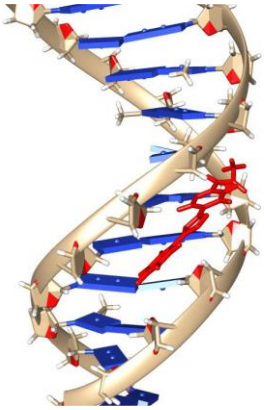
Novel Purine Nucleotide Analogs

Novel 2'-Deoxyguanine Analogs with Enhanced Binding Affinity and Selectivity in Duplex Formation

Background

Development of novel oligonucleotide analogs that possess enhanced binding affinity and selectivity in the formation of duplexes with complementary DNA sequences would be instrumental for numerous applications, from biotechnology and medicine to material sciences and nanotechnology. A number of artificial oligonucleotides have been developed that stabilize duplexes by maximizing stacking interaction, by forming additional hydrogen bonds, or by minimizing electrostatic repulsion between DNA strands. The phenoxazine dC analogue or "G-clamp" utilizing these effects was developed that is capable of bringing to complementary guanine with high affinity and specificity. Unfortunately, the nucleotides with comparable affinity towards purines are currently not known.



Lukin 2015. The canonical B-type double helical conformation is preserved in the duplex **II**, and the diphenyloxodiazole moiety occupies the minor groove.

Technology

Dr. Mark Lukin from the Department of Pharmacology at Stony Brook University has developed novel purine nucleotide analogs bearing a polyaromatic moiety attached to the nucleobase via N2. The stabilizing effects of the purine analogues is comparable to G-clamp, yet the dA and dG analogs demonstrate only moderate sensitivity towards the DNA sequence context. In addition, the new purine analogs demonstrate increased mismatch discrimination, especially when the mismatched base in the opposite strand is adenine or guanine making them a useful tool for creation of various DNA hybridization methods, (point mutation detection, single nucleotide polymorphism). The new nucleotide analogs can be incorporated into the oligonucleotides using standard phosphoramidite chemistry, and no modification of the synthetic protocol is necessary.

Patent number/Publication:

Provisional application

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Advantages

- **Sequence independent**
- **High thermal stability**
- **Double helical conformation is preserved**

Applications

- **Research Tool**
- **Diagnostics**

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