Avidin-Based Nanocomplex for siRNA Delivery
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Avidin-biotin interaction is one of the strongest non-covalent interactions in the nature. Recently, there has been a growing interest in exploiting this non-covalent interaction in nanoscale drug delivery systems for pharmaceutical agents, including small molecules, proteins, vaccines, monoclonal antibodies, and nucleic acids. Particularly, the ease of fabrication without losing the chemical and biological properties of the coupled moieties makes avidin-biotin system a very promising platform for nanotechnology.

We have developed a streptavidin-based multi-component siRNA nanocomplex to deliver siRNA to hepatic stellate cells (HSCs). Biotin-siRNA and biotin-cholesterol were mixed with streptavidin to form the streptavidin-biotin complex, which was further condensed electrostatically with positively charged protamine to form the final multicomponent siRNA nanocomplex in the size range of 150-250 nm. The nanocomplex can efficiently protect siRNA from degradation in the serum and efficiently deliver the siRNA into HSC in a specific manner.

We studied the post internalization trafficking of this siRNA nanocomplex and its multiple components like siRNA, protamine, and streptavidin, in HSCs. After internalization, the nanocomplex entrapped in early endosomes undergoes three possible routes including endosomal escape, exocytosis, and entrapment in lysosomes. Significant amount of siRNA dissociates from the nanocomplex to exert silencing activity. After escaping from endosomes, protamine dissociates from the nanocomplex and stays inside the cytoplasm. We also compared different siRNA nanocomplexes prepared from avidin, neutravidin, and streptavidin. Neutravidin shows the most promising capability to deliver siRNA into the cells. Moreover, the neutravidin nanocomplex can be used as a platform for other diseases by changing the siRNA sequence and targeting ligand.