

Genetic tradeoff: Harmful genes are widespread in yeast but hold hidden benefits

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The genes responsible for inherited diseases are clearly bad for us, so why hasn't evolution, over time, weeded them out and eliminated them from the human genome altogether? Part of the reason seems to be that genes that can harm us at one stage of our lives are necessary and beneficial to us at other points in our development.

The idea that the same gene can be both beneficial and harmful, depending on the situation, is called antagonistic pleiotropy. The theory has been around since the 1950s and has been used to explain aging, cancer and [genetic diseases](#).

But until now, no one has been able to determine just how common antagonistic pleiotropy is—on a genome-wide scale—in any organism. In a paper to be published online Oct. 25 in the journal *Cell Reports*, Jianzhi "George" Zhang of the University of Michigan and his coworkers report that antagonistic pleiotropy is very common in yeast, a single-celled organism used by scientists to provide insights about genetics and [cell biology](#).

Zhang and his colleagues say the findings have broad biomedical and evolutionary implications.

"In any given environment, yeast expresses hundreds of genes that harm rather than benefit the organism, demonstrating widespread antagonistic pleiotropy. The surprising finding is the sheer number of such genes in the [yeast genome](#) that have such properties," said Zhang, a professor in

the Department of Ecology and [Evolutionary Biology](#).

"From our yeast data we can predict that humans should have even more antagonistic pleiotropy than yeast," he said. "This suggests that special cautions are needed when treating inherited diseases, because a treatment that removes a disease-causing [genetic effect](#) may lead to [adverse effects](#) in other aspects of life."

Yeast has about 6,000 genes, about 1,000 of which are essential – eliminate any of them and the organism dies. Zhang and his colleagues worked with a set of 5,000 laboratory strains of yeast in which one non-essential gene had been deleted from each strain. Each strain was tagged with a genetic "barcode" to allow researchers to identify it later.

Zhang and his [coworkers](#) grew all 5,000 strains together in a single test tube and compared the growth rates of each strain, under various environmental conditions, to the growth rates of "wild type" yeast strains without gene deletions.

This side-by-side comparison allowed them to determine which genes were beneficial (increased growth rate) and which ones were harmful (decreased growth rate) under the six environmental conditions. Different mixes of nutrients and chemical stressors, such as ethanol, were added to the yeasts' growth media to create the six environmental conditions.

The researchers found that for each of the six conditions, on average, the yeasts expressed about 300 genes that slowed their growth and were therefore classified as harmful. Deleting those genes resulted in more rapid growth.

But many of the [genes](#) that were harmful under one set of environmental conditions proved to be beneficial under another, demonstrating

widespread antagonistic pleiotropy, Zhang said.

"There are a lot of theories – some of them relating to aging, cancer and genetic disease – that invoke antagonistic pleiotropy. But it's not easy to measure, and empirically we have not known much about it," Zhang said. "Now, in yeast, we have found that antagonistic pleiotropy is very common."

Provided by University of Michigan

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