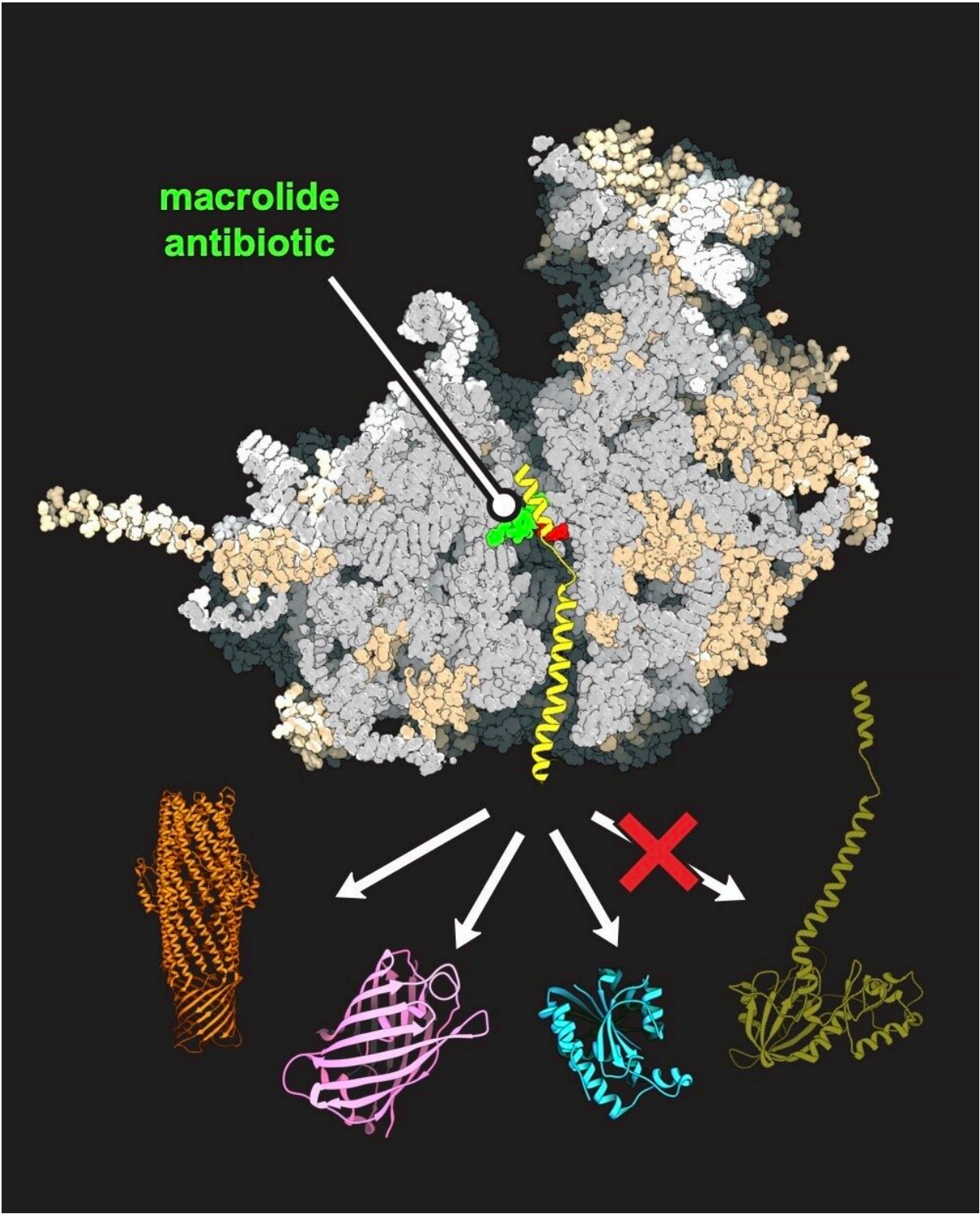


# **Can antibiotics treat human diseases in addition to bacterial infections?**

May 25 2021, by Jacqueline Carey

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An antibiotic (green), bound in the human-like yeast ribosome (gray), allows for synthesis of some proteins (represented in orange, purple, and blue) but not

others (dark green). Credit: Maxim Svetlov/UIC

According to researchers at the University of Illinois Chicago, the antibiotics used to treat common bacterial infections, like pneumonia and sinusitis, may also be used to treat human diseases, like cancer. Theoretically, at least.

As outlined in a new *Nature Communications* study, the UIC College of Pharmacy team has shown in laboratory experiments that eukaryotic ribosomes can be modified to respond to antibiotics in the same way that prokaryotic ribosomes do.

Fungi, plants, and animals—like humans—are eukaryotes; they are made up of cells that have a clearly defined nucleus. Bacteria, on the other hand, are prokaryotes. They are made up of cells, which do not have a nucleus and have a different structure, size and properties. The ribosomes of eukaryotic and prokaryotic cells, which are responsible for the [protein synthesis](#) needed for [cell growth](#) and reproduction, are also different.

"Some antibiotics, used for treating bacterial infections, work in an interesting way. They bind to the [ribosome](#) of bacterial cells and very selectively inhibit protein synthesis. Some proteins are allowed to be made, but others are not," said Alexander Mankin, the Alexander Neyfakh Professor of Medicinal Chemistry and Pharmacognosy at the UIC College of Pharmacy and senior author of the study. "Without these proteins being made, bacteria die."

When people use antibiotics to treat an infection, the cells of the patient are not affected because the drugs are not designed to bind to the differently shaped ribosomes of eukaryotic cells.

"Because there are many human diseases caused by the expression of unwanted proteins—this is common in many types of cancer or [neurodegenerative diseases](#), for example—we wanted to know if it would be possible to use an antibiotic to stop a human cell from making the unwanted proteins, and only the unwanted proteins," Mankin said.

To answer this question, Mankin and study first author Maxim Svetlov, research assistant professor with the department of pharmaceutical sciences, looked to yeast, a eukaryote with cells similar to human cells.

The research team, which included partners from Germany and Switzerland, performed a "cool trick," Mankin said. "We engineered the yeast ribosome to be more bacteria-like."

Mankin and Svetlov's team used biochemistry and fine genetics to change one nucleotide of more than 7,000 in yeast ribosomal RNA, which was enough to make a macrolide antibiotic—a common class of antibiotics that works by binding to bacterial ribosomes—act on the yeast ribosome. Using this yeast model, the researchers applied genomic profiling and high-resolution structural analysis to understand how every protein in the cell is synthesized and how the macrolide interacts with the [yeast](#) ribosome.

"Through this analysis, we understood that depending on a protein's specific genetic signature—the presence of a 'good' or 'bad' sequence—the macrolide can stop its production on the eukaryotic ribosome or not," Mankin said. "This showed us, conceptually, that antibiotics can be used to selectively inhibit [protein](#) synthesis in human [cells](#) and used to treat human disorders caused by 'bad' proteins."

The experiments of the UIC researchers provide a staging ground for further studies. "Now that we know the concepts work, we can look for [antibiotics](#) that are capable of binding in the unmodified eukaryotic

ribosomes and optimize them to inhibit only those proteins that are bad for a human," Mankin said.

**More information:** Maxim S. Svetlov et al, Context-specific action of macrolide antibiotics on the eukaryotic ribosome, *Nature Communications* (2021). [DOI: 10.1038/s41467-021-23068-1](https://doi.org/10.1038/s41467-021-23068-1)

Provided by University of Illinois at Chicago

Citation: Can antibiotics treat human diseases in addition to bacterial infections? (2021, May 25) retrieved 26 April 2024 from <https://phys.org/news/2021-05-antibiotics-human-diseases-addition-bacterial.html>

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