ARNA **Seminar Series**

Tuesday, September 16 at 11 am (BBS auditorium)

Antibiotic recalcitrance in infection

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Infections caused by antibiotic-persistent bacteria remain a major challenge in clinical settings, as they often lead to relapse and treatment failure. The first part of this talk will focus on *Salmonella* persisters and the host-driven mechanism that maintains them in a non-growing state during infection. Reactive nitrogen species (RNS), produced by immune cells, intoxicate persisters by targeting the Krebs cycle and blocking respiration, thereby locking them into persistence. When RNS levels decrease, this lock is released, allowing persisters to resume growth—particularly when antibiotic treatment has ceased—thus driving relapse. Notably, chemical modulation of RNS levels in combination with antibiotics was shown to reduce persister survival and limit relapse risk.

The second part will present a study on the *Enterobacter cloacae* complex, where whole-genome sequencing of clinical isolates revealed that more than 85% of recurrent infections were true relapses caused by the same persistent strain. Mutations were also detected in the RCS regulatory system controlling capsule synthesis, and these genetic changes correlated with phenotypic differences in capsule production observed between infection episodes.

Together, these projects linked host-immune signals to bacterial persistence, and uncovering genetic determinants of relapse in clinical strains—thereby shedding light on the mechanisms underlying bacterial recalcitrance in infection

Host: Anaïs Le Rhun, ARNA laboratory