

Small variations in genetic code, previously thought to be inconsequential, can team up to have a big impact

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(Medical Xpress)—Scientists at USC have definitively demonstrated that large sets of variations in the genetic code that do not individually appear to have much effect can collectively produce significant changes in an organism's physical characteristics.

Studying the budding yeast *Saccharomyces cerevisiae*, USC's Matthew B. Taylor and Ian M. Ehrenreich found that the effects of these genetic variants can depend on four or more other variants in an individual's genome.

Most genetic analyses of heritable [physical characteristics](#), including genome-wide association studies in human populations, focus on so-called "additive" variants that have effects that occur regardless of the organism's genetic background. Taylor and Ehrenreich, however, found that higher-order interactions of five or more places along the genome can have major impacts, and may help explain the so-called "missing heritability" problem, in which additive genetic variants do not entirely explain many inherited diseases and traits.

"Studies focused only on additive effects often explain just a fraction of the genetic basis of many traits. The question is, what are we missing?" said Ehrenreich, assistant professor of molecular biology at the USC Dornsife College of Letters, Arts and Sciences, and corresponding author of a paper on the study that was published by *PLOS Genetics* on May 1.

An alternative view of Taylor and Ehrenreich's findings is that genetic variants that have the potential to cause major changes in an organism's phenotype can be completely canceled out if they occur in the "wrong" genomic background.

"It's exciting to provide a characterized example of

how [genetic background](#) can influence the effects of mutations. We hope that this will open the door for future studies to tease apart how these complex interactions happen," said Taylor, a PhD student in the Molecular and Computational Biology Section at USC.

Their work could impact genetic mapping studies, suggesting that researchers will need to take an approach to understanding the genotype-phenotype relationship that encompasses complex non-additive effects.

Taylor and Ehrenreich plan to take a closer look at the molecular mechanisms that underlie these interactions, in the hopes of providing basic insights into how they occur in biological systems.

Provided by University of Southern California

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