

October 26, 2019

Dear Editor, *mBio*

We submit this article entitled, “Genetic Capitalism and Stabilizing Selection of Antimicrobial Resistance Genes in *Escherichia coli*” for your consideration. This original work, completed by Colby T. Ford, Gabriel Lopez Zenarosa, Kevin Smith, John Williams, and Daniel Janies, has not been submitted for publication elsewhere.

Antimicrobial resistance (AMR) in pathogenic bacteria is a severe health challenge that lacks clear solutions. In this study, we examine competing hypotheses for explaining the rise of AMR:

- 1) Genetic capitalism: Genes that confer antibiotic resistance are gained and not often lost in bacterial lineages, and;
- 2) Stabilizing selection: Genes that confer antibiotic resistance are gained and lost often in bacterial lineages.

Using a very large comparative genomic dataset for *Escherichia coli* analyzed through phylogenetics and data science methods, we show that patterns of gain and loss of most AMR genes support the hypothesis for genetic capitalism and few genes behave as if under stabilizing selection.

Moreover, we found a statistically significant difference between biochemical mechanisms of resistance represented in the groups of genes associated with the competing theories. By understanding these differences, we pinpoint where antibiotic cycling and drug development is likely to work due to stabilizing selection and where it is not due to genetic capitalism.

On behalf of all authors, we thank you for considering our manuscript for publication.

Sincerely,



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