EXCLUSIVE SPEAKER INTERVIEW

6th Annual

CNS Drug Delivery Summit

Innovating Optimized Delivery to Specific CNS Targets

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How has the CNS drug delivery landscape evolved over the last 12 months, and where do you see it heading in the next few years?

Over the past 12 months, the CNS drug delivery landscape has made significant strides, especially in addressing the challenges posed by the blood-brain barrier (BBB). One of the most exciting developments has been the emergence of nanoparticle-based combinational strategies. By combining nanoparticles with various delivery methods-like cell-based drug delivery, viral vectors, focused ultrasound, magnetic fields, and intranasal delivery-we're seeing a real enhancement in brain penetration, improving drug delivery efficiency, therapeutic efficacy, and reducing off-target effects.

I'm especially encouraged by the growing interest in receptor-mediated transcytosis and peptide shuttles, which use natural transport mechanisms like transferrin receptors to more effectively and selectively deliver drugs across the BBB. Complementing these advances, the development of organ-on-chip and iPSC-derived models has been crucial. These models are helping us better mimic human BBB physiology and pathology, giving us a much-needed controlled environment to study drug delivery and efficacy. This is particularly important given the time and resources often lost when BBB-targeted therapeutics fail in clinical trials due to inadequate models.

Looking forward, I believe the integration of AI and machine learning will become even more pivotal in predicting drug responses and optimizing delivery systems. Precision medicine is another area where I see a lot of promise, with nanoparticle development increasingly tailored to individual patient needs. There's also going to be a stronger focus on translating these innovative technologies from the lab to the clinic, which is where I think we can make the most impact in providing faster and more effective solutions for CNS disorders.

Another promising frontier is the intersection between BBB dysfunction and immune responses. I'm particularly interested in how BBB dysfunction might lead to the breaking of immunological tolerance, causing the immune system to recognize antigens from BBB breakdown in the periphery. Understanding these immune responses could open up new pathways for drug development, potentially leading to therapies that not only restore BBB integrity but also modulate immune activity in neurodegenerative conditions.

Being an expert in in vitro blood-brain barrier models including microfluidics, how is the field looking to enhance their human relevance?

As someone deeply involved in in vitro blood-brain barrier models, I've seen firsthand how the field is making significant strides in enhancing their human relevance. Microfluidic platforms, often referred to as organ-on-chip technologies, are leading the way. These systems allow us to create dynamic, complex models that closely mimic the human BBB environment. By incorporating multiple cell types and simulating the conditions brain microvascular endothelial cells experience under shear stress, we can better replicate the in vivo BBB.

Furthermore, the use of iPSC-derived cells from patients allows us to develop patient-specific BBB models, which are crucial for studying individual drug responses and understanding disease-specific BBB dysfunctions. The integration of advanced imaging techniques and multi-omics approaches further enhances our understanding of BBB function and drug interactions, moving us closer to more effective and personalized treatments.

What role does BBB dysfunction play in neurodegenerative diseases, and how can understanding this help in developing new treatments?

BBB dysfunction is increasingly recognized as a critical factor in the development of neurodegenerative diseases like Alzheimer's, Parkinson's, and ALS. When the blood-brain barrier loses its integrity, it allows neurotoxic substances, immune cells, and pathogens to enter the brain, exacerbating neuronal damage.

Understanding this dysfunction is key to developing new treatments. It opens the door to strategies that either restore BBB integrity or leverage its altered state to enhance drug delivery. By targeting the pathways involved in BBB breakdown and promoting repair mechanisms, we can develop therapeutic approaches with the potential to slow or even halt disease progression.

How are current in vitro models contributing to our understanding of BBB dysfunction in neurodegenerative diseases?

Current in vitro models, particularly those leveraging microfluidic platforms and iPSC-derived cells, have revolutionized our understanding of BBB dysfunction. I've personally witnessed how these models enable us to recreate the complex disease environments that were once challenging to study in depth. For instance, using these models to explore specific factors like amyloid-beta in Alzheimer's (Shin et al., Advanced Science, 2019) or alpha-synuclein in Parkinson's (Pediaditakis et al., Nature Communications, 2021), it feels like we're uncovering new insights into how these diseases impact BBB integrity and function. What excites me most is the ability to closely examine and observe these interactions in a controlled setting, which not only helps us identify potential therapeutic targets but also allows us to test the effectiveness of drugs designed to protect or even repair the BBB.

Which other sessions on the agenda are you most looking forward to at the 6th CNS Drug Delivery Summit?

I'm particularly excited about the sessions on the latest advancements in nanoparticle drug delivery and focused ultrasound for BBB disruption-areas that hold immense promise for transforming CNS drug delivery.

Equally important to me are the discussions on how these innovations can be translated from lab-based BBB models to clinical settings. Bridging the gap between bench science and real-world treatments is what keeps me passionate about this work. I can't wait to explore these topics further and see how we can push the boundaries even more.