic peptides offers new therapeutic targets in the treatment of CNS diseases to prevent BBB dysfunction and dysregulation.

Symposium 31

Saturday, March 25, 2017
8:30 - 10:30, Lecture Hall 105

Chairs: *Petra Henrich-Noack, Ingolf E. Blasig and Gert Fricker, Magdeburg, Berlin and Heidelberg*

08:30 **Opening Remarks**

08:40 Gert Fricker, Heidelberg
DRUG DELIVERY TO THE BRAIN BY COLLOIDAL CARRIERS (S31-1)

09:00 Svetlana Gelperina, Moscow, Russia
NANOMEDICINE FOR EFFICIENT CHEMOTHE RAPY OF BRAIN TUMOURS: FROM BENCH TO BEDSIDE (S31-2)

09:20 Ingolf E. Blasig, Berlin
CLAUDINS AND CLAUDIN MIMETICS - TIGHT JUNCTION PROTEINS IN NORMAL AND ISCHEMIC BLOOD-BRAIN BARRIER (S31-3)

09:40 Anne Mahringer, Heidelberg
INTERACTION AND CAUSAL RELATIONSHIP OF BLOOD-BRAIN BARRIER DAMAGE AND CNS DISEASE (S31-4)

10:00 Sophie Dithmer, Berlin
CLAUDIN PEPTIDOMIMETICS TO MODULATE THE BLOOD-BRAIN BARRIER FOR ENHANCED DRUG DELIVERY (S31-5)

10:10 Qing You, Magdeburg
GUIDING NANOPARTICLES' DESIGN BY IN VIVO VISUALIZATION AND QUANTIFICATION OF THEIR BLOOD-BRAIN BARRIER PASSAGE (S31-6)

10:20 **Concluding Remarks**