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APPLICATION OF NUCLEIC ACID MIMICS IN THE TREATMENT OF BACTERIA

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The emergence of pathogenic bacteria resistant to most, if not all, currently available antimicrobial agents has become a critical problem in modern medicine. As we are apparently entering the post-antibiotics era, the development of alternative antibacterial therapies is of the utmost importance. One of the alternatives that have been exploring is the antisense technology that is based on the introduction of an oligonucleotide complementary to a given mRNA, thereby inhibiting translation. The development of a new generation of nucleic acid mimics (NAMs) with promising antisense characteristics together with several studies reporting successful modifications of gene expression has put the antisense technology in the spotlight. In fact, some of these molecules are already being developed for therapeutic applications *in vivo*, and protocols involving hybridization inside higher-order animals are available. The success of the antisense technique using NAMs obtained in eukaryotic cells has not been reproduced in microorganisms. In fact, all studies in microorganisms have so far showed limited ability to completely eliminate bacterial populations in a reproducible way. This might be due to a multitude of factors, and several studies have shown that the difficulty of these mimics to cross the bacterial cell envelope as one of the most critical factors. This work focus on the development of an integrated approach focused on the targeted delivery of different nucleic acid mimics using multiple delivery strategies into microorganisms. We will discuss and compare not only the influence of different nucleic acid mimics, such as peptide nucleic acids (PNA), locked nucleic acids (LNA) and 2´-O-Methyl-RNA, but also of different delivery strategies such as liposomes/nanoparticles and cell penetrating peptides (CPPs).

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