Teaching life a new trick: Bacteria make boron-carbon bonds

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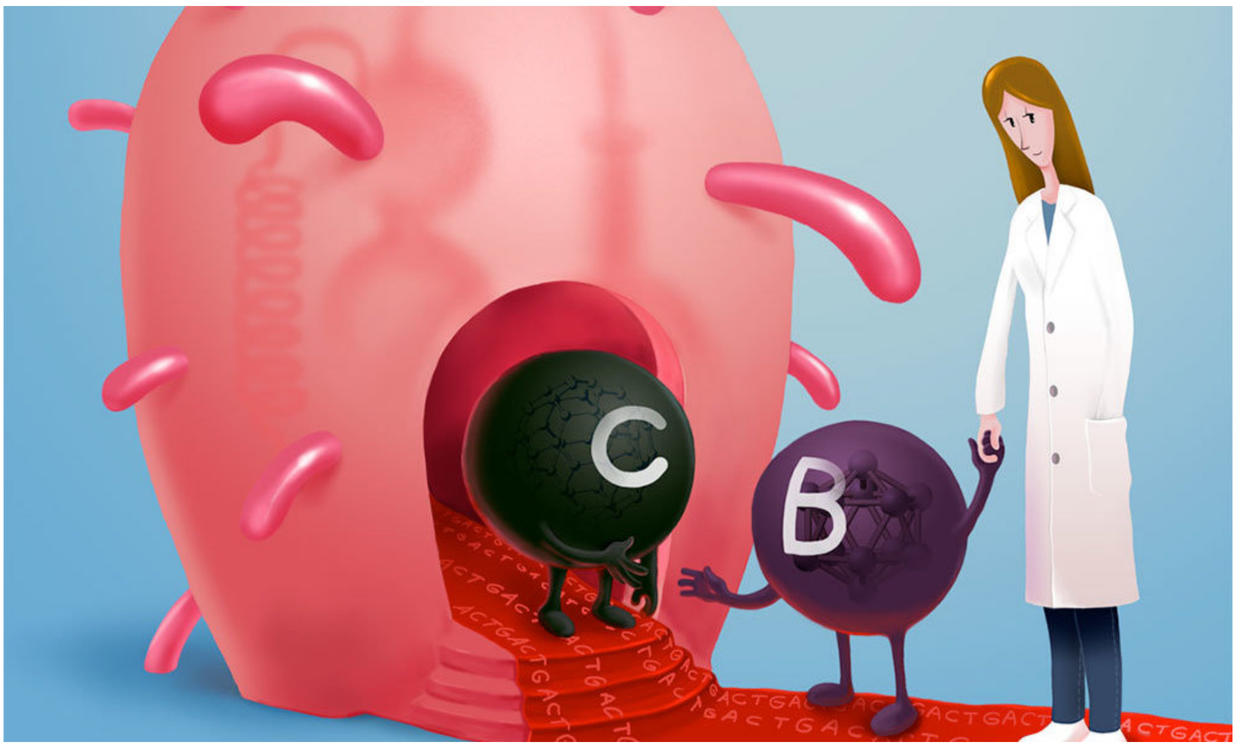

Artist's interpretation of a scientist introducing boron to the carbon-based chemistry of life. Jennifer Kan, Xiongyi Huang and their team from the Caltech laboratory of Frances Arnold have created bacteria that can make compounds with boron-carbon bonds for the first time. Credit: David Chen and Yan Liang (BeautyOfScience.com) for Caltech

In another feat of bioengineering, Caltech's Frances Arnold, the Linus

Pauling Professor of Chemical Engineering, Bioengineering and Biochemistry, and her team have created bacteria that can, for the first time, make chemical compounds containing bonds between boron and carbon. Before now, such boron-carbon bonds came only from the laboratories of chemists and could not be produced by any known life form.

The finding is part of a new wave in synthetic biology, in which living organisms are taught to make chemical compounds needed for pharmaceuticals, agricultural chemicals, and other industrial products. Last year, Arnold's team also engineered bacteria to produce molecules with silicon-carbon bonds, called organosilicon compounds, which can be found in everything from pharmaceuticals to semiconductors.

By using biology instead of synthetic processes, researchers can potentially make the chemical compounds in "greener" ways that are more economical and produce less toxic waste, according to Arnold.

The results are published in the November 29 online edition of the journal *Nature*. Lead authors of the report are Jennifer Kan and Xiongyi Huang, postdoctoral scholars in Arnold's laboratory.

"We have given life a whole new building block that it did not have before," says Arnold, who is also the director of the Donna and Benjamin M. Rosen Bioengineering Center. "This is just the beginning. We've opened a new space for biology to explore, a space that includes useful products invented by humans."

"Nature has created beautiful machinery that we can benefit from," says Huang. "We're repurposing nature's best inventions."

To coax the bacteria into making boron-containing compounds, the scientists used a method pioneered by Arnold in the early 1990s called directed evolution, in which enzymes are evolved in a lab to perform desired functions—such as creating chemical bonds that aren't found in the biological world. As was done in the previous silicon-based research, the scientists started with a common protein called cytochrome c—but with a variant naturally found in bacteria living in Icelandic hot springs. They mutated the DNA that encodes the protein and then put the mutated DNA sequences into thousands of bacterial cells to see whether the resulting bacteria could create the desired boron-carbon bonds. The DNA of successful mutant proteins was then mutated again, and the cycle was repeated until the bacteria making the proteins were highly proficient at assembling the boron-carbon compounds.

The researchers made six versions of these proteins, each with slightly different penchants for making various molecules with boron-carbon bonds. Their final bacterial creations were up to 400 times more productive than synthetic chemical processes used for the same reaction.

Kan says that researchers can use this technique to easily generate even more proteins with specific functions.

"The protein DNA is like software that researchers can go in and rewrite," says Kan. "In traditional chemistry, you have to resynthesize a whole chemical catalyst if you want it do something new. But we can do this by simply altering the DNA that tells the bacteria what to make."

Boron, which comes from the mineral borax, sits just to the left of carbon on the periodic table. It is a common ingredient found in composite materials and in fertilizers. It's also an essential nutrient of plants, and recent research from NASA's Curiosity rover showed that it is present on Mars, a sign of possible habitable conditions.

Says Kan, "Boron is one of chemistry's unsung heroes. It is not an element we hear about every day, but its contribution to chemistry is tremendous. We are excited to add this element to the synthetic biology toolbox for the first time."

The *Nature* study is titled "Genetically programmed chiral organoborane synthesis."

More information: Genetically programmed chiral organoborane synthesis, *Nature* (2017). nature.com/articles/doi:10.1038/nature24996

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