Universität Basel

Research Project

Keeping one step ahead: understanding evolution of pathogens to manage their virulence and to stop their transmission

Third-party funded project

Project title Keeping one step ahead: understanding evolution of pathogens to manage their virulence and to stop their transmission
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The current antibiotic resistance crisis testifies that technological progress is lagging behind bacterial evolution. Understanding the general principles underlying the evolution of pathogens will be essential to design strategies shifting away from classical approaches that rely entirely on antimicrobial chemotherapy. I propose to study both the molecular mechanisms supporting virulence in entero-pathogens and to assess their evolutionary dynamics in response to factors limiting the infection (i.e., the colonization resistance, mediated by the intestinal microbiota, and the adaptive immunity in vaccinated hosts, which dampen the fitness of targeted pathogens). This will lay the foundation for preventive treatments based on rational control of pathogens in populations of hosts. My group will focus on the model organism Salmonella enterica Typhimurium, in which the expression of virulence is metabolically costly. This favors the emergence of attenuated mutants (defectors) during infections. Moreover, the expression of virulence is bimodal in S. Typhimurium, i.e., the bacteria switch phenotypically back and forth from virulent to avirulent. Bimodality in virulence expression is a feature of general relevance observed in many pathogens. However, its selective value remains poorly understood. In S. Typhimurium, bimodality seems to offset the cost of virulence and to slowdown the rise of defectors. This suggests that tightly regulated bimodal expression of virulence could represent an unexploited ”Achilles’ heel”. This will be addressed by further developing theoretical and experimental frameworks to quantify the within-host and between-host evolutionary dynamics of S. Typhimurium. This should reveal both the conditions required to drive loss of virulence and pathogen fitness in a population of hosts, and potential drug-able molecular targets that could generate these conditions.

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