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"Bioenergetic stress enhances antimicrobial resistance evolution and persistence"

By

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M.D./Ph.D. Program
B.A. 2017, Rutgers University, New Brunswick, NJ

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Wednesday, April 2nd, 2025
ICPH Auditorium
9:00 A.M.

Join Zoom presentation
https://rutgers.zoom.us/j/96592294406?pwd=Xu2gcKxiwcMlrpIYOZAli99e4fIiMY.1
Meeting ID: 965 9229 4406
Password: ecoli2025

ABSTRACT

Antimicrobial resistance (AMR) is a global health crisis and there is an urgent need to better understand AMR mechanisms. Antibiotic treatment alters several aspects of bacterial physiology, including increased ATP consumption, cellular respiration, and reactive oxygen species (ROS) formation. However, the impact of "bioenergetic stress" caused by increased ATP consumption on treatment outcomes remains unclear. Here, we defined bioenergetic stress as a state characterized by diminished ATP/ADP ratio and we utilized a synthetic biology approach to study the direct effects of bioenergetic stress on antibiotic efficacy. We engineered a genetic system that constitutively hydrolyzes ATP or NADH in *Escherichia coli*. While bioenergetic stress did not directly confer antibiotic resistance, we found that bioenergetic stress potentiates AMR evolution and antimicrobial persistence. Mechanistic studies revealed that bioenergetic stress accelerates AMR evolution via enhanced ROS production, mutagenic break repair, and transcription-coupled repair. Further, we found that bioenergetic stress potentiates antimicrobial persistence via the stringent response. These findings support a model in which the balance between ATP consumption versus production regulates antimicrobial resistance and persistence. By elucidating how cellular energy dynamics influence antibiotic outcomes, this work provides new insights into AMR mechanisms and informs potential strategies for curbing the spread of AMR infections.