Evaluation of 3D Tumor Spheroid Penetration and Drug Delivery of Peptide Amphiphiles

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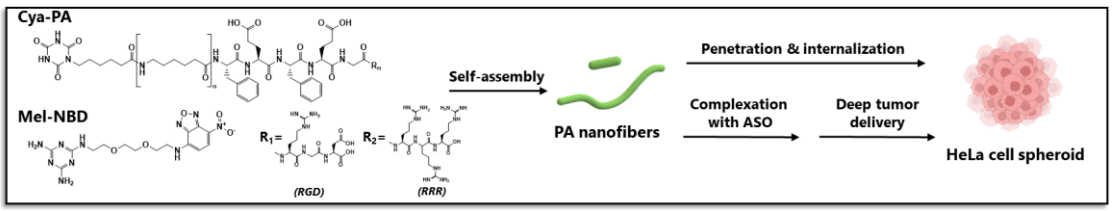
The majority of cancer tumors are solid, characterized by their compact structure and low vascular density, which together present significant challenges for effective drug delivery. To study tumor drug penetration, tumor cell spheroids have been used as a model as they closely mimic the main features of human solid tumors[1]. This study aims to characterize the 3D tumor spheroid penetration kinetics of a peptide amphiphile (PA) system. PAs are short-chain peptides attached to a hydrophobic tail, capable of self-assembly into nanostructures in water. Additionally, molecular modification was performed on the PA monomers to explore its potential as a platform for deep tumor drug delivery.

Here, the PA system consists of cyanuric acid-modified PA (Cya-PA) and melamine-nitrobenzofurazan (Mel-NBD)[2]. In aqueous conditions, complementary hydrogen bonding and amphiphilicity of the PAs direct the formation of Cya-PA/Mel-NBD co-assembled nanofibers. These nanofibers exhibit rapid and non-endocytic internalization in cells. Upon incubation with HeLa cell spheroids, fluorescence microscopy revealed rapid and deep penetration of the nanofibers. Through flow cytometry analysis, it was confirmed that the nanofibers not only penetrated the cell spheroid structure but also internalized into the interior cells. Further PA monomer modification to include positive-charge amino acid sequence (triple-arginine) allowed the co-assembled nanofibers to be electrostatically complexed with nucleic acid drugs, such as antisense oligonucleotide (ASO). When HeLa cell spheroids were treated with the complex, penetration of both the nanofibers and ASO was observed. In this presentation, the penetration characteristic and kinetics of the PA system, and their delivery of ASO will be discussed.



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