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RESEARCH NEWS SCAN

Evolution-proof Antibiotics

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ABSTRACT

Evolving resistance in pathogenic bacteria has compromised the efficacy of current antibiotics. The need of the hour dictates producing antibiotics to which the bacteria cannot produce resistance. Attractive options possible are first, formulating 'evolution-proof' antibiotics *via* mutation or horizontal gene transfer which bacteria cannot resist and secondly by producing compounds to which resistance may develop, but rarely at a rate that can make it become epidemic.

Keywords: Antimicrobial resistance, Evolution-proof antibiotics, Horizontal gene transfer.

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INTRODUCTION

A team of researchers from McGill University, Canada, and Oxford University the United Kingdom has formulated a method to predict the development of antimicrobial resistance within a host and subsequent chances of transmission among hosts of such resistant strains.[1] Ensuring efficient use of the next generation of antibiotics mandates a thorough understanding of antibiotic resistance mechanisms in the pathogenic bacteria. Considering that antibiotic targets in a bacterial cell are a highly conserved feature which cannot be modified, a scenario can be envisaged that absence of resistance-conferring mutations or horizontal gene transfer does not lead to the development of resistance in the first place. Alternatively, it may be argued that resistance may arise, but excessive fitness cost, high stochastic loss, and low transmission rates may prevent a full-blown epidemic spread. Resistance mutations that modify the essential cell functions targeted by antibiotics may compromise these essential functions, incurring a fitness cost to bacteria and may lead to prevention of such mutations in the first place. But this argument is flawed as has been observed by demonstration of antimicrobial peptide resistance[2] and rifampicin resistance.[3]

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Authors have designed tests such as fluctuation test[4] and antibiotic ramp experiment[5] which may help estimate chances of developing resistance to a particular drug by spontaneous mutation. Unfortunately, the inability to reproduce the complex ecological interactions involved in *in vivo* horizontal gene transfer resistance makes an *in vitro* analysis of this mechanism quite difficult. Authors have employed functional metagenomics[6] and amplifying bioreactor experiments[7] to evade this problem.

Understanding and integrating the concepts of 'within-host' antibiotic resistance development and proliferation and subsequent 'between-host' resistance transmission and epidemiological spread should provide clues to prevent evolutionary resistance development.

To prevent the evolution of resistance to new antibiotics reducing the mutation rate, treating infections rapidly and optimizing antibiotic doses to limit "within-host" proliferation seems a reasonable option followed by limiting antibiotic treatment, reducing encounter rates, immunizing hosts and increasing resistance costs as they may limit "in-between host" transmissions.

Though the concept of an "evolution-proof" antibiotic seems more of a dream rather than a reality, in the present scenario, nevertheless the model of "within-host" and "between host" antibiotic resistance proposed by Bell and MacLean[1] may be considered a stepping stone to more rigorous and concrete models in the hopeful future.

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