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to either inhibit (antisense) or stimulate (sense) the expression of a desired target mRNA, which contains complementary sequences to the antisense oligonucleotide. Today, there are nine licensed antisense drugs. Among these are ONTARGET, NUPR1, AMP-26, BLU-651, for treating viral infections, dementia, heart disease, diabetes and asthma, respectively. It has been shown that antisense oligonucleotides can be used for a wide range of gene therapy and diagnostics. An antisense oligonucleotide can be used to inhibit the expression of a particular mRNA. In this case it is called antisense. Alternatively, an oligonucleotide can be used for the detection of an mRNA

sequence in a sample or as a guide sequence for RNA polymerase to facilitate the expression of a particular gene. The efficiency of oligonucleotides to perform their therapeutic function is dependent on several factors. The oligonucleotides must be delivered to their site of action (or target cell) in sufficient amounts. Once delivered, they need to be transported to their site of action and taken up by cells/tissues. Several barriers exist to facilitate the passage of the oligonucleotides across the cell membrane into the cytoplasm and from there into the cell nuclei where the antisense effect is exerted. It is generally accepted that the major barrier to the passage of

oligonucleotides across cell membranes is their negative charge. The oligonucleotides have a high degree of negative charge due to the phosphodiester backbone and the negatively charged sugars. In addition, the efficiency is also dependent on the half-life of the oligonucleotides. The oligonucleotides also need to be properly modified to enhance their pharmacokinetic properties. Unmodified c6a93da74d

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