Control of DNA Packaging for Efficient Gene Delivery

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Recently, there is a strong impetus for the development of biocompatible materials directed for biomedical applications, particularly nanocarriers delivering therapeutic agents such as drugs and nucleic acids to the target cells. We have developed supramolecular "smart" nanocarriers including polymeric micelles and polymeric vesicles and have demonstrated nanocarriers-mediated cell therapy by facilitating the translation of basic achievements into clinical applications. Upon fabricating efficient nanocarriers, understanding their underlying structural formation and regulating the process into appropriate structure that can fully demonstrate their therapeutic potency is crucial. Among the nanocarrier system, this talk focuses polymeric micelles applied for gene therapy, which task is to deliver therapeutic gene to target nucleus and demonstrate gene expression. The gene carrier are constructed by electrostatic-based self-assembly process between plasmid DNA (pDNA) and block copolymers composed of biocompatible poly(ethylene glycol) (PEG) and polycations.[1] The assembly spontaneously forms distinct core-shell polymeric micelle structure where pDNA is packaged in the core, which is covered by PEG palisade. Through intensive study on structure formation of the assembly, we have finally established controlling methodology of folding structure of pDNA packaged within the core.[2,3] Moreover, we found interesting correlation between the folding structure and the tethering PEG shell, where the tethering PEG crowdedness plays an important role in determining pDNA folding pattern.[3,4] The polymeric micelles could induce gene expression at the target site and ultimately accomplished significant tumor growth suppression on a pancreatic tumor model by anti-angiogenesis way through systemic application.[4,5]

References:
(1) K. Osada, et al., *J. R. Soc. Interface* 6 S325-S339 (2009)
(2) K. Osada, et al., *J. Am. Chem. Soc.* 132 (35) 12343-12348 (2010).
(3) K. Osada, et al., *Biomaterials* 33, 325-332 (2012).
(4) Q. Chen et al., *Biomaterials* 33 (18) 4722-4730 (2012).
(5) M. Oba et al., *Biomaterials* 32 (2) 652-663 (2011).