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Lipid Oligonucleotide Bioconjugates: Applications in Medicinal Chemistry

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4.2.1 Introduction

Crossbreeding is often referred to as the art, or science, of modulating the traits of biological species (animals, plants) by mixing two different populations in order to obtain desired characteristics. Interestingly, this idea can be transferred to biomolecules. In theory, the synthetic combination of two chemical species would lead to chimerical structures featuring new characteristics belonging to both molecular species. Nucleic acids and lipids are the fundamental molecules in biology. While the former store and propagate genetic information, the latter, as the structural components of cell membranes, act as boundaries and allow for compartmentalization. Thus, the combinations of lipids with oligonucleotides have been realized and new bioconjugates termed Lipid OligoNucleotides (LONs) have been synthesized and studied [1]. These amphiphiles are currently attracting a considerable degree of interest owing to their unique physicochemical and biological properties. These hybrid compounds feature the molecular code of the nucleic acids and the self-assembly properties that lead to aggregates such as micelles [2], liposomes [3], and nanoparticles [4]. Excitingly, LONs have been investigated for biomedical applications [4], for example, in the design of new therapeutic strategies.

In this chapter we highlight recent advances in the area of LONs with an emphasis on molecular and biomedical applications. In the first section, we focus on the design and the synthesis of LONs. This will include several examples of synthetic oligonucleotide based amphiphiles. In the next section, we describe recent biomedical applications involving LONs.