

Common use of antibiotics in cells grown for research could distort tests

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A UCSF researcher prepares cell cultures in a lab. Credit: Susan Merrell

When growing cells in the lab, researchers routinely add antibiotics to prevent contamination. But a new study by UC San Francisco researchers raises a red flag against this standard practice, finding that it can induce unintentional genetic changes in the cells and distort test results.

These changes may be especially concerning in pharmacogenomics experiments looking at how human [cells](#) respond to drugs, an important part of precision medicine.

Nadav Ahituv, PhD, professor of bioengineering in the School of Pharmacy and senior author of the paper published Aug. 8, 2017, in *Scientific Reports*, didn't set out to challenge standard laboratory protocol. But as is often the case in science, one question led to another.

Antibiotics and Gene Expression, Gene Regulation

One area of study in Ahituv's lab is how genetic variations affect our response to drugs. Recently, his lab found that rifampin, a common antibiotic prescribed for tuberculosis and other infections, can cause significant changes in the expression of genes and regulatory elements in human liver cells.

"While we were doing this experiment, I was thinking: we treat cells with antibiotics all the time in cell culture and nobody's looked at how this might affect [gene expression](#) and [gene regulation](#)," said Ahituv.

He and graduate student, Ann Hane Ryu, first author of the study, designed a simple experiment in which they compared a human liver cell line, HepG2, grown with and without the standard antibiotic cocktail, PenStrep, a combination of penicillin and streptomycin. They chose liver cells because the liver helps clear foreign materials from the body and would be the most responsive to drugs, said Ahituv.



The lab of Nadav Ahituv, PhD, studies how genetic variations affect our response to drugs. Credit: Susan Merrell

They let the cells grow for three weeks and analyzed them to identify changes in both coding and non-coding DNA.

They found altered expression in 209 genes, particularly in those related to drug and stress response. These included higher expression of genes known to be involved in apoptosis and the unfolded protein response.

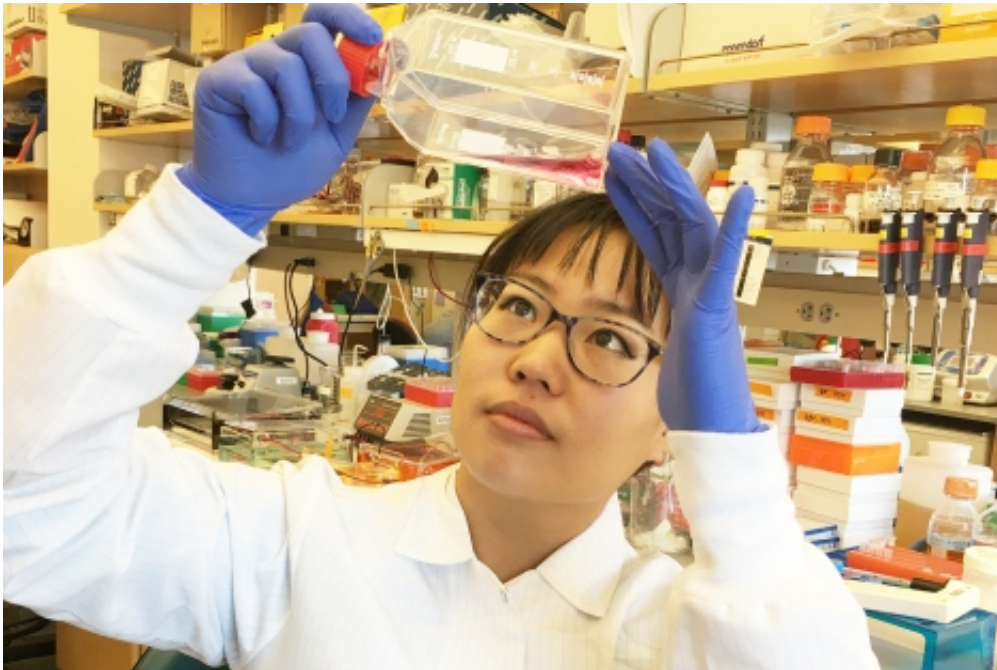
Of particular concern, said Ahituv, is that several of the affected genes are transcription factors, which can in turn control the expression of many other genes.

They also found changes in more than 9,500 gene regulatory elements, part of the 98 percent of our genome that is non-coding. These [regulatory elements](#) were located near genes involved in cell

differentiation, nuclease activity and tRNA modification.

A Systematic Look at Antibiotics' Effects

Ahituv believes this is the first study to look systematically at the effect of antibiotics on cell culture using genomic tools. Researchers have raised concerns before, said Ahituv, "but they see it as more of a cost-benefit issue, they're more worried about contamination than this having an effect on their experiment."



Ann Hane Ryu, a graduate student in the lab of Nadav Ahituv, PhD, works with cell cultures. Credit: Ann Hane Ryu

He hopes the study will serve as a warning for other researchers to take into account the effect of antibiotics, and perhaps even examine other variables in the laboratory – like growing medium and hood temperature

– that may unintentionally influence an experiment.

At the same time, Ahituv isn't alarmist about the new findings. He said that changes to the expression of 209 genes, out of some 20,000 genes in our entire genome, is a relatively small effect.

"So 209 is not a big number, but I think it's important to know the identity of these [genes](#) and to know what they're doing," he said. "If you do a study, for example, and you see a certain gene expressed very highly, it could be not related to the study but because you're treating with antibiotics."

He would recommend that researchers studying drug response avoid the use of antibiotics, and instead take other precautions against contamination. "Definitely, for us, based on these results, from now on if we don't need to use antibiotics, we'll not use [antibiotics](#)."

More information: Ann H. Ryu et al. Use antibiotics in cell culture with caution: genome-wide identification of antibiotic-induced changes in gene expression and regulation, *Scientific Reports* (2017). [DOI: 10.1038/s41598-017-07757-w](#)

Provided by University of California, San Francisco

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