Expanding the code of life with new 'letters'

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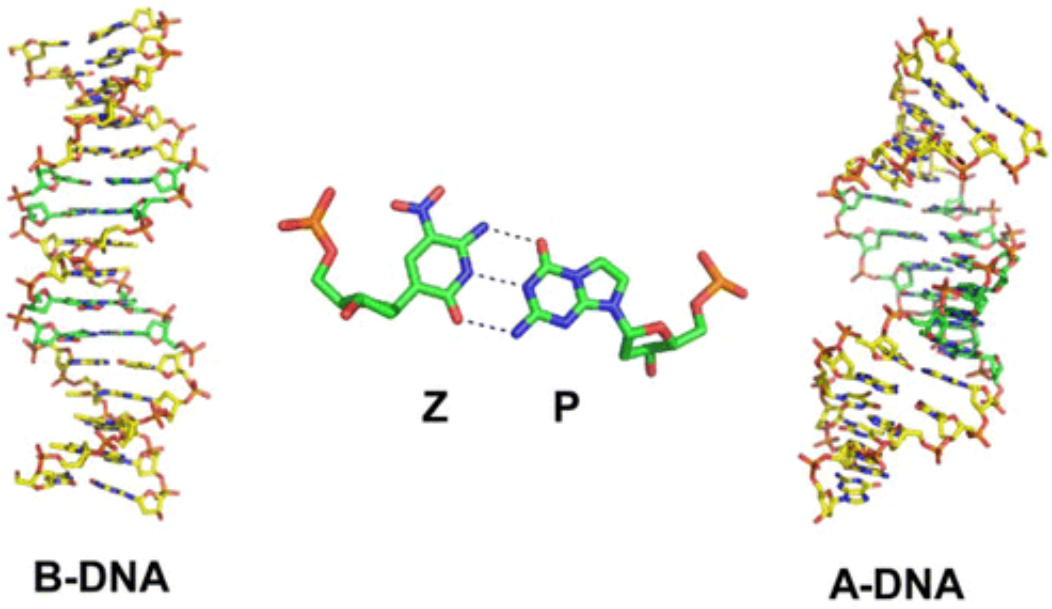
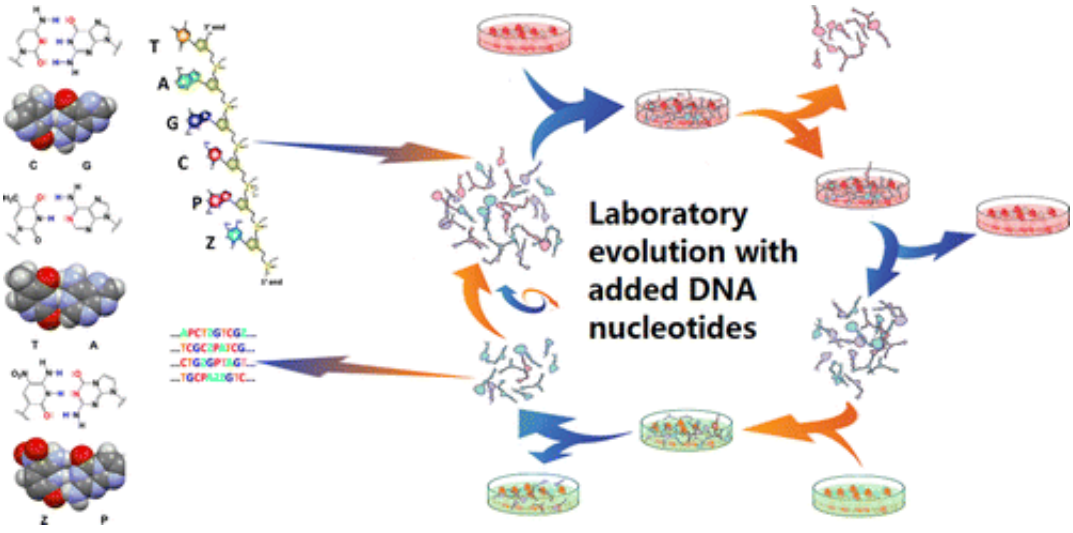


The DNA encoding all life on Earth is made of four building blocks called nucleotides, commonly known as "letters," that line up in pairs and twist into a double helix. Now, two groups of scientists are reporting for the first time that two new nucleotides can do the same thing—raising the possibility that entirely new proteins could be created for medical uses. Their two studies appear in ACS' *Journal of the American Chemical Society*.

Synthetic biologists have been attempting for years to expand on nature's genetic "alphabet," consisting of the nucleotide bases cytosine, guanine,

adenine and thymine—also represented by the letters "C," "G," "A" and "T," respectively. But so far, the potential additions they've tested have shown limited promise. For example, one duo pairs up but doesn't form a nice helix, an important criterion given that the bases would have to incorporate fairly seamlessly with the original four to be useful. Millie M. Georgiadis, Steven A. Benner and colleagues from Indiana and Florida wanted to see if another potential set of letters, "Z" (6-amino-5-nitro-2(1H)-pyridone) and "P" (2-amino-imidazo[1,2-a]-1,3,5-triazin-4(8H)one), would form a helix—and evolve.

The researchers found that multiple Z-P pairs can contribute to a double helix, just as C-G and A-T pairs do, with the same combination of flexibility and rigidity required for natural DNA to function. They also showed that the Z-P pairs integrate well with conventional pairs and that six-letter GACTZP DNA can evolve. The evolution of DNA containing the new building blocks endows the structures with new properties that could be useful in protein recognition.



More information: Structural Basis for a Six Nucleotide Genetic Alphabet, *J. Am. Chem. Soc.*, Article ASAP. DOI: 10.1021/jacs.5b03482

Evolution of Functional Six-Nucleotide DNA, *J. Am. Chem. Soc.*, Article ASAP. DOI: 10.1021/jacs.5b02251

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