Making Oligonucleotides Better Biopharmaceuticals with Brush Polymers

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Nucleic acids are programmable biomolecules that hold great promises as therapeutics. However, with over 40 years of development, only a handful of nucleic acid drugs ever reached the market. The lack of greater success is in part due to the poor biopharmaceutical properties of naked nucleic acids, which require extensive chemical modification and/or the use of an (often toxic) carrier system. This presentation focuses on the development of two new strategies for transferring genetic materials to cells, which are mechanistically distinct from existing methods. The new systems rely upon the three-dimensional arrangement of oligonucleotides or the use of biologically benign brush polymers to enhance the properties of the nucleic acids. For instance, the oligonucleotide can acquire steric selectivity towards complementary strands vs. proteins, which allows it to bypass many of the side effects associated with protein-DNA interactions (Figure 1).

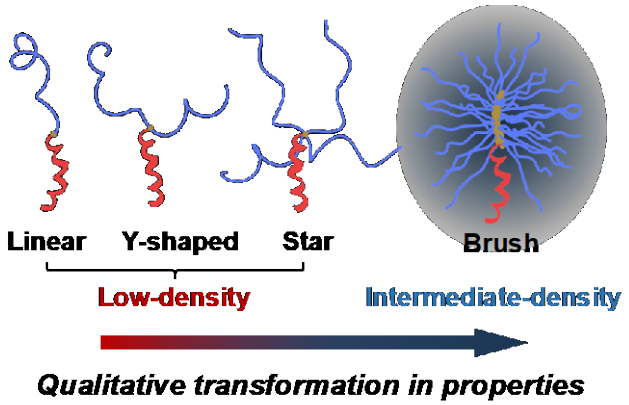

Figure 1: Brush polymer-assisted compaction of DNA (pacDNAs) as a new platform for non-hepatic, systemically delivered oligonucleotide therapeutics.

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