

January 13, 2020

Dear Prof. Dr. Rudolf Meier, Editor, *Cladistics*

We submit this article entitled, “Genetic Capitalism and Stabilizing Selection of Antimicrobial Resistance Genotypes in *Escherichia coli*” for your consideration. This original work, completed by Colby T. Ford, Gabriel Lopez Zenarosa, Kevin Smith, David Brown, John Williams, and Daniel Janies, is not under consideration for publication elsewhere. Dan Janies did present a talk on the subject at the Hennig meeting in Berkeley in May 2019.

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

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

Moreover, we found a statistically significant difference between biochemical mechanisms of resistance represented in the groups of genotypes 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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