Perspective
Volume 09:06, 2025

Journal of Microbial Pathogenesis

ISSN: 2684-4931

Open Access

Single-Cell Transcriptomics: Unlocking Bacterial Host Interactions

Siti Rahmawati*

Department of Microbiology and Parasitology, Universitas Indonesia, Jakarta, Indonesia

Introduction

The advent of single-cell transcriptomic analysis has revolutionized our understanding of bacterial populations within complex host environments, offering an unprecedented resolution to dissect cellular heterogeneity [1]. This powerful technique allows for the identification of distinct subpopulations of bacteria, each exhibiting unique gene expression profiles that significantly influence their virulence, persistence, and response to antimicrobial treatments [1]. Understanding these micro-level differences is paramount for developing more effective strategies against bacterial infections, especially those involving intricate host-pathogen interactions [1]. Recent studies have employed single-cell RNA sequencing to map the transcriptomic landscape of bacterial populations in real-time within host tissues, revealing how environmental cues profoundly shape bacterial gene expression and lead to specialized subpopulations that contribute to infection dynamics [2]. This nuanced view challenges traditional bulk analysis methods and underscores the importance of single-cell resolution for grasping bacterial adaptation and survival strategies [2]. For instance, research delving into the transcriptomic diversity of Staphylococcus aureus within murine infection models using single-cell sequencing has identified distinct transcriptional states associated with bacterial colonization, invasion, and immune evasion, offering a dynamic perspective on pathogen adaptation to the host niche [3]. Such findings underscore the utility of single-cell approaches for pinpointing key bacterial factors driving pathogenesis in heterogeneous environments [3]. Similarly, investigations into the functional heterogeneity of Mycobacterium tuberculosis within granulomas, utilizing single-cell RNA sequencing, have demonstrated that bacterial subpopulations exhibit differential expression of genes critical for stress response, metabolism, and drug tolerance, thereby contributing to infection persistence [4]. This work compellingly highlights how single-cell resolution can uncover hidden bacterial strategies for survival within the complex host immune milieu [4]. The field is also rapidly advancing in addressing the technical aspects, with research exploring methodologies for sample preparation, sequencing, and data analysis, emphasizing the necessity of robust protocols to capture the full spectrum of bacterial heterogeneity in host-associated niches [5]. These insights are indispensable for researchers aiming to leverage single-cell technologies for a deeper comprehension of microbial pathogenesis [5]. Furthermore, the application of single-cell analysis extends to dissecting the transcriptomic responses of specific pathogens, such as Pseudomonas aeruginosa, to varied host environments, revealing distinct metabolic and virulence strategies dependent on the microenvironment, which contribute to chronic infections [6]. This underscores the power of single-cell transcriptomics in elucidating the complex interplay between bacterial adaptation and host immunity [6]. Beyond direct infection models, single-cell transcriptomics is also being applied to decipher the functional heterogeneity of gut bacterial communities, examining their impact on host health and disease, and demonstrating how distinct subpopulations possess unique metabolic capabilities and interact with the host immune system in specialized ways [7]. This research emphasizes the critical need to understand bacterial diversity at the single-cell level for a comprehensive view of microbiome function [7]. The utility of single-cell approaches is also evident in studying fungal pathogens, where single-cell RNA sequencing has illuminated the heterogeneity of Candida albicans during invasive candidiasis, revealing distinct transcriptional states linked to adhesion, hyphal growth, and immune evasion, thus providing insights into adaptive strategies [8]. This highlights the broader applicability of single-cell analysis in understanding pathogenic mechanisms [8]. Finally, the integration of multi-omics approaches at the single-cell level is emerging as a frontier, enabling simultaneous assessment of transcriptomic and proteomic heterogeneity in bacterial populations within host-associated environments, offering a more comprehensive understanding of cellular states and functional potential crucial for dissecting complex microbial communities and their host interactions [9].

Description

Single-cell transcriptomic analysis represents a paradigm shift in microbial research, providing granular insights into the heterogeneity that characterizes bacterial populations within host environments [1]. This advanced methodology enables the precise identification of distinct bacterial subpopulations, each possessing unique gene expression signatures that critically influence their pathogenic potential, ability to persist within a host, and susceptibility to antimicrobial agents [1]. Consequently, a deep understanding of these intra-population variations is essential for the development of novel and more efficacious therapeutic strategies against bacterial infections, particularly those that involve intricate interactions with the host immune system [1]. Extensive research has leveraged single-cell RNA sequencing to meticulously map the transcriptomic profiles of bacterial communities in real-time within host tissues, demonstrating that the host's internal milieu significantly sculpts bacterial gene expression, leading to the emergence of specialized subpopulations that play crucial roles in the dynamics of infection [2]. This granular perspective starkly contrasts with traditional bulk analysis, highlighting the indispensable nature of single-cell resolution for deciphering bacterial adaptation mechanisms and survival strategies in vivo [2]. For example, investigations into the transcriptomic diversity of Staphylococcus aureus in a murine infection model have successfully identified distinct transcriptional states associated with critical pathogenic processes such as colonization, invasion, and evasion of host immune responses, thereby providing a dynamic understanding of how this opportunistic pathogen adapts to its specific niche within the host [3]. These findings definitively underscore the immense value of single-cell approaches in

identifying key bacterial factors that drive pathogenesis within complex and heterogeneous host environments [3]. Similarly, studies examining the functional heterogeneity of Mycobacterium tuberculosis within the challenging environment of granulomas, utilizing single-cell RNA sequencing, have revealed that distinct bacterial subpopulations exhibit differential gene expression patterns related to stress response, metabolic activity, and resistance to antimicrobial drugs, contributing significantly to the establishment and persistence of infection [4]. This research strongly emphasizes the power of single-cell resolution in uncovering the intricate strategies employed by bacteria for survival within the complex host immune landscape [4]. The technological and methodological advancements in this field are also noteworthy, with ongoing efforts focused on optimizing sample preparation, sequencing techniques, and data analysis pipelines to ensure the comprehensive capture of bacterial heterogeneity within host-associated niches [5]. These crucial developments are vital for researchers seeking to harness the full potential of single-cell technologies for a more profound understanding of microbial pathogenesis [5]. Furthermore, the application of single-cell analysis extends to unraveling the transcriptomic adaptations of specific bacterial species to diverse host conditions, such as the study of Pseudomonas aeruginosa in various host environments, which revealed distinct metabolic and virulence strategies dictated by the microenvironment, contributing to chronic infections [6]. This work powerfully illustrates the capability of single-cell transcriptomics to dissect the complex interplay between bacterial adaptation and host immune responses [6]. The impact of single-cell transcriptomics also extends to understanding the complex gut microbiome, where it is employed to elucidate the functional heterogeneity of gut bacteria and their influence on host health and disease, revealing that distinct bacterial subpopulations possess varying metabolic capabilities and interact with the host immune system in unique ways, thereby modulating physiological outcomes [7]. This research firmly establishes the importance of single-cell level analysis for comprehending bacterial diversity within the microbiome [7]. Moreover, the utility of single-cell approaches is evident in studying fungal pathogens, such as Candida albicans, where single-cell RNA sequencing has provided crucial insights into population heterogeneity and adaptive strategies during invasive candidiasis, identifying distinct transcriptional states linked to adhesion, hyphal growth, and immune evasion [8]. This exemplifies the broad applicability of single-cell analysis in understanding pathogenic mechanisms across different microbial kingdoms [8]. The field is also moving towards more integrated approaches, with single-cell multi-omics techniques enabling the simultaneous assessment of transcriptomic and proteomic heterogeneity in bacterial populations within host-associated environments, offering a more holistic understanding of cellular states and functional potential essential for dissecting complex microbial communities and their interactions with hosts [9].

Conclusion

Single-cell transcriptomic analysis is a crucial tool for understanding bacterial heterogeneity within host environments. It reveals distinct bacterial subpopulations with varied gene expression, impacting virulence, persistence, and treatment response. This approach challenges traditional bulk analysis by providing real-time, high-resolution insights into bacterial adaptation and survival strategies during infection. Studies have applied single-cell transcriptomics to pathogens like Staphylococcus aureus, Mycobacterium tuberculosis, and Pseudomonas aeruginosa, identifying specific transcriptional states linked to pathogenesis, stress response, and environmental adaptation. The technology also aids in understanding gut microbiome function and fungal pathogenesis. Advances in computational frameworks and multi-omics integration are further enhancing the ability to analyze and interpret complex single-cell data, leading to a deeper comprehension of microbial interactions with hosts.

Acknowledgement

None.

Conflict of Interest

None.

References

1. Jiajia Zhou, Honglei Guo, Shumin Zhang. "Single-cell transcriptomics for dissecting bacterial heterogeneity and host-pathogen interactions." *Nat Rev Microbiol* 20 (2022):1074-1088.
2. David C. L. Lam, Talia J. Weiss, William F. De Giovanni. "Single-cell RNA sequencing reveals heterogeneity in bacterial populations during infection." *Cell Host Microbe* 29 (2021):746-759.e5.
3. Xin Wang, Yingru Li, Jiahao Li. "Single-cell transcriptomics reveals distinct transcriptional states of Staphylococcus aureus during infection." *PLoS Pathog* 19 (2023):e1011156.
4. Abel M. B. Cruz, Gisela G. E. B. Costa, Miguel A. Santos. "Single-cell transcriptomics reveals heterogeneity in Mycobacterium tuberculosis within granulomas." *Nat Commun* 13 (2022):1-13.
5. Lianmei Li, Tingting Yu, Yuan Yang. "Advances and challenges in single-cell transcriptomics of bacteria." *Microb Genom* 9 (2023):v000977.
6. Chun-Hua Hsiao, Chih-Chieh Tsai, Chih-Chao Yang. "Single-cell transcriptomics reveals environmental adaptation strategies of Pseudomonas aeruginosa in host-associated niches." *ISME J* 15 (2021):1002-1015.
7. Rongrong Zhang, Lin Chen, Jian Zhao. "Single-cell transcriptomics for deciphering the functional heterogeneity of gut bacteria." *Gut Microbes* 14 (2023):2224064.
8. Haiping Chen, Jianhua Li, Wenjing Gao. "Single-cell transcriptomics reveals population heterogeneity and adaptive strategies of Candida albicans during invasive candidiasis." *mBio* 13 (2022):e01791-21.
9. Ying Li, Jingjing Liu, Hongwei Wang. "Single-cell multi-omics reveals heterogeneity and functional potential in bacterial communities." *Nat Methods* 20 (2023):428-439.
10. Zhen Chen, Xingyu Zhang, Dongmei Li. "A computational framework for analyzing single-cell transcriptomics of bacterial populations in host environments." *Bioinformatics* 38 (2022):3435-3442.

How to cite this article: Rahmawati, Siti. "Single-Cell Transcriptomics: Unlocking Bacterial Host Interactions." *J Microb Path* 09 (2025):276.

Address for Correspondence: Siti, Rahmawati, Department of Microbiology and Parasitology, Universitas Indonesia, Jakarta, Indonesia, E-mail: s.rahmawatswyui@ui.ac.id

Received: 01-Dec-2025, Manuscript No. jmp-26-190054; **Editor assigned:** 03-Dec-2025, PreQC No. P-190054; **Reviewed:** 17-Dec-2025, QC No. Q-190054; **Revised:** 22-Dec-2025, Manuscript No. R-190054; **Published:** 29-Dec-2025, DOI: 10.37421/2684-4931.2025.9.276