Nucleic acids as targets for Drug Delivery and Drug Design

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DNA and RNA are highly charged polyelectrolytes. Accordingly transport of such macromolecular ions across cell membranes does not take place on its own. This requires special strategies and/or design of appropriate molecular entities. This is an important goal in medicine as attempts to cure a disease could be initiated by supplementing an aberrant gene (DNA) or by the delivery of a suicide gene or via transfer of genes for the synthesis of new therapeutic proteins. Traditionally, DNA delivery systems are broadly based on either viral or non-viral vectors. Viral vectors are more efficient in delivering the gene as well as in inducing gene expression as a result of their highly evolved and specialized components. However, their use in clinic is limited due to inherent drawbacks, such as adverse immunogenic reactions, restricted targeting of specific cell types, size limitation on DNA, and potential for mutagenesis.

Among the non-viral vectors, appropriately designed lipids, peptides and lipopolymers have shown excellent potential for the gene delivery applications. Of these the lipid-mediated DNA delivery is one of the most practical approaches for gene delivery and much progress have been made in the development of various cationic liposomes for gene delivery to mammalian cells. The factors such as lipid architecture, composition, lipid/DNA charge ratios, lipoplex structures, role of different cell types, ionic strength, and presence of serum have been considered for the successful and efficient gene delivery. I shall present efforts made by us towards this end.