

Structured DNA nanoparticles for delivery of RNA therapeutics

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Nanoparticles are useful for delivering therapeutics into cells. However, size, shape, surface chemistry and the presentation of targeting ligands on the surface of nanoparticles can affect circulation half-life and biodistribution, cell specific internalization, excretion, toxicity, and efficacy. A variety of materials have been explored for delivering small interfering RNAs (siRNAs) - a therapeutic agent that suppresses the expression of targeted genes. However, conventional delivery nanoparticles such as liposomes and polymeric systems are heterogeneous in size, composition and surface chemistry, and this can lead to suboptimal performance, lack of tissue specificity and potential toxicity. Here, we show that self-assembled DNA tetrahedral nanoparticles with a well-defined size can deliver siRNAs into cells and silence target genes in tumours. Monodisperse nanoparticles are prepared through the self-assembly of complementary DNA strands. Because the DNA strands are easily programmable, the size of the nanoparticles and the spatial orientation and density of cancer targeting ligands (such as peptides and folate) on the nanoparticle surface can be precisely controlled. We show that at least three folate molecules per nanoparticle is required for optimal delivery of the siRNAs into cells and, gene silencing occurs only when the ligands are in the appropriate spatial orientation. *In vivo*, these nanoparticles showed a longer blood circulation time ($t_{1/2} \sim 24.2$ min) than the parent siRNA ($t_{1/2} \sim 6$ min).

Biography

Hyukjin has received his Ph.D. from KAIST and did postdoctoral studies from chemical engineer department and Koch institute for integrative cancer research at MIT. Currently, he is working at the graduate school of pharmaceutical science in Ewha Womans University.

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