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Single cell RNA-seq reveals heterogeneity of salmonella and macrophage factors that control infection outcome

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Encounters between innate immune cells and invading pathogens ultimately set the stage for the outcome of infection. Current methodologies to study infection capture these interactions only at the population level, which may obscure subpopulation dynamics critical for outcomes. We present an experimental system that combines single-cell transcriptional measurements with fluorescent monitoring of infection phenotypes. Using mouse macrophages infected with *S. enterica*, we identify host and bacterial pathways that are activated in response to infection and give rise to unique subpopulations with widely different infection dynamics. Specifically, we show that variability of host response may be propagated by TLR4-TRIF sensing of intracellular bacteria and differential activity of the bacterial two-component system PhoPQ, which alters the extent of LPS modification in single invading bacteria. We further demonstrate that population heterogeneity is a fundamental factor of the host-pathogen dynamics in an in-vivo mouse infection model. The method presented herein offers a generalizable approach to characterize infection at the single cell level that can be applied in diverse infection models to reveal a wide spectrum of the host-pathogen interface.

Biography

Roi Avraham has completed his PhD at the Weizmann Institute of Science in Israel and is currently doing his postdoctoral studies at the Broad Institute under the guidance of Dr. Deb Hung. His current research focuses on host-pathogen interactions, and studying genetic perturbations that can alter infection outcome.

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