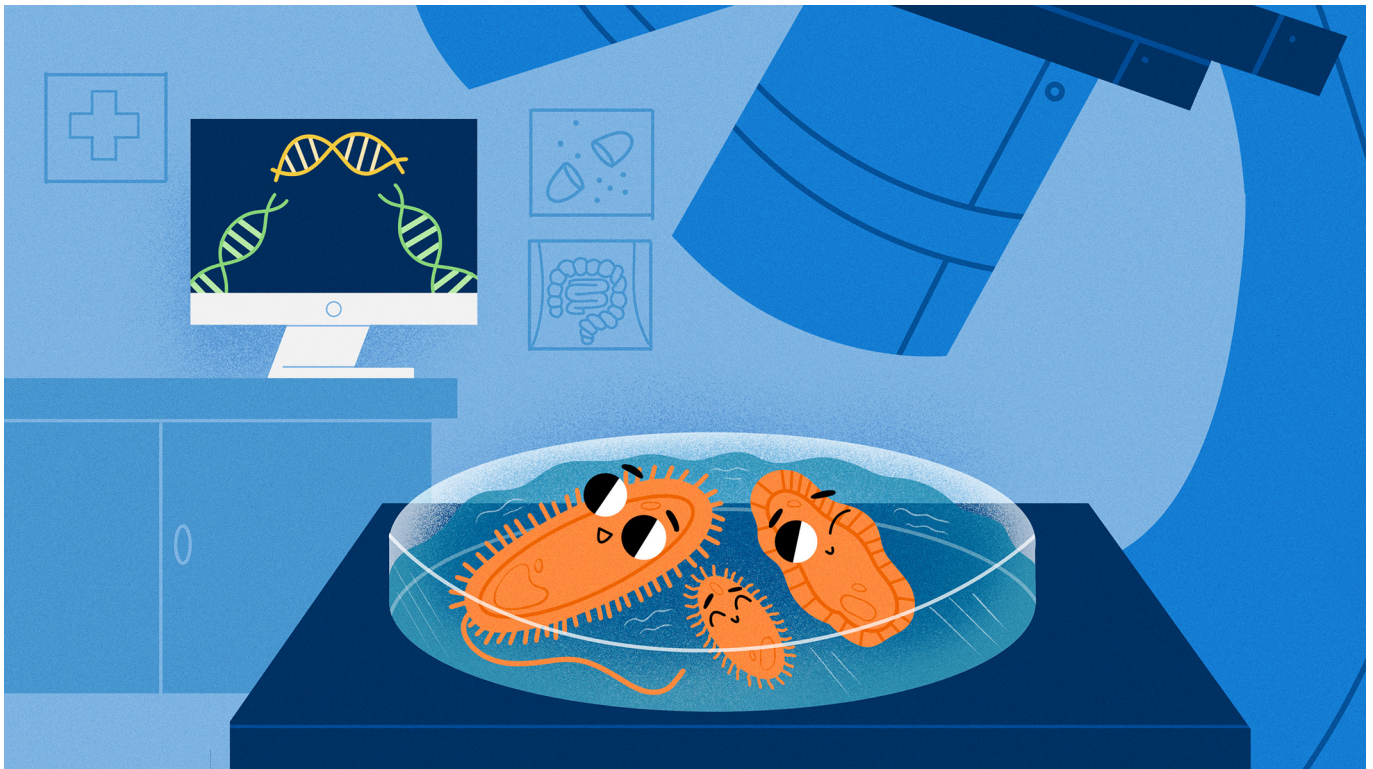




HOW CAN WE ENGINEER BACTERIA TO TREAT HUMAN DISEASES?

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YOUNG REVIEWERS:



MANNAN

AGE: 9



WILLIAM

AGE: 10

Bacteria are microscopic single-celled organisms that are invisible to the naked eye. They live all over the human body, and they can help keep people healthy by producing vitamins and breaking down food. Scientists can even use bacteria to treat disease by changing their genetic code to give them new instructions to produce a medicine from inside a person's body—like tiny factories! This can be better than traditional medicine because the bacteria have instructions to only produce the medicine where it is needed in the body, reducing the side effects of treatment. In this way, people can work *with* the bacteria in their bodies to fight disease together.

HOW DO BACTERIA KEEP PEOPLE HEALTHY?

Bacteria are living things made up of just one cell, but they come in all kinds of shapes and sizes. Bacteria are so tiny that they cannot

be seen without a microscope, but they can be very different from each other, allowing them to live in lots of different places and perform many jobs. Bacteria are everywhere, from deep in the ocean to active volcanoes, in the air, and on every plant and animal on the planet—even people! Even though you cannot see them with your eyes, bacteria are responsible for supporting life on Earth. They can break down nutrients in the soil to help plants grow, and they help you digest the food in your gut [1].

SPECIES

A group of similar organisms that can exchange DNA.

PATHOGEN

Harmful microorganisms, like bacteria, that can cause disease.

Bacteria often get a bad reputation, as some **species** (specific types of bacteria) can make people sick—which is why it is important to always wash your hands! But there are many other species that actually help you to stay healthy. Many bacteria and other microbes live in and on your body, and they can protect you from harmful bacteria (called **pathogens**) and help your immune system. In your intestines, you have many types of bacteria all working together and performing important jobs. **Intestinal bacteria** help you digest the food you eat, produce essential vitamins, and fight against harmful bacteria or microbes you accidentally ingest (Figure 1). In fact, the human gut hosts approximately 100 trillion microbes, which play a vital role in human health [2]. This bacterial community is important not just for your physical health [3]—some studies have even shown that the bacteria in and on your body can affect your mental health, too [4]. Now that you know how bacteria work in your body to keep you healthy, let us look at how scientists are trying to change the job of bacteria to help fight diseases!

Figure 1

Bacteria are present all over your body, performing various jobs including helping to digest food, producing vitamins, combating harmful pathogens, and affecting your mental health and overall mood.

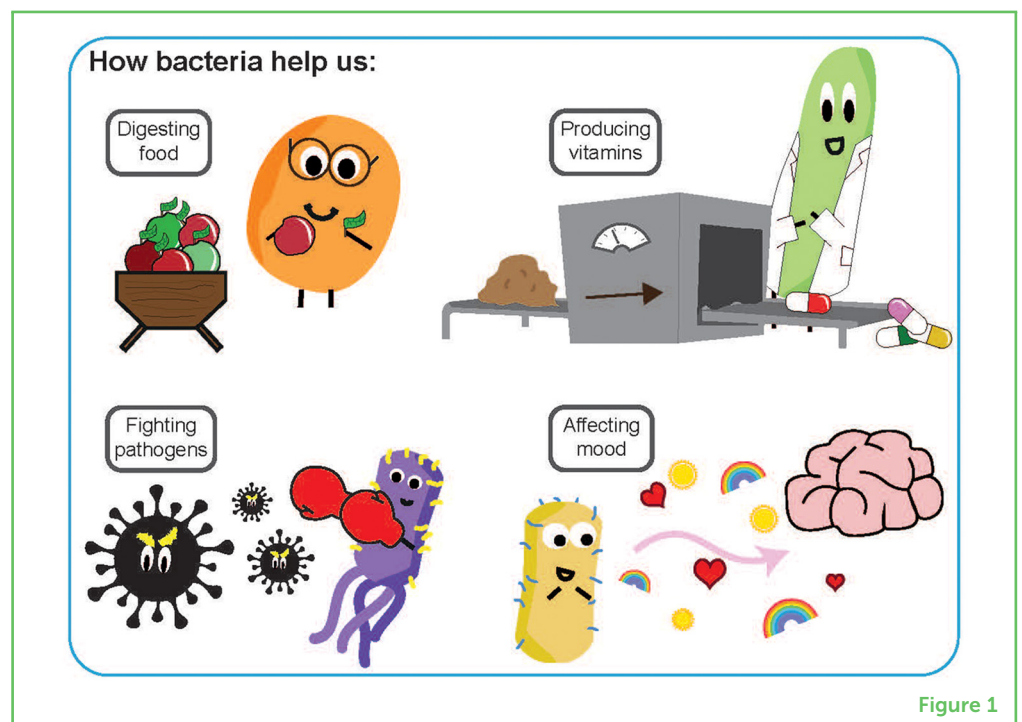


Figure 1

PROBIOTIC

Beneficial bacteria or other microorganisms that help keep your body healthy, especially your digestive system.

DNA

Genetic material that contains instructions for how living things look and function.

GENETIC ENGINEERING

A way scientists change an organism's DNA to give it new traits or abilities.

GENE

A section of DNA that controls a specific trait, which is inherited from your parents.

HOW DO WE USE BACTERIA TO TREAT DISEASE?

Scientists can take two main approaches if they want to use bacteria to treat diseases. The first is to use bacteria that exist in the environment naturally, either on their own or working together in groups. The second is to engineer bacteria in a laboratory to carry out a specific task. Many foods contain natural bacteria that help to keep people healthy—for example, the bacteria in natural yogurt break down food in the gut, which helps the body to access the nutrients it needs to grow. These natural bacteria can also be taken as a tablet, called a **probiotic**, to make sure people get enough of the helpful bacteria. Probiotics are currently being tested in humans, to help researchers discover new ways of helping patients [5].

Every cell in the body has a job, whether it is making the hair on your head or forming the muscle in your heart, so every cell contains a set of instructions called **DNA** that tell the cell what to do. Researchers can edit the DNA of bacteria to give them new instructions, so they can perform specific tasks for people, and this is called **genetic engineering**. For example, if your body does not produce enough of a protein it needs, we can take the **gene** (a section of DNA that performs a specific function) that produces that human protein and add it to the DNA of bacteria. Once the bacteria have the new instructions, they will produce the lacking protein, and we can use those bacteria to make a medicine that you can take when your body needs it. In this way, we can work with bacteria so that they can make the medicine people need [6]. This allows scientists to correct errors in people's bodies and prevent patients from getting sick.

To design engineered bacteria to combat disease, there are many questions that we need to consider. Firstly, depending on the disease we want to treat, we can use different species of bacteria. For example, if we want to treat a disease in the gut, we could use bacteria that already live inside the intestines.

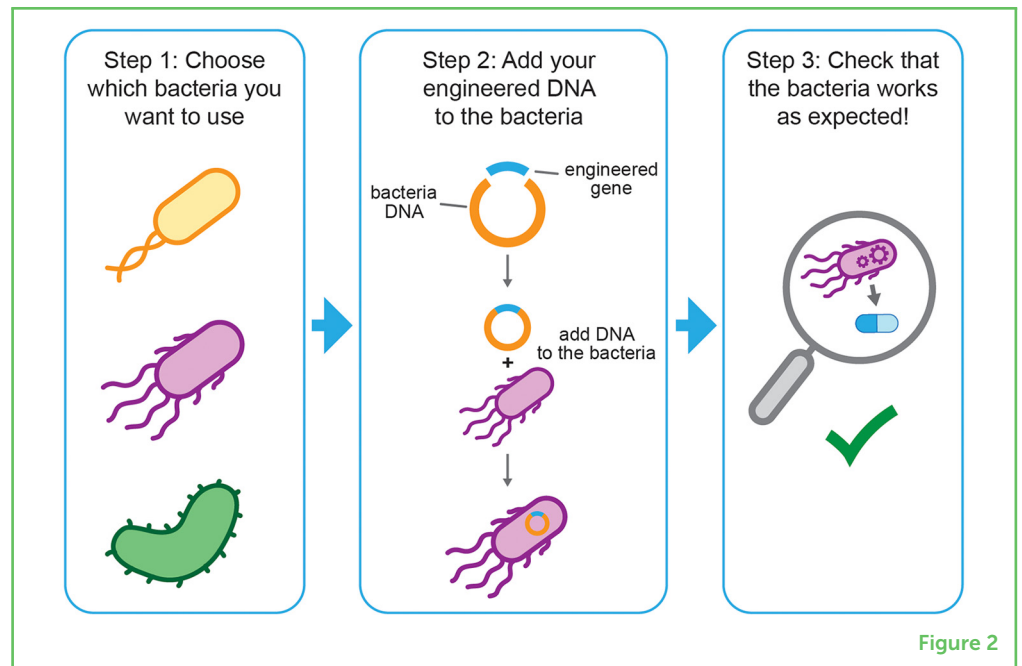
Some commonly used species are *Escherichia coli* Nissle 1917 [7], which was discovered in the gut of a First World War soldier, and *Lactobacillus* bacteria, which are often found in the yogurt at your local supermarket. Once the right bacteria for the job are chosen, we need to engineer their DNA to produce the medicine or drug we want, and then check that everything is working as expected (Figure 2).

WHY USE BACTERIA WHEN WE HAVE MEDICINE ALREADY?

Normally, when you are sick, you might take medicine to make you feel better or to fight the disease. Unfortunately, there are diseases that do not yet have medicines that can treat them, and many current treatments can cause unpleasant side effects. For example, the

Figure 2

A simplified cartoon of how scientists can engineer bacteria to treat disease. First, we must choose the bacteria we want to use. Second, we change the DNA of the bacteria so that it can make the medicine we want. The final, very important, step is to check that the bacteria work as we intended.



medicines used to kill harmful bacteria often kill the helpful bacteria at the same time and then those helpful bacteria cannot do their jobs. Instead of using medicine made from plants or chemicals, scientists can change the DNA of bacteria so that they can produce the medicine for us. Let us take diabetes as an example. Diabetes occurs in people who cannot make the chemical insulin, which regulates blood sugar, and so they need to take insulin as a drug. In the past, insulin from cattle and pigs was used to treat diabetes in humans, but it caused allergic reactions in many patients [8]. Scientists have since engineered bacteria to include the gene for making human insulin. Today, these bacteria are grown in large containers where they make insulin, which can be collected and used for diabetes treatment, instead of taking it from animals!

Using bacteria in this way offers many advantages over traditional drugs: bacteria are cheaper, grow quickly, and can make lots of the medicines we need. Scientists are even working on making engineered bacteria in a pill form—where the helpful bacteria go into your body and make the medicine right where it is needed. In the future, doctors might give patients special bacteria to treat diseases, so we will not always need to rely on regular drugs or chemicals to feel better.

CLINICAL TRIALS

Carefully designed scientific studies that test whether new medicines or treatments are safe and effective in people.

LOOKING FORWARD

Scientists have now engineered many bacteria to treat human diseases, but none of these engineered bacteria have been approved for use in humans yet. This is because they are still new therapies and need to be tested in properly designed experiments in humans called **clinical trials**, to prove they are safe and effective for patients to use.

If helpful bacteria escape into nature, they might spread in ways that we cannot control and cause problems. Also, if they grow too much in patient's bodies, they might make people sick instead of helping them. That is why scientists are careful when using bacteria as medicine. How can we make sure that engineered bacteria only go where we want them to? How can we make sure patients feel comfortable taking these new treatments? If they pass clinical trials, would you feel safe about using engineered bacteria to help treat disease?

While there are still many questions left to be answered, engineering bacteria to help treat disease is an amazing technology that has the potential to transform how patients are treated in the future. Without the bad side effects of some of the medicines used now, and with increased creation of medicines that only go where they need to go in the body, people could get better a lot faster—and that leaves more time for the fun things in life!

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YOUNG REVIEWERS

MANNAN, AGE: 9

Mannan, a 9-year-old soon-to-be 4th grader, loves gymnastics, soccer, reading, and coding. His book collection includes titles such as Franny K. Stein: Mad Scientist, Encyclopedias, The Wild Robot, and The City of Ember, among others. Inspired by his grandparents, doctors, and his parents, biological scientists, Mannan is passionate



about scientific breakthroughs. He shares his excitement and curiosity in his reviews, making tricky ideas fun and easy to understand.



WILLIAM, AGE: 10

My name is William and I am going into 5th grade. I like to play baseball. My favorite animals are fish and whales. I like to play video games and guitar. I have one pet dog and four chickens.

AUTHORS



JACK W. RUTTER

I am a scientist at UCL and I work with bacteria and research how we can design them to help us fight harmful microbes that can make us unwell. All sorts of different bacteria live on and in our bodies, and I love finding new ways in which we can engineer them to produce useful proteins, detect important chemicals, or fight infections.



CHANIA CLARE

I am a PhD student at UCL, where I investigate how bacteria interact with each other in our bodies so we can learn how to control the levels of harmful bacteria and prevent them from making us unwell. I have previously investigated electrotopism in plants (that is plant roots bending toward an electrical current!), engineering algae to produce the nutrients crops need to grow, and how to make mosquitoes immune to the malaria parasite so we do not get sick!



KIMBERLEY A. OWEN

I am based at UCL and I engineer bacteria, which means getting bacteria to do useful jobs for me. I want to engineer bacteria to kill harmful bacteria that are found in the human body. This would be beneficial to us as humans because these bacteria can act as drugs, and they are more specific and have fewer side effects that make people unwell. They would be particularly useful where antibiotics (drugs that kill bacteria when you are sick) do not work. This is a global challenge that scientists are working on, and my engineered bacteria could be an answer.



CHRIS P. BARNES

I am a professor in the Faculty of Life Sciences at University College London. My career has spanned multiple fields including particle physics, genetics, statistics, computational systems biology, and synthetic biology. In addition to my research, I am also actively engaged in training the next generation of researchers; I develop and run programs to train life scientists in computational and mathematical skills.



LINDA DEKKER

I am a researcher at UCL who studies bacteria and how we can engineer them to do useful things. Right now, I am working on special bacteria that act like tiny sensors to detect chemicals important for gut health. In the past, I have worked on projects that used bacteria to make medicines, fight harmful germs, and even create new materials. I love exploring how we can use microbes to solve problems in medicine and technology! *linda.dekker.09@ucl.ac.uk