Biomimetic Strategies in Engineering Nanoparticles for Gene Delivery

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Cellular delivery of plasmid DNA (pDNA) has fostered great success in gene therapy and DNA vaccine over the past decades. Holding the promise in turning DNA into next-generation medication, the key challenge of this field lies in the development of safe and efficient nano-vectors for gene transfection. Indeed, nature has inspired significant advances in the development of delivery systems. For instance, spiky pollen particles enhance adhesion toward insects to allow effective delivery of genetic materials via pollination, infectious viruses pack and stabilize gene molecules inside of capsid for efficient cellular delivery, and bacteria can also carry gene molecules for cell invasion and replication. Mimicking these delivery routes will underpin the development of novel nano-delivery systems for DNA vaccine and therapeutics. Here, pollen-inspired silica nanoparticles[1] with either a head-tail morphology[2] or a tailored coverage of spiky surface[3] will be first introduced, which showed enhanced interactions with pDNA molecules and boosted intracellular transfection efficacy. Then, a virus-mimicking zeolitic imidazolate framework (ZIF) nanoparticle was assembled with *in-situ* encapsulation of pDNA into the pH-responsive matrix. A designer core-shell structure enabled strong protection and controlled release of DNA molecules, leading to superior transfection in dendritic cells and DNA vaccine performance *in vivo*. Besides, our latest studies on utilizing bacteria as gene delivery vectors through nanoparticle engineering will also be presented, where the design and evaluations on anti-tumor gene delivery will be discussed.

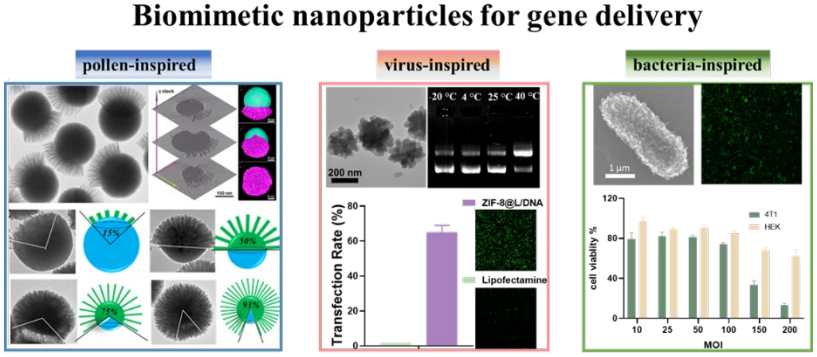

Figure 1: Novel strategies in developing biomimetic nanoparticles for gene delivery

References:
[1] Song, H. et al. *J Am Chem Soc* **2017**, *139*, 18247-18254
[2] Lin, X.; Wu, W.; et al. *ACS Appl Mater Interfaces* **2021**, *13*, 50695-50704.
[3] Wu, W. et al. *J Mater Chem B* **2022**, *10*, 7995-8002.