

New and more detailed map of antimicrobial resistance

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Collection of sewage sample in Tamale, Ghana - one of 101 countries to have taken part in a global surveillance of infectious diseases and antimicrobial resistance via sewage. Credit: Courage Kosi Setsoafia Saba

During the COVID-19 pandemic, the world has become aware of the value of using sewage analyses to monitor disease development in an area. However, at DTU National Food Institute, a group of researchers has been using sewage monitoring from throughout the world since 2016

as an effective and inexpensive tool for monitoring infectious diseases and antimicrobial resistance.

By analyzing sewage samples received by DTU from 243 cities in 101 countries between 2016 and 2019, the researchers have now mapped where in the world the occurrence of resistance [genes](#) is highest, how the genes are located, and in which types of bacteria they are found.

The results from the new metagenomic study—which have just been published in *Nature Communications*—have surprised the researchers. In fact, the study shows that the genes have appeared in many different genetic contexts and bacterial types, indicating greater transmission than the researchers had expected.

"We've found similar resistance genes in highly different bacterial types. We find it worrying when genes can pass from a very broad group of bacteria to a completely different group with which there is no resemblance. It's rare for these gene transmissions to occur over such long distances. It's a bit like very different animal species producing offspring," explains Assistant Professor Patrick Munk.

If the genes are in bacteria that don't usually make people sick—such as [lactic acid bacteria](#)—it's of less concern. However, if the resistance genes find their way into bacteria that are important to human health—such as salmonella—it's a completely different story.

"This makes it much more likely that the bacteria will actually kill people—for example in a hospital—because no treatment is available," says Patrick Munk.

Like an intricate puzzle

The Research Group for Genomic Epidemiology at DTU National Food

Institute has developed and maintains one of the world's most comprehensive resistance databases. It currently includes 3,134 known resistance genes.

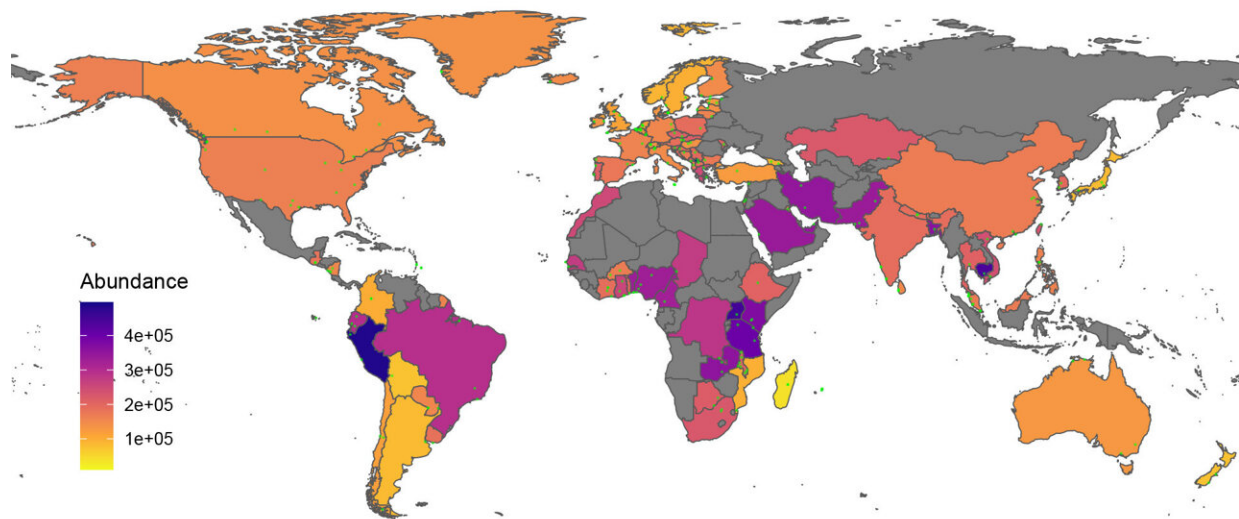
The researchers have used the database to map resistance genes in the sewage samples in the new study.

The samples contain a very large number of microorganisms from different sources, including human feces. The frozen sewage samples have been sent to DTU, where laboratory technicians extract all the bacteria from the thawed samples.

The bacteria are then broken up and their collective DNA is broken into [smaller pieces](#), which state-of-the-art DNA sequencing equipment can read all at once.

A supercomputer can then compare the billions of recorded DNA sequences with known genes and construct larger pieces of the original genomes contained in the samples.

This process provides insight into several areas such as in which bacteria and genetic neighborhoods the resistance genes are located.



The world map shows the occurrence of resistance genes in different countries. The darker a colour used for a country, the higher the frequency of resistance genes in bacteria. Grey countries have not provided sewage samples. Credit: Technical University of Denmark

Hotspots for transmission of genes

In [different places](#) in Sub-Saharan Africa, the researchers have found the same resistance gene in a number of different bacteria.

"We interpret this to mean that we may be quite close to a transmission hotspot, where there is a gene transmission from one to another to a third bacterium. That's why we're seeing the gene in so many different contexts precisely there," Patrick Munk explains.

He adds that many of the surprising transmissions appear to occur in the

Sub-Saharan Africa. These are also countries with the least developed programs for monitoring resistance, which means that there is very little data on the resistance situation.

"We risk overlooking important trends because we don't have data," he suggests, stressing that solid data is exactly what is needed to develop effective strategies for combating resistance:

"Right now, we have huge knowledge about how resistance behaves in the West and—based on that knowledge—we plan how to combat resistance. It now turns out that if we look at some new locations, the resistance genes may behave very differently—presumably because they have more favorable transmission conditions. Therefore, the way in which you combat resistance must also be adjusted and tailored to the local conditions."

Successor

The global sewage project—which is supported by the Novo Nordisk Foundation and the VEO research project—concludes in 2023. The researchers find that it has proved to be a good supplement to existing monitoring initiatives, which mainly operate at national or regional level and measure resistance in [bacteria](#) from sick people.

They therefore hope that a successor to the project will appear, so that the world can continue to benefit from the important knowledge generated by the monitoring program. This also applies to countries that have solid monitoring programs and control strategies in place.

"There are many analogies with climate change, where what happens on the other side of the globe isn't unimportant to you. One day or another, the problem will come back to bite us, as we've seen time and again," Patrick Munk stresses.

Reuseable data

Unlike data from conventional analysis methods, raw data from metagenomic studies can be reused to shed light on other problems. For example, the researchers in the sewage project have used their dataset to analyze the occurrence of other pathogenic microorganisms in the sewage.

The whole dataset from the sewage monitoring has been made freely available to researchers worldwide. For example, it has already been used to detect many new viruses globally and to map the ethnic composition of different populations.

As new resistance genes are discovered—even far into the future—researchers will be able to reuse raw data to quickly establish where they have first appeared and how they have spread.

In the study, the researchers have analyzed 757 [sewage](#) samples from 243 cities in 101 countries. The samples were collected and sent to DTU's campus in Lyngby between 2016 and 2019.

Genomic analysis of wastewater is fast and fairly inexpensive relative to how many people you can cover. Wastewater analyses do not require ethical approval, as the sample material cannot be linked to individuals.

More information: Patrick Munk et al, Genomic analysis of sewage from 101 countries reveals global landscape of antimicrobial resistance, *Nature Communications* (2022). [DOI: 10.1038/s41467-022-34312-7](https://doi.org/10.1038/s41467-022-34312-7)

Provided by Technical University of Denmark

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