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Newly engineered microbes could help prevent contamination in industrial tanks like these.

'Genetic firewall' holds engineered microbes captive

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By Erik Stokstad (/author/erik-stokstad) | 21 January 2015 6:45 pm | Comments (/biology/2015/01/genetic-firewall-holds-engineered-microbes-captive#disqus_thread)

Human-engineered microbes are workhorses of the pharmaceutical and chemical industries, churning out biofuels, drugs, and many other products. But they can cause big problems if they become contaminated by other microbes or viruses or escape into the environment. Now, a new type of microbe that can survive only on artificial nutrients promises better security against such mishaps. The strategy, described in two papers in this week's

issue of *Nature*, might ultimately be used to control genetically engineered plants or other organisms released into the wild to create products or clean up pollution.

Contamination is one of many risks involved in using engineered microbes to produce biological pharmaceuticals and high-value chemicals. Viruses, for example, can hijack bacteria and spoil a batch of drugs. "It can be disastrous," George Church of Harvard Medical School in Boston, who helped lead the new research, told reporters during a telephone briefing. Engineered microbes themselves can also accidentally end up in a product or the environment. That's why government regulators require that most engineered microbes be physically contained in sealed vats or other containers.

In principle, a microbe could be confined more securely by modifying its genome so that it can reproduce only in the presence of certain nutrients or chemicals. But microbes can usually evolve to get around these obstacles. Now, Church and colleagues say they've overcome those issues by redesigning the *Escherichia coli* genome so that the microbe depends on a synthetic amino acid (http://www.nature.com/nature/journal/vaop/ncurrent/full/nature14121.html) to create proteins necessary for survival and reproduction. When the microbes are grown without this synthetic nutrient, their genetic machinery grinds to a halt and they die. The modification also prevents viruses from contaminating the culture, as they can't replicate inside the altered microbes. Farren Isaacs, a former postdoc in Church's lab now at Yale University, describes similar results (http://www.nature.com/nature/journal/vaop/ncurrent/full/nature14095.html) in the same issue of *Nature*.

To lower the chances that any of the engineered microbes can mutate and survive without the special diet, the groups altered three genes to require the synthetic amino acids. "It really adds increasing layers of security onto this system," says Tom Ellis, a synthetic biologist at Imperial College London, who was not involved in the research. Neither group has yet detected any successful mutations in the microbes. "They're opening a door into a completely new area for investigation in biosafety," adds Markus Schmidt, a biosafety expert and consultant in technology assessment at Biofaction KG in Vienna.

Several steps remain before the microbes are ready for prime time. One

important question is the cost of the synthetic amino acids used to feed the engineered microbes. For example, Ellis says that the amino acid used in Isaacs's experiment would be prohibitively expensive for most commercial applications. Church engineered microbes to require a cheaper synthetic amino acid.

***Correction, 26 January, 10:07 a.m.:** A previous version of this story incorrectly stated that Church's microbes reproduced less quickly than those in the experiments by Isaacs. In addition, neither group measured the ability of the microbes to produce chemicals.*

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