DIACARTA

TRANSFORMING CANCER CARE WITH SPOT ON PRECISION DIAGNOSTICS

XNA (Xenonucleic Acid) Molecular Clamp Technology

XNA technology is employed to improve the sensitivity of mutation detection by suppressing amplification of wildtype alleles. XNA are essentially innovative nucleic acid molecular oligomers that hybridize with target DNA sequences and can be employed as molecular clamps in quantitative real-time polymerase chain reactions (qPCR) providing a high level of sensitivity to diagnostic tests.

What is XNA?

XNA is a synthetic DNA analog in which the phosphodiester backbone has been replaced by a novel synthetically modified backbone chemistry. XNAs are highly effective at hybridizing to targeted normal DNA sequences and can be employed as highly specific molecular probes for detection of nucleic acid target sequences. Binding of XNA to its target sequence blocks strand elongation by DNA polymerase in PCR assays. When there is a mutation in the target site, either a point mutation or indels, and therefore a mismatch, the XNA-DNA duplex is unstable, allowing strand elongation by DNA polymerase.

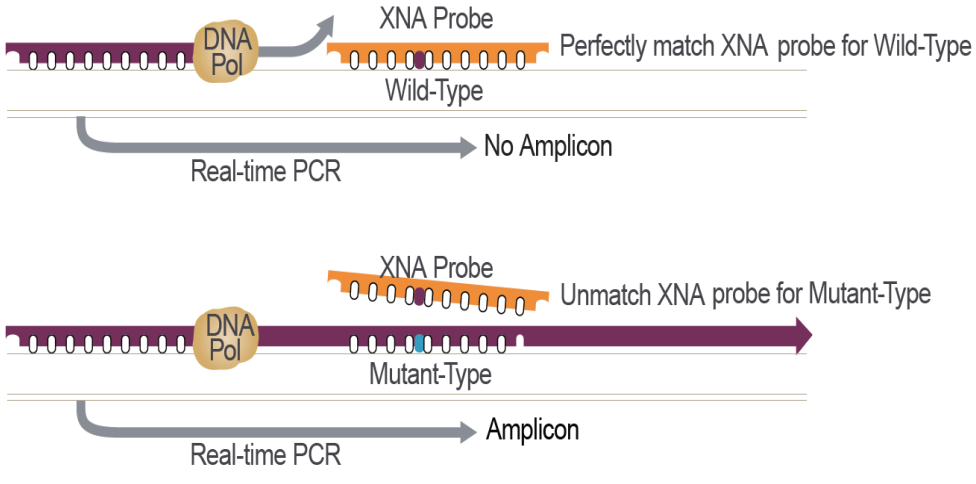

Figure 1: XNA Technology Overview

XNA Applications

A key application of XNA technology is to identify cancer mutations and to provide meaningful information for cancer treatment. Applying the XNA technology in diagnostics can yield more accurate and rapid results as follows:

XNA can enrich mutant sequence in a population. Therefore, it can detect the mutant with higher sensitivity. For instance, with every 3.3 (100 in total with 30 enriched mutations) sequence checked, rather than every 100 (100 in total with no enrich mutations) sequence checked, a mutation is found. This greatly benefits finding mutations in liquid biopsy samples as rare somatic mutations are buried among the wildtype cell-free DNA (cfDNA) background. Quantitative real-time PCR (qPCR) can be easily used to identify single or a few mutations in one reaction.

For targeted Next Gen Sequencing (NGS) that contains 50 genes for instance, one can add the XNAs to the panel to increase the NGS sensitivity from 1% to 0.1%. This will:

- Reduce the materials amount one needs for sequencing
- Reduce the sequencing depth (by not sequencing the same region many times)
- The panel can be used for minimal or molecular residual disease (MRD) monitoring at 20,000X depth, which is normally done with ultra-deep sequencing 100,000X depth

Less sequencing depth means less time for sequencing to get the mutation detected. This means less cost for sequencing (less flow cell space needed) and thereby less data for the bioinformatician to analyze (less man power cost).

Use of regular NGS could result in missing the mutation, unless more sample input is added (for instance, instead of 10 ng, one may need 100 ng DNA, which is not realistic to get from liquid biopsy samples)

number using OptiSeq™ Nano Panel V2

XNA is a powerful technology that can be used

- as an effective and precise method to identify rare somatic mutations
- when combined with NGS it will yield higher sensitivity and more cost-effective (less sequencing depth and less material needed).