Abstract

Abstract Tite: Anti-cancer Drug Design

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The emerging future of antisense oligonucleotides depends on rational modifications of its nucleotide repeating units. Currently the most prevalent design features that are crucial for continued antisense development are nuclease resistance, cellular uptake, hybridization properties, and disruption of RNA functions through terminating events.

Very few structure-activity relationship (SAR) studies have been directed to these problems and these have typically used binding affinities and nuclease sensitivities as activity end points rather than in vitro or in vivo biological activities. Further SAR studies may be approached by sequence selection SARs which hold a certain uniform modification type constant (e.g. phosphorothioates) while varying the sequence of the oligonucleotide.The more traditional approach is to modify the oligonucleotide while keeping the sequence constant. This review is concerned with the latter approach and summarizes modifications of the phosphorus atom, pentofuranosyl (sugar) linker, pentofuranosyl ring and its 2'-substituents, and the heterocycles. The review covers the 1989-91 literature of various modified oligonucleotides designed and synthesized to enhance pharmacokinetic and pharmacodynamic properties of antisense oligonucleotides.

Keywords- *oligonucleotides, nuclease, RNA, SAR, pentofuranosyl, hetercycles,*

Professional Biography

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