The future of cancer treatment may lie in genetically engineered bacteria

By Kevin Wheeler
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Researchers from Yale University and Yale School of Medicine have genetically engineered E. coli bacteria to resist viral infection and undesirable gene transfer, opening up new pathways for medical research as well as better production of medicines, chemicals and numerous other products derived from biological sources.

By removing a section, or codon, of the bacterium's genetic code, the inventors can generate immunity because viruses use this code to infiltrate an organism and replicate inside it. Without the right code to exploit, the viruses are powerless to infect. Adding or manipulating code, on the other hand, can help researchers simulate and study the processes that lead to cancer and other diseases much faster than before.

The inventors are seeking to patent their technology with the U.S. Patent and Trademark Office, which published their application on April 29.

"We have effectively changed our cell and made the code different from every other organism on the planet," said

co-inventor Jesse Rinehart, an associate professor of cellular and molecular physiology at Yale School of Medicine.

The technology works because genetic code, present in DNA, has roughly the same function, and even the same makeup, across all cellular organisms. DNA contains three-letter sequences of nucleic acids that form amino acids — that doesn't change. There are only 20 amino acids that form the "building blocks" of life.

Rinehart and his colleagues clipped the genetic code of E. coli bacterium in 321 different places using a gene editing technique developed by inventor Farren Isaacs of the Yale School of Medicine. According to Rinehart, the basic idea behind the technique resembles editing text in a word processor.

"If you misspelled a word, you would literally cut and replace the letter, and that's exactly what's being done to the organism's genome," Rinehart said in an interview with *Fastinform*.

One of the primary goals of this technology is to help combat viral contamination of pharmaceutical products. This is a rare but costly problem in the production of insulin, medicines and vaccines, which often rely on bacteria to create the materials that eventually make up these products. If a virus infects any batch of such products, it could ruin an entire facility's worth of material, according to Rinehart.

From 1955 to 1963, simian virus 40, a virus that can infect humans and monkeys and could increase cancer risk, contaminated as much as 30% of administered polio vaccines. If future vaccines rely on Rinehart and his colleagues' technology, this risk could be completely avoided.

Because the bacteria are genetically isolated, they are immune to horizontal gene transfer as well as viruses. Horizontal gene transfer is a form of evolution that involves the movement of genetic material from one species to another rather than parent to offspring. Typically, it occurs over millions of years in larger organisms, but bacteria possess direct and indirect processes that make horizontal gene transfer much faster, according to Rinehart.

A major concern in bacteriology is now the proliferation of antibiotic-resistant bacteria and the horizontal transfer of antibiotic-resistant genes. As with viral resistance, editing the genetic code of bacteria to make it unlike any other type can help stop the transfer and movement of antibiotic-resistant genes.

"We're really excited about all the products that could come out of these cells, but there's also excitement about the factory itself. The cell is the factory, right?" Rinehart said. "The factory is safer, it's more robust, it's more scalable, it's controlled. It doesn't escape and wreak havoc."

Rinehart's bacterial "factory" may not only help create insulin and vaccines, but also more effective cancer drugs. By removing and altering the genetic code of E. coli bacteria, Rinehart and his colleagues can engineer their bacteria to express certain proteins that replicate processes that lead to cancer.

"If I had to study cancer using a cancer cell, it's going to take me 20 years, but if I use the bacterial technology, I can get the same answer in one year," Rinehart said.

Studying these processes helps identify new targets for cancer drugs, and Rinehart and his colleagues plan to soon release a paper describing how they discovered a new drug to treat breast cancer using their engineered bacteria.

"We all know the power and the amazing potential of cellular life, and so to have full writing and editing capability of a genome gives you full access to engineering cellular life," Rinehart said. "That's the most exciting thing. We're now focused on using these same approaches for the products of cellular life."

The application for the patent, "Engineering organisms resistant to viruses and horizontally transferred genetic elements," was filed on Nov. 30, 2020, to the U.S. Patent and Trademark Office. It was published April 29 with the application number PCT/US2020/048471. The earliest priority date was Oct. 29, 2019. The inventors of the pending patent are Farren Isaacs and Jesse Rinehart, Yale School of Medicine; and Natalie Ma and Colin Hemez, Yale University. The assignee is Yale University.