**Abstract**

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

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Blood-Brain Barrier (BBB), a crucial physiological structure between blood and brain tissues, strictly regulates the movement of cells, molecules and ions between the circulatory system and brain to protect the brain, heavily limiting the delivery of drug to the brain circulation. [1] This BBB remains the therapy of central nervous diseases (e.g. amyotrophic lateral sclerosis, Alzheimer’s disease, Parkinson’s disease, brain tumour) a formidable challenge although tremendous efforts to develop effective strategies for neurological disorders treatment have been made in the past decades.[2] Nanoparticles are emerging as a new class of delivery vehicles that mediate and/or improve transendothelial penetration of drugs to the specific regions of the brain.[[3]](#_ENREF_9)Systematic investigation on how nanoparticles surface and shape affect BBB penetration will provide key information for the design and development of BBB penetrable nanoparticles for brain disease theranostics, however, few study has been reported.

Most recently, we investigate how nanoparticles with different surfaces and shapes affect BBB penetration using upconvertion nanoparticles (UCNPs), because the unique advantages of UCNPs such as fine-tuning shape/size/surfaces, background free, photo stable, and high deep tissue penetration, [4] results them as ideal model nanoparticles to investigate the underlying mechanisms of how nanoparticles cross 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.

**Key words:** Blood-Brain Barrier (BBB), Penetration, Upconvertion nanoparticles, Brain disease.

**References:**

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