

All known life on Earth, except possibly a few viruses, makes its DNA out of four bases for the most part: adenine, cytosine, guanine, and thymine, which is where the genetic letters A,C,G, and T come from.

Occasionally there are other bases, usually modifications of these four, that cells use, but the big four are never replaced. That's why it's possible to take a gene from humans, say for insulin production, and put it in bacteria so that they make insulin for medical use.

It would take a lot of changes in a cell's machinery to be able to substitute an unusual base for one of the four, since they are so essential to the cell's function.

But now, an international team of scientists publishing this past July has evolved bacteria to be able to substitute a synthetic analog of thymine called 5-chlorouracil into their genomes.

The researchers grew *Escherichia coli*, a strain that couldn't make its own thymine, in a device consisting of two growth chambers connected to each other and to some medium reservoirs. The culture was transferred between the chambers so that the chamber not in use could be cleaned, to prevent biofilm formation, which would allow the bacteria to escape selective pressure.

The medium they were growing in contained varying amounts of thymine, the natural base, and 5-chlorouracil, the synthetic analog. This way, cells would get the thymine they needed to grow, but those that could use more 5-chlorouracil would be able to replicate faster and would come to dominate the population. This is how they encouraged evolution. Then they gradually increased the amount of synthetic base and decreased the natural one until the bacteria could grow on 5-chlorouracil alone, with no thymine added.

They ended up with two strains that actually required 5-chlorouracil to replicate; they could no longer grow with thymine instead, though it wasn't too hard for them to regain that ability.

Then they took a sample and chopped up the DNA to analyze its composition, and found that almost all of the thymine had been replaced with the synthetic analog, as expected.

This is a very cool result with many implications for microbial biotechnology. For example, using these methods, strains of industrial organisms could be developed that produce useful products, like biofuels or pharmaceuticals, growing in media that contains synthetic analogs of natural biomolecules, that only those organisms engineered to grow on them could use. This could make it much easier to avoid contamination with undesirable organisms, which would have to evolve to use the synthetic compounds before they could grow, reducing the cost of such processes.

Also, there could be less concern about what industrial organisms might do if they escaped from a plant, because they wouldn't be able to grow at all without their synthetic food present, which it wouldn't be out in nature.

They might also be useful for medical purposes, like for drug delivery: if they could be engineered to target a specific type of cell, like cancer or other harmful bacteria, they could attack it but otherwise be unable to replicate in the body because they would be lacking their synthetic compound.

I wonder, though: there are viruses whose genomes are made of RNA, not DNA, so they might not be affected by the results of this study. It might be necessary to engineer some other kind of difference if this turns out to be a problem.