

'Flipping the switch' reveals new compounds with antibiotic potential

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The fungus *Fusarium* overproduces various pigments in concentric rings because formerly silenced genes are expressed in a *kmt6* mutant. Credit: Lanelle Connolly, courtesy of Oregon State University

Researchers at Oregon State University have discovered that one gene in a common fungus acts as a master regulator, and deleting it has opened access to a wealth of new compounds that have never before been studied – with the potential to identify new antibiotics.

The finding was announced today in the journal *PLOS Genetics*, in research supported by the National Institutes of Health and the American Cancer Society.

Scientists succeeded in flipping a genetic switch that had silenced more than 2,000 [genes](#) in this fungus, the cereal pathogen *Fusarium graminearum*. Until now this had kept it from producing novel [compounds](#) that may have useful properties, particularly for use in medicine but also perhaps in agriculture, industry, or biofuel production.

"About a third of the genome of many [fungi](#) has always been silent in the laboratory," said Michael Freitag, an associate professor of biochemistry and biophysics in the OSU College of Science. "Many fungi have antibacterial properties. It was no accident that penicillin was discovered from a fungus, and the genes for these compounds are usually in the silent regions of genomes.

"What we haven't been able to do is turn on more of the genome of these fungi, see the full range of compounds that could be produced by expression of their genes," he said. "Our finding should open the door to the study of dozens of new compounds, and we'll probably see some biochemistry we've never seen before."

In the past, the search for [new antibiotics](#) was usually done by changing the environment in which a fungus or other life form grew, and see if those changes generated the formation of a compound with antibiotic properties.



The corn stem on the left is infected with *Fusarium graminearum* -- a common fungus that researchers have genetically altered in work that may aid the discovery of new antibiotics. Credit: Eric Schmelz, courtesy U.S. Department of Agriculture

"The problem is, with the approaches of the past we've already found most of the low-hanging fruit, and that's why we've had to search in places like [deep sea vents](#) or corals to find anything new," Freitag said. "With traditional approaches there's not that much left to be discovered. But now that we can change the genome-wide expression of fungi, we may see a whole new range of compounds we didn't even know existed."

The gene that was deleted in this case regulates the methylation of

histones, the proteins around which DNA is wound, Freitag said. Creating a mutant without this gene allowed new expression, or overexpression of about 25 percent of the genome of this [fungus](#), and the formation of many "secondary metabolites," the researchers found.

The gene that was deleted, *kmt6*, encodes a master regulator that affects the expression of hundreds of genetic pathways, researchers say. It's been conserved through millions of years, in life forms as diverse as plants, fungi, fruit flies and humans.

The discovery of new antibiotics is of increasing importance, researchers say, as bacteria, parasites and fungi are becoming increasingly resistant to older drugs.

"Our studies will open the door to future precise 'epigenetic engineering' of gene clusters that generate bioactive compounds, e.g. putative mycotoxins, antibiotics and industrial feedstocks," the researchers wrote in the conclusion of their report.

Provided by Oregon State University

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