New Strategy for Blood-Brain Barrier Crossing and Brain Disease Therapy

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A key challenge for treating neurodegenerative diseases is the delivery of drugs across the blood–brain barrier (BBB). To overcome this, our group has been developing nanoparticles-based strategy to transport drugs across the BBB into brain, offering high-performance therapy for brain diseases.

The BBB is a natural protective cellular barrier separating the brain and spinal cord from the rest of the body, preventing toxic chemicals and molecules from entering the brain. However, the BBB also stops most therapeutic drugs from reaching the brain. Over many years, various strategies have been proposed to increase BBB penetration efficiency, including chemical modification of compounds to facilitate their membrane permeability across the BBB, and carrier- or receptor-mediated transcytosis. Unfortunately, these approaches are relatively unsuccessful, with the best techniques clinically verified taking less than 1% of drugs through the BBB. Nanoparticles (NP) are emerging as a new class of delivery vehicles that can mediate and/or improve transendothelial penetration of drugs to specific regions of the brain. Conventional nanoparticles, including polymeric nanoparticles, gold nanoparticles and silica nanoparticles, have all been reported to improve molecule transportation across the BBB, but face a list of obvious challenges. One outstanding bottleneck is the difficulty in mapping the distribution of nanoparticles and tracking their entry pathways into the deep tissue of the living brain, where high background noise is generated by blood circulation. This issue stops further systematic study of the mechanism of the nanoparticles-based BBB penetration, how sizes, shapes, and surface of nanoparticles affect BBB penetration for advanced BBB penetration. Another fundamental problem is how to avoid particle clearance by the immune system, and how to target the delivery of nanoparticles (and controlled release of drugs) to specific cells or tissues in sufficient quantities for therapeutic efficacy. Clearly further multidisciplinary research is needed to identify a robust biocompatible strategy that combines the multiple functions of BBB penetration, excellent biocompatibility and on-demand targeted delivery of compounds.

Most recently, we firstly investigate how nanoparticles with different surfaces and shapes affect BBB penetration using upconversion nanoparticles (UCNPs), because the unique advantages of UCNPs such as fine tuning shape/size/surfaces, background free, photo stable, and high deep tissue penetration, results them as ideal model nanoparticles to investigate the underlying mechanisms of how nanoparticles cross the BBB. Furthermore, we also study the strategy that employ the cell membrane of red blood cell to coat the nanoparticles for the fabrication of biomimetic BBB penetrative delivery system, to avoid particle clearance by the immune system. Most importantly, we have discovered that some targeting molecules, for example peptides and transferrin, which can help nanoparticles to pass the BBB. Based on the key information from this study, we further developed a toolbox of efficient BBB penetrable nanoparticles for brain disease therapy and diagnostics.
Profile: Dr Bingyang Shi is currently a NHMRC-ARC dementia fellow and group leader of Brain Drug Delivery at Macquarie University. Dr Shi’s research focuses on the development of nanobiotechnology and advanced multifunctional bionanosystems for neurodegenerative disease diagnosis and therapy. He has been recognised as an emerging leader on brain drug delivery by receiving many awards including Macquarie University research fellowship, NHMRC Peter Doherty fellowship, NHMRC-ARC Dementia fellowship, Australian Endeavour fellowship and ACS rising star awards. Dr Shi has been attracted more $1 M competitive research grant as CIA including his new NHMRC Project grant on brain drug delivery and delivered more than 40 peer-review pubs including Nature Nanotechnology, Advanced Materials, Angewandte Chemie and Trends in Biotechnology.

Research Interests:
1. The mechanism and strategies for Blood brain barrier penetration
2. Advanced brain drug delivery system
3. Brain diseases preclinical therapeutic evaluation

Selected publications in last five years:


