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Replication System, Novel Polymerases, and Uses for Threose Nucleic Acid

Synthetic genomics, though a relatively nascent field, is generating a lot of excitement in the scientific community, especially with the advent of unnatural nucleic acid polymers. Threose nucleic acid (TNA) is one such unnatural nucleic acid polymer that is particularly promising because of its high resistance to nuclease degradation, making it much more stable than natural DNA and RNA. DNA and RNA have had limited utility in diagnostics and therapeutics because of their rapid degradation by nucleases, further highlighting the desire to use TNA in these applications. Unfortunately, limitations in the availability of enzymes and the conditions that allow for storage and replication of unnatural nucleic acid polymers have decreased their utility.

Researchers at the Biodesign Institute of Arizona State University have developed a two-enzyme replication system and novel polymerases which allows for the transcription and reverse-transcription of genetic information back and forth between TNA and DNA. This process allows for the in vitro synthesis, selection, amplification and evolution of TNA molecules for information storage as well as SELEX with TNA. Moreover, they've created stable, nuclease-resistant TNA and TNA-DNA (mosaic) oligonucleotides which are completely resistant to enzymatic degradation for a range of 24 to 72 hours, enabling the use of TNA in diagnostic and therapeutic applications.

This novel technique will greatly advance our understanding unnatural genetic coding, and provide a source of custom ligands, catalysts and nanostructures for applications in biotechnology and medicine.

Potential Applications

- Replication of TNA
- Replacement of RNA or DNA in biotechnological and medical applications
  - Diagnostics
  - Therapeutics
  - Aptamers
  - Can be used in SELEX process

Benefits and Advantages

- These are some of the most nuclease-resistant nucleic acid analogues developed to date
  - Tested with RNAseA, RQ1 DNAse and Turbo DNAse
  - Stable for a range of 24 to 72 hours, depending ont he oligonucleotide created
- Replication with high efficiency and fidelity

- Can utilize all four TNA - previous polymerases were limited to a 3 letter genetic alphabet
- The polymerases function in the absence of manganese, significantly improving TNA transcription fidelity

For more information about the inventor(s) and their research, please see Dr. Chaput's departmental webpageDr. Chaput's laboratory webpage