Small apoptotic bodies: Nirvana, birth and death

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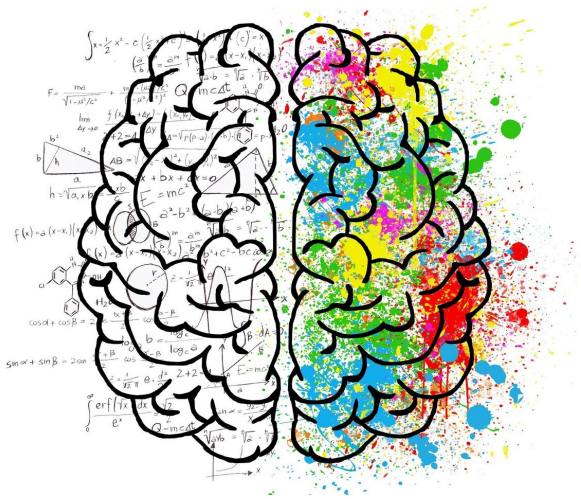

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Scientists from Nanjing University and University of Macau have discovered nano-scaled apoptotic bodies (ABs) as a new brain-targeting drug carrier, bringing new promise for the Parkinson's Disease as well as other brain diseases.

The blood-brain barrier (BBB) is the most restrictive barrier that keeps most biomolecules and drugs from the brain, setting "barriers" for the treatment of cerebrovascular diseases. With the increasingly serious aging problem, the treatment of brain diseases now faces tough challenges, and therefore efficient brain drug delivery strategies are urgently needed.

Apoptotic bodies (ABs), secreted from dying cells, have been discovered for half a century but their roles are underestimated. ABs are rarely considered for drug delivery, due to their uneven size distribution (varying from hundreds to thousands of nanometres) and complex composition (especially large chromosomal DNA fragments and various kinds of cytoplasmic proteins). However, with the natural bioactive lipids and affluent proteins, ABs should be more functional than being just an in vivo recycling unit.

In this paper, the team separated the small apoptotic bodies (sABs) and revealed their potential advantages as a delivery system for brain targeting. First, compared with the micron-sized apoptotic bodies, sABs have a more uniform size, with few DNA fragments and abundant RNAs. Second, sABs are stable in serum and has a long circulating time in vivo, not easily engulfed by the phagocytes. Third, the drug loading efficiency into sABs is high and the process is productive and controllable. Additionally, sABs are vesicles shed from the cell membrane, so the molecules in the cell membrane are preserved on the vesicles, providing a way for incorporating targeting ligands. With these advantages, sABs are likely a new candidate for drug delivery.

This paper, "Delivering Antisense Oligonucleotides across the Blood-Brain Barrier by Tumor Cell-Derived Small Apoptotic Bodies," is recently published in *Advanced Science*. Professor Lei Dong of Nanjing University, the leading author of this work, believes that sABs would be able to overcome the bottleneck of the exosome-based therapeutics and become a new class of drug delivery careers. They successfully loaded TNF-a antisense oligonucleotide (ASO) into sABs secreted by melanoma cells with high brain metastasis. The drug-loaded sABs could penetrate BBB, delivering the anti-inflammatory ASO to microglia and showing a remarkable efficacy in alleviating the development of Parkinson's disease in mice.

With the outstanding encapsulation and delivery efficiency to the microglia within the brain, the cancer cell-derived sABs might revolutionize the diagnosis, prevention and treatment of many brain diseases.

More information: Yulian Wang et al, Delivering

Antisense Oligonucleotides across the Blood?Brain Barrier by Tumor Cell?Derived Small Apoptotic Bodies, *Advanced Science* (2021). DOI: 10.1002/advs.202004929