Cooperative Bacterial Growth Dynamics Predict the Evolution of Antibiotic Resistance

TATIANA ARTEMJOVA, YLAINE GERARDIN, SOPHIA HSIN-JUNG LI, JEFF GORE — Since the discovery of penicillin, antibiotics have been our primary weapon against bacterial infections. Unfortunately, bacteria can gain resistance to penicillin by acquiring the gene that encodes beta-lactamase, which inactivates the antibiotic. However, mutations in this gene are necessary to degrade the modern antibiotic cefotaxime. Understanding the conditions that favor the spread of these mutations is a challenge. Here we show that bacterial growth in beta-lactam antibiotics is cooperative and that the nature of this growth determines the conditions in which resistance evolves. Quantitative analysis of the growth dynamics predicts a peak in selection at very low antibiotic concentrations; competition between strains confirms this prediction. We also find significant selection at higher antibiotic concentrations, close to the minimum inhibitory concentrations of the strains. Our results argue that an understanding of the evolutionary forces that lead to antibiotic resistance requires a quantitative understanding of the evolution of cooperation in bacteria.