Locked Nucleic Acid (LNA™) Technology

Introduction

Locked nucleic acid (LNA™) nucleosides are a class of nucleic acid analogues in which the ribose ring is "locked" by a methylene bridge connecting the 2'-O atom and the 4'-C atom (Figure 1). LNA™ nucleosides contain the common nucleobases (T, G, A, and mC) and are able to form base pairs according to standard Watson-Crick base pairing rules. However, by "locking" the molecule with the methylene bridge the LNA™ is constrained in the ideal conformation for Watson-Crick binding. When incorporated into a DNA oligonucleotide, LNA™ therefore makes the pairing with a complementary nucleotide strand more rapid and increases the stability of the resulting duplex.

The affinity-enhancing effect of incorporation of LNA™ monomers into an oligonucleotide is demonstrated by an increase in the duplex melting temperature (*T* m) of 2-8 ºC per LNA™ monomer (see table 1).

See how LNA™ works. View 3D visualization
Read more about LNA™

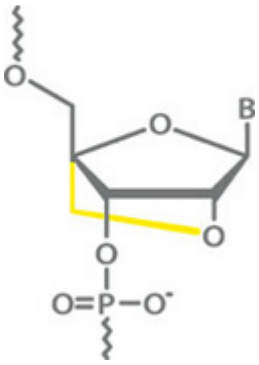

Figure 1

Benefits of the LNA™ technology

Some of the benefits of using LNA™ include:

- Ideal for the detection of short RNA and DNA targets
- Increases the thermal stability of duplexes
- Capable of single nucleotide discrimination
- Resistant to exo- and endonucleases resulting in high stability in vivo and in vitro applications
- Increased target specificity
- Facilitates *T* m normalization
- Strand invasion properties enables detection of "hard to access" samples
- Compatible with standard enzymatic processes

The placement of the LNA™ monomers is of great importance for the performance of the oligonucleotide. Exiqon has developed in-house algorithms that enable the design of LNA™-enhanced oligonucleotides with high melting temperatures (*T* m), optimal mismatch discrimination and high binding specificity while avoiding unacceptable secondary structure and self-complementarity.

For more detailed information about the LNA™ technology, please see "Technical Literature" and "Scientific Publications" in the right hand menu.

Applications

LNA™ can be used with great advantage in a large variety of applications and innovative products. In particular, LNA™-enhanced oligonucleotides are widely used to add unique specificity and sensitivity to the analysis of very

short sequences. They are also ideal for discriminating between highly similar nucleic acid sequences.

In addition, the therapeutic and diagnostic use of LNA™ is under intense investigation.

LNA™ applications include:

- Small RNA research
- SNP genotyping
- mRNA antisense oligonucleotides
- Allele-specific PCR
- RNAi
- DNAzymes
- Fluorescence Polarization probes
- Molecular Beacons
- Microarray gene expression profiling
- Gene repair/exon skipping
- Splice variant detection
- Comparative genome hybridization (CGH)

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