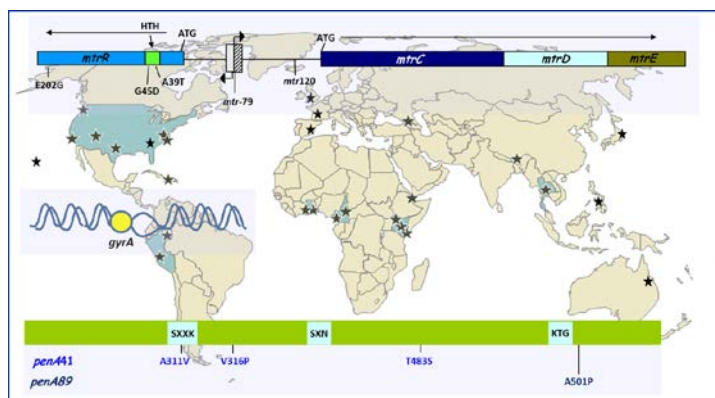




Tit for Tat: Antibiotic resistance and microbial fitness in *Neisseria gonorrhoeae*



An estimated 106 million cases of gonorrhea occur each year. These infections seriously impact reproductive and neonatal health, and increase the spread of human immunodeficiency virus. Concern about gonorrhea is intensified by the threat of untreatable gonorrhea, which reached headline news in the summer of 2012 upon removal of the sole use of extended-spectrum cephalosporins (ESCs), the last remaining monotherapy for gonorrhea, from treatment guidelines. The world has responded with increased surveillance measures, which while helpful, can only temporarily slow the global spread of resistant strains. The relationship between resistance mutations and microbial fitness can help explain and predict the spread of antibiotic resistance. Fitness studies can also further our understanding of bacterial adaptation to the host. Here, resistance mutations in *Neisseria gonorrhoeae* that increase fitness *in vivo* but not *in vitro* will be discussed, including clinically relevant antibiotic resistance mutations in the *mtr* locus, which increase expression of the MtrC-MtrD-MtrE active efflux pump, and mutations in the quinolone resistance-determining region of *gyrA*, which leads to differential expression of gonococcal genes. The fitness impact of mosaic *penA* alleles that confer ESC resistance will also be presented. These mutant alleles reduce gonococcal fitness *in vitro* and *in vivo*; however, compensatory mutations can be selected *in vivo* to restore fitness to that of the sensitive parent strain. This finding is consistent with prevailing theories about how compensatory mutations promote the spread of resistant bacteria that are otherwise compromised in the absence of antibiotic pressure.

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