Salmonella Biofilms Provide an Adaptive Advantage in the Persistently Infected Heterologous Host *Caenorhabditis elegans*

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*Salmonella enterica* is an intracellular pathogen that switches its lifestyle to form biofilms on gallstones of asymptomatic patients. Carriers then disseminate *S. Typhimurium*, as well as the more dangerous human-restricted serovar, *S. Typhi*. Adhesion of sessile bacteria to various biotic and abiotic surfaces to form multicellular communities is also essential for environmental persistence, and is the basis of periodic *Salmonella* outbreaks worldwide. Our understanding of biofilm formation *in vivo* is severely limited due to the lack of suitable infection models and our reliance on the murine model for studying *Salmonella* pathogenesis. A limitation of the murine model is the difficulty in visualizing bacteria inside the tissues. The soil nematode *Caenorhabditis elegans* is a heterologous host for *Salmonella* and represents an exciting model to investigate how *Salmonella* regulates the lifestyle switch from the infectious to the dormant form at various phases of infection. In our recent studies, we characterized the molecular events leading to *Salmonella* biofilms *in vitro*. We discovered that SsrB, a response regulator acquired during the evolution of *Salmonella* as a pathogen, sits at a pivotal position in governing *Salmonella* lifestyle fate: to either exist inside the host (in the vacuole) as a promoter of virulence; or as a surface-attached multicellular biofilm, maintaining the carrier state. Unphosphorylated SsrB relieves H-NS-mediated repression at *csgD*, which encodes the master regulator of biofilms, favoring formation of *S. Typhimurium* biofilms (Desai et al., eLife 2016). Using confocal time-lapse imaging, we now establish that *Salmonella* exists as sessile aggregates, or *in vivo* biofilms, in the persistently infected *C. elegans* gut. Interestingly, formation of *in vivo* biofilms in the worm intestine also required the SsrB-CsgD pathway. A combination of cell biological, genetic and molecular approaches enabled dissection of the adaptive advantages conferred by the *Salmonella* carrier state in persistent infections. We discovered that *Salmonella* rapidly killed the host in the absence of *in vivo* biofilm formation. Overall our studies involving the *C. elegans* infection model lead to a detailed understanding of how *Salmonella* has evolved to form biofilms in persistent infections and why *in vivo* biofilms are fundamental to successful pathogenesis. Supported by RCE in Mechanobiology, NUS Ministry of Education, Singapore, NIHR21-A1123640 and VA 5101BX000372 to LJK.