Precision Nanomedicine for Brain Gene Delivery: From Engineered Nanoparticles to Microgel-Based Disease Models

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Brain disease therapeutics are increasingly dominated by biotherapeutics, including monoclonal antibodies, gene therapies, and nucleic acid-based medicines. However, their translation remains severely limited by the blood–brain barrier (BBB), poor brain accumulation, and insufficient tissue and cell specificity. For gene therapeutics, successful delivery requires nanoparticle systems that can protect nucleic acid cargo, cross the BBB, target diseased cells, escape endosomes, and release cargo intracellularly.[1]

To address these challenges, our group has developed polymer-engineered magnetic nanoparticles using reversible addition–fragmentation chain-transfer polymerisation.[2] This platform enables modular control over nanoparticle surface chemistry, allowing the integration of bioinert, stimuli-responsive, and functional moieties.[1, 3] We have applied this approach to develop magnetic nanoparticles with reduced immunogenicity, prolonged circulation, and, more recently, siRNA delivery capability across BBB models for tumour microenvironment-responsive gene silencing in medulloblastoma.[4] In parallel, we are developing droplet-engineered microgel platforms that provide controlled, scalable, and physiologically relevant 3D cellular microenvironments. These microgels enable tunable matrix composition, stiffness, size, and biochemical cues, supporting organoid culture, disease modelling, and in vitro BBB model development.

This presentation will discuss how rational nanoparticle surface engineering and microgel-based tissue models can be integrated to overcome key barriers in brain delivery and accelerate the translation of next-generation precision nanomedicines for neurological disease and brain cancer therapy.

References:

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