Antibiotic-resistant bacteria are a global problem

Antibiotic-resistant bacteria carry resistance genes and often become dominant in microbial populations. Bacteria can also mutate and receive genes from other microbes that make them resistant to antibiotics. Katariina Pärnänen, post-doctoral researcher at the Academy of Finland, searches for and identifies these genes that have been collected from different environments around the world and stored in databases.

Antibiotics, or drugs produced by microbes that kill other microbes, especially bacteria, have been used to fight infections since the 1930s. Use of antibiotics, particularly overuse or inappropriate use, results in bacteria becoming resistant to antibiotics. This is a growing problem, and because of it people die from infections that cannot be treated with antibiotics.

Katariina Pärnänen studies antibiotic resistance at the University of Turku.

“When a person has been infected with an antibiotic-resistant bacteria, they will not respond to treatment with antibiotics. These days antibiotic-resistant bacteria are typically resistant not just to one but as many as 15 different antibiotics.”

A problem for human and environmental health

Antimicrobial resistance genes are a growing problem globally. They are found not just in the human gut but also in soil, wastewater, fish farms and animal farms. Resistance genes found in our environment may ultimately end up in the human gut.

“Everything about microbes is of interest to me. From research perspective, it is quite useful that I have some understanding of what happens in pig farms, fish farms or in a river flowing through a big city in Indonesia. At the University of Helsinki, I studied the infant gut microbiome and the connection between formula or breastfeeding and the number of resistance genes. In a way, my research represents the ‘One Health’ approach,” Pärnänen says.

Discovery of new viral diseases and threats of such diseases in the early 2000s led to the emergence of the One Health and Global Health research concepts: a broad understanding of the need to protect human and animal health and the ecosystem. The movement initiated by physicians and veterinarians represents an interdisciplinary approach that covers the local, regional, national and international levels.

“I want to address antibiotic resistance as a problem that affects human health, animal and food production, and environmental health. Previously I studied the ways in which resistance genes were passed on from mothers to children, and how the duration of breastfeeding affected the number of these genes. Now my focus is on the various factors linked to antibiotic resistance of the gut microbiota. These include overuse of antibiotics, living environment and health history. These may provide an indication of whether the person is likely to carry antibiotic-resistant bacteria.”

New sequencing techniques a breakthrough in the study of microbes

The study of environmental bacteria and their genes took a giant leap forward with
In some species of bacteria, it is possible to identify genes that appear in its genome only once. By comparing these with genes in the databases of other species, we can identify the species in question. We look for matches with resistance genes stored in databases. Then we can say that the person has ten resistance genes in their stool sample, or that they carry a certain amount of coliform bacteria.

“Resistance genes are everywhere”

Pärnänen was one of the researchers in a study where resistance genes from human feces were analysed. The study involved a comparative analysis of bacteria found in wastewater treatment plants in seven countries. Half of the world’s population carry the CrAssphage virus – a bacterial parasite – in their intestines. The gene sequence of this phage was used in the study as a marker to indicate feces-based infection.

“Antibiotic resistance has been studied for a long time, but with NGS we can now analyse all resistant genes from a single sample instead of just individual genes,” Pärnänen explains.

Metagenomics related studies have shown that antibiotic resistance genes are commonly found in our environment. The risk of these genes transferring to bacteria that cause infections in humans is significant.

Pärnänen uses metagenome sequence data that is stored in extensive open databases. She uses supercomputers at CSC – IT Center for Science to analyse the data, allowing her to identify different species of bacteria and their resistance genes.

“The same resistance genes can be found all over the world. Antibiotic resistance is often called an invisible pandemic, because the same resistance genes are spreading beyond country borders. However, certain genes are more common in some parts of the world than others.”

These genes may be found in larger numbers in India than, for example, in Northern Europe. There are also significant differences between Southern and Northern Europe.
The E. coli strains that cause urinary tract infections in southern Europe can be very resistant.

Bacteria do not cause a serious disease in a healthy person, but sometimes an intestinal infection may be caused by a resistant bacterium.

An infection caused by resistant bacteria is difficult to treat. Usually the most difficult resistant infections found in Finland are diagnosed in persons who had travelled abroad.

In 2002, stool samples were collected from Finnish adults as part of the FINRISK study by Finnish Institute of Health and Welfare (THL), and the sequence data of the microbes found in the samples was analysed.

Together with THL researchers we analysed samples from the Finnish population to see what the potential impacts of resistance could be and how a large number of resistant bacteria would affect a person’s health. Are high levels of antibiotic resistance genes associated with risk of death during the follow-up period?

It has been predicted that in 2050 more people will die from antibiotic-resistant infections than from cancer. Infectious diseases would be the most common cause of death. Antibiotics are currently being used more on farm animals than on humans, and at the same time our consumption of animal protein is growing. According to Pärnänen, the best way to fight the resistance crisis is to use antibiotics only to treat bacterial infections and only when there is evidence to prove that antibiotics will help. Similarly, an appropriate diet or lifestyle may reduce resistance genes in the intestinal microbiota.

In studies conducted recently in the United States, fibre intake was linked to a low rate of resistance genes while animal protein in the diet was linked to a high rate of genes. You could say your gut microbiota is what you eat.

Katariina Pärnänen works in the research team of assistant professor Leo Lahti. The team develops machine learning models that screen microbial groups from large data collections.

“Antibiotic resistance is one example of a research area where we use new measurement methods and computing capacity in a way that has not been done before. This research naturally combines different measurement environments from the human body to the environmental microbiome. This type of research generates ideas for method development that benefits researchers in various fields,” Leo Lahti comments.

Katariina Pärnänen would like to extend her research to the world’s entire human population and study the gut microbiome samples that have been metagenome sequenced and are openly available in databases.

“It would be interesting to discuss the technical feasibility of such a project with CSC experts. It would also promote open science, because the identified resistance genes and species found in microorganisms could also be stored for use by other researchers.”

Ari Turunen