Enzymatic Synthesis of DNA Containing Non-Standard Nucleotide Basepairs

The solution is a strategy for enzymatic synthesis of double-stranded DNA oligonucleotides that contain modified natural bases and xenonucleobases, including up to 12 different nucleotides that form six orthogonal pairs.

What is the Problem?

DNA is composed of the four-letter standard genetic alphabet (A,T,G,C) and has the ability to store and transfer biological information. The manipulation of the four letters of DNA has led to major advances in biotechnology, information storage, and healthcare. For example, the four nucleic acids are key components for diagnostic tests, therapeutics, and long-term storage of digital information. However, nature's standard nucleic acids are non-exhaustive and there is an opportunity to expand the current DNA alphabet.

What is the Solution?

The solution is a strategy for enzymatic synthesis of double-stranded DNA oligonucleotides that contain modified natural bases and xenonucleobases, including up to 12 different nucleotides that form six orthogonal pairs. The enzyme-assisted method involves inserting a singular, orthogonal xenonucleic acid (XNA) base pair into standard DNA sequences using various DNA polymerases. The two standard base pairs (A=T, G=C) can be combined with any of the four mutually orthogonal xenonucleobases (B=S, P=Z, X=K, J=V).

What is the Competitive Advantage?

The competitive advantage of this technology lies in its ability to provide an expanded 12-letter supernumerary DNA alphabet as a fusion of the standard nucleobases (A, T, G, C) with synthetic hydrogen bonding xenonucleobases (B, S, P, Z, X, K, J, V). These xenonucleotides significantly expand DNA's chemical, structural, and binding capabilities. This technology can be used to create more sensitive diagnostic tests, therapeutics, semi-synthetic organisms, catalytic nucleic acids, and increased digital information storage. As the global genomics market size is valued at $32.7 billion in 2023 with an expected CAGR Of 16.5%, there is a significant opportunity for this technology to expand the capabilities of current DNA technologies.

References

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