A model to investigate anti-virulence strategies against *Salmonella*

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Anti-virulence therapies disarm pathogens without killing them, preserving the host microbiome and offering a promising alternative to antibiotics. Despite their potential, the outcomes of stopping anti-virulence treatment remain unclear. Do bacteria regain virulence and cause relapse, or are they cleared by the host immune system? Addressing these issues in an *in vivo* infection model is essential to understand the potential impact and limitations of anti-virulence strategies. In this work, we developed a switchable anti-virulence system to mimic an efficient anti-virulence treatment in *Salmonella*-infected mice. We complemented a *ssrB* null mutant with a doxycycline-inducible *ssrB* expression cassette to obtain a strain with switchable activity of the SPI-2 injectisome. This inducible strain was avirulent in mice in absence of doxycycline, but regained full virulence when doxycycline was provided in the drinking water. Withdrawal of doxycycline stopped disease progression and prevented escalating *Salmonella* loads. Reintroducing doxycycline restarted disease progression. Thus, the inducible-virulence strain provides a suitable model to investigate and optimize the impact of anti-virulence on disease progression, inflammation, and post-exposure relapse, including in combination with antibiotics.