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Omar Rossi

University of Cambridge, UK

Use of isogenic tagged strains to study the impact of antimicrobials on the within-host dynamics of *Salmonella* bacterial infections

Antimicrobials do not always determine the rapid and complete resolution of acute infections, resulting in carrier states or in the relapse of infections upon cessation of the treatment. More effective treatments and eradication of infections will benefit from a better understanding of how bacterial growth dynamics are modified under antimicrobial pressure. We have studied in vivo the effects of two widely used classes of antimicrobials (the β -lactam ampicillin and the fluoroquinolone ciprofloxacin) on the early stages of treatment using wild-type (fast-growing), Δ aroC (slow-growing) and Δ sseB (reduced ability to spread from cell to cell) Isogenic Tagged Strains (ITS) of *Salmonella*. We have followed the dynamics of bacterial populations before, during and upon the cessation of antimicrobial treatment by combining total bacterial counts in the infected organs and numerical and spatial fluctuations of ITS sub-populations using a sequencing-based approach and a novel method for Bayesian bottle-neck analysis. We found that both antibiotics reduced (up to ~95%, with ciprofloxacin producing the highest reduction) bacterial loads of the wild type bacteria in spleen, liver and blood with a marked and constant drop during the first days of treatment followed by a phase of more moderate effect. Cessation of the treatment resulted in an immediate relapse of the infection. The antimicrobials had smaller effect on bacterial counts in mesenteric lymph nodes during treatment but a strong increase in bacterial numbers was still observed upon cessation of antibiotic therapy. Treatment of infections with the Δ aroC strain and Δ sseB strains showed a smaller but continuous reduction in bacterial counts in spleens and livers and in both infections cessation of the treatment resulted in a carrier state. The antimicrobials acted homogeneously on all the bacterial populations within various organs and at all the time-points. We have concluded that the efficacy of ampicillin or ciprofloxacin treatment is more pronounced in infections with fast-growing strains and more marked in the early stages of treatment. Antibiotic pressure does not select for ITS sub-population and chronic and relapsing infections do not appear to be caused by the persistence or amplification of selected subpopulations of *Salmonella*.

Biography

Omar Rossi has received his BSc in Biology and MSc in Cellular and Molecular Biology at the University of Florence, Italy. He has completed his PhD in 2014 and Postdoctoral studies at Novartis Vaccines Institute for Global Health in Siena, Italy, working on vaccines' development. From April 2015, he is working as a Research Associate at the Department of Veterinary Medicine of the University of Cambridge, UK, studying the impact of antimicrobials on the within-host dynamics of *Salmonella* infections in Dr. Pietro Mastroeni's group. He has published more than 10 papers in reputed journals.

or265@cam.ac.uk

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