

Researchers discover DNA shift never before seen in nature

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A team of MIT researchers and others has discovered that bacteria employ a type of DNA modification never before seen in nature.

The researchers, led by Peter Dedon, professor of biological engineering, and Zixin Deng at Shanghai Jiaotong University in China, published their results in the November issue of *Nature Chemical Biology*.

For several decades, researchers have known that it is possible to modify synthetic oligonucleotides (short strands of DNA) by adding sulfur to the sugar-phosphate DNA backbone as a phosphorothioate. Researchers often use such modifications in the laboratory to make DNA resistant to nucleases (enzymes that snip DNA in certain locations) as a step toward gene and antisense therapies of human diseases.

Dedon said he and his co-workers were surprised to discover that a group of bacterial genes, known as the *dnd* gene cluster, gives bacteria the ability to employ the same modification on their own.

"It turns out that nature has been using phosphorothioate modifications of DNA all along, and we just didn't know about it," he said.

The discovery raises many new questions.

"To find that bacteria do it naturally opens up a whole new set of issues to deal with," Dedon said.

"What is it doing? Why would bacteria conserve this system which requires five enzymes, each with different co-factors?"

He theorizes that the modification system might serve as either protection against foreign (unmodified) DNA, or as a "bookmark" to assist with transcription or replication of DNA.

The researchers found that the sulfur was incorporated as a phosphorothioate about every several thousand base pairs in the bacterial

genome, but they are not sure why it appears in those specific locations. They found the sulfur in many different strains of bacteria, and they believe the gene cluster can be passed between bacteria, much like genes for antibiotic resistance.

Other MIT authors of the paper are lead author Lianrong Wang, a visiting graduate student in the Department of Biological Engineering; Shi Chen, a postdoctoral scientist in the Department of Chemistry; Koli Taghizadeh, a research scientist in the Center for Environmental Health Sciences; and John Wishnok, senior research scientist in the Department of Biological Engineering and the Center for Environmental Health Sciences.

Source: MIT, by Anne Trafton

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