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CRITICAL REVIEW

# Hybrid lipid oligonucleotide conjugates: synthesis, self-assemblies and biomedical applications†

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Hybrid lipid oligonucleotide conjugates are finding more and more biotechnological applications. This short *critical review* highlights their synthesis, supramolecular organization as well as their applications in the field of biotechnology (111 references).

## Introduction

Bioconjugates combining lipids and oligonucleotides (LONs) are currently attracting considerable attention owing to their unique physicochemical and biological properties. Interestingly, these amphiphiles, which feature molecular recognition capabilities and the ability to store and transfer encoded information, can self assemble to give aggregates such as micelles,[1] liposomes[2] and nanoparticles.[3] In parallel, LONs have been developed for cell biology, and medicine[4] as for example in the design of artificial molecular devices[5–9] and novel therapeutic strategies.[10]

In this contribution we highlight recent advances in the area of amphiphilic structures derived from LONs with an emphasis on molecular and supramolecular properties, and biotechnological applications. In the first section, we focus on the design and the synthesis of LONs. This part includes several examples of synthetic oligonucleotide based amphiphiles. In the next section, we present the use of LONs as supramolecular building blocks and their aggregation properties. Finally, in the last section of this short critical review, we describe recent biomedical applications involving LONs. Fig. 1 shows the capabilities of forming supramolecular assemblies and biomedical applications of LONs.

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## 1. Design and synthesis of LONs

Development of efficient and reproducible methods for convenient preparation of various types of LONs has become a subject of considerable importance. Scheme 1 describes the possible ways of hydrophobic conjugation to the different moieties of the oligonucleotide (*i.e.* at sugar, phosphate backbone or base unit). The hydrophobic part can be a lipid

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