Friday, November 21, 2025

Poster abstract submission

Approval Status Not Started

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Poster title

Long-term host control of Salmonella after transient virulence inhibition

Poster abstract

Anti-virulence therapies disarm pathogens without killing them, thereby preserving the host microbiome and representing a promising alternative to conventional antibiotics. Several inhibitors show impressive activities in animal infection models, but the relative contribution of specific virulence inhibition vs. off-target effects on either the bacteria or the host remain unclear. Moreover, the long-term outcomes of stopping anti-virulence treatment remain unclear. Do bacteria regain virulence, cause relapse, or are they cleared by the host immune system? Answering these questions is essential to understand the potential impact and limitations of anti-virulence strategies. Here, we addressed these issues in a mouse model of human typhoid (enteric) fever. We developed Salmonella with switchable virulence (S-VIR) by putting the type 3 secretion system-2 (T3SS-2), which is essential for systemic virulence, under doxycycline control. This inducible system enables precise on–off regulation of the T3SS-2, allowing us to mimic an effective anti-virulence therapy in Salmonella-infected mice and to assess the consequences of dynamically suppressing virulence.

In infected mice given low-dose doxycycline in drinking water, S-VIR showed wild-type levels of fitness and virulence. Doxycycline withdrawal shut down T3SS-2, arrested Salmonella replication and resolved disease symptoms. After ten days of T3SS-2 inhibition, reintroducing doxycycline restored virulence and replication, but bacterial loads remained stable, indicating partial control by host immunity. These effects were comparable to treatment with fluoroquinolone antibiotics, a highly effective therapy for human systemic salmonellosis. Thus, selective T3SS-2 inhibition may offer a suitable alternative for controlling invasive Salmonella infections, such as typhoid fever.

Research topic Microbiology