Anticipating Resistance to Antivirulence Compounds Employing Directed Evolution for Drug Development

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Description

T e need for new antibiotics and new approaches to treating bacterial infection is critical due to the rise in antimicrobial resistance (AMR) [1].Traditional antibiotics target essential physiological processes and do not discriminate between pathogenic bacteria and the commensal microbiome. T is approach disrupts normal microbial fora and places tremendous selective pressure on susceptible bacteria. T us, resistance can arise either within the target population or the microbiome. Mutations in either population can subsequently spread through horizontal gene transfer [2]. A promising approach to combat AMR is the use of Anti-virulence therapies (AVTs). T ese compounds specifcally target virulence factors and do not afect the normal microbial fora. T e rationale behind AVTs is that they prevent selective pressure on non-pathogenic microbial fora. T us, resistance will likely arise more slowly or not at all [3,4]. T is notion is predicated on the fact that many virulence targets are specifcally upregulated in the host or are only essential in the host environment. In the a le ntt Q u ionwioheres in ei io uEs u K i i oc hM ₂₀ lence u al [ac cc ˏ c auP ap q u ets ₩ect ₄₄ o a ₽