International Journal for Research in Biology & Pharmacy
(ISSN: 2208- 2093)
Vol. 12, Issue 03, August 2026
DOI: 10.65327/bp.v12i3.2530

SINGLE-CELL OMICS IN PHARMACOLOGY: DECIPHERING CELLULAR HETEROGENEITY, DRUG RESPONSE, RESISTANCE, AND THERAPEUTIC TARGETS

Dr. Mohammad Anas Shamsi[1*], Dr. Sai Hanuman Sagar Boddu[2], Dr. Akram Ashour Ashames[3], Dr. Samir Issa Bloukh[4]

[1*]College of Pharmacy and Health Sciences, Ajman University, Ajman, United Arab Emirates
[2,3,4]College of Pharmacy and Health Sciences, Ajman University, Ajman, United Arab Emirates

[*] *Corresponding Author: dr.mohammadanasshamsi@gmail.com*

Received:16/05/2026 Revised:15/07/2026 Acceptance:17/08/2026 Published:30/08/2026

ABSTRACT

Single-cell omics has emerged as an important approach in pharmacology by enabling molecular analysis at individual-cell resolution. It provides deeper insight into cellular heterogeneity, therapeutic response, resistance mechanisms, and disease-associated molecular states that may be obscured by bulk analyses. This review aimed to synthesize current evidence on the role of single-cell omics in understanding cellular heterogeneity, drug response, therapeutic resistance, therapeutic target and biomarker discovery, multi-omics integration, and emerging pharmacological applications. A comprehensive review design was used to identify and synthesize relevant peer-reviewed literature from major academic databases. Studies addressing single-cell sequencing, multi-omics, spatial omics, drug response, resistance, biomarkers, and precision pharmacology were screened and organized into major thematic areas. The review showed that single-cell omics can distinguish functionally diverse cellular populations, identify drug-sensitive and resistant states, and reveal mechanisms involving clonal selection, cellular plasticity, epigenetic reprogramming, metabolic adaptation, and microenvironmental interactions. Integration with spatial and multi-omics technologies further improves therapeutic target identification, biomarker discovery, and interpretation of treatment-related cellular changes. Single-cell omics provides a valuable framework for precision pharmacology by improving understanding of heterogeneous therapeutic responses and resistance. Further standardization, functional validation, and clinical translation are needed to support broader pharmacological application.

Keywords: Single-cell omics, Pharmacology, Drug response, Drug resistance, Precision medicine

International Journal for Research in Biology & Pharmacy
(ISSN: 2208- 2093)
Vol. 12, Issue 03, August 2026
DOI: 10.65327/bp.v12i3.2530

1. Introduction

The concept of single-cell omics has become a significant breakthrough in biomedical and pharmacological studies as it has become possible to perform the molecular analysis of single cells. Conventional bulk omics methods give a mean result of high population of cells and might fail to capture the significant biological variations within single cell types and cellular states. Conversely, single-cell technologies allow a researcher to study the complex biological system with significantly more precision by offering high-resolution data on genomic, transcriptomic, epigenomic, and proteomic, and other molecular features. Combination of these techniques has enhanced systems biology and precision medicine as they allow comprehensive characterization of cellular diversity, which cannot be sufficiently addressed by standard population-level techniques (Li et al., 2021).

The heterogeneity of cells is of special concern in pharmacology as the cells in tissues or disease might vary significantly in their molecular properties, functional conditions, and reaction to therapeutic interventions. An example is tumors, which harbor genetically and phenotypically heterogeneous malignant cells alongside immune, stromal, endothelial and other microenvironmental factors that may affect disease progression and treatment responses. Multi-omics studies have revealed that such heterogeneity plays a role in cancer evolution, interaction with microenvironment, and development of therapeutic resistance (Ibekwe et al., 2025). Single-cell analyses have also indicated a high level of heterogeneity within tumor endothelial populations, with an increased focus on the fact that even non-malignant elements of the tumor microenvironment can have specific biological functionality and therapeutic value (Zeng et al., 2023). The same complexity has been revealed in prostate cancer, in which single-cell omics has permitted the thorough description of cancerous cells and their microenvironment (Yu et al., 2023).

Variable drug response and therapeutic resistance is one of the most significant pharmacological uses of single-cell omics. The individual populations of cells may have varying sensitivities to the same drug due to variation in gene expression, signaling pathways, developmental stages, and molecular adaptations. Single-cell methods have thus been useful in future prognosis of drug reactions and determining subpopulations that might be less responsive to treatment (Wu et al., 2020). The multi-omics analysis of single-cells in neuroblastoma has given insights into developmental diversity, immune composition and mechanisms of therapeutic resistance, demonstrating the usefulness of cell-resolved analysis in understanding treatment failure (He et al., 2026). Similarly, multi-omics in single cells in biliary tract cancers has demonstrated links between cellular heterogeneity, the tumor microenvironment, and potential treatment approaches (Tang et al., 2025).

Single-cell omics is also involved in the process of identifying therapeutic targets and clinically relevant biomarkers. These technologies can identify disease-related cell populations in the presence of other cells, identify certain molecular defects, pathways, and resistance-related markers that can be targeted using pharmacological means. Genomic profiling using multi-omics can thus be used to aid in the identification of possible therapeutic targets, and molecular markers related to drug resistance (Rajendran, 2024). The combination of the various layers of molecules has also been useful in prostate cancer, as integrated multi-omics approaches have also enhanced insights into pathways related to the disease and therapeutic opportunities, thus showing the relevance of combining multiple layers of molecules in the discovery of therapy (Yan et al., 2025).

The combination of multi-omics and spatial technologies with single-cell techniques extends their pharmacological usefulness. Multi-layered models give a more detailed view of cellular conditions, whereas spatial techniques are able to maintain data regarding the location of the cells in tissues and their interactions with adjacent populations. This kind of integration is especially important when treating cancer by immunotherapy, where multi-omics of single cells can bridge the gap between heterogeneity of the tumor, immune population, and response to treatment to provide more personalized therapy (Le et al., 2025). The usefulness of combining genomic, transcriptomic, and proteomic data, particularly at bulk and single-cell scales, to enhance the characterization of disease heterogeneity, has also been demonstrated by breast cancer studies (Zhu et al., 2023).

International Journal for Research in Biology & Pharmacy
(ISSN: 2208- 2093)
Vol. 12, Issue 03, August 2026
DOI: 10.65327/bp.v12i3.2530

Although there has been a rapid advancement, there is still a fragmentation of evidence in various technologies, types of disease and pharmacological applications. Research tends to concentrate on individual aspects of cellular heterogeneity, drug response, resistance, target discovery, or individual cancers and fails to provide a comprehensive view of how these domains interrelate. There is thus a need to synthesize comprehensively how single-cell omics can help throughout the pharmacological spectrum. This review will explore how single-cell omics is used to solve cellular heterogeneity, drug response, therapeutic resistance, and discovery of therapeutic targets, as well as how multi-omics integration and new translational uses are being considered.

2. Methodology

This study uses a comprehensive review design to combine the available academic evidence on the use of single-cell omics in pharmacology with a specific focus on cellular heterogeneity, drug response, therapeutic resistance, and therapeutic target discovery. Peer-reviewed journal articles and academic sources found in databases like Google Scholar, DOAJ, and ScienceDirect were identified as the sources of relevant literature. The review consisted of empirical studies and review articles that were directly related to single-cell sequencing, multi-omics, spatial omics, pharmacological response, drug resistance, biomarkers, and precision therapy, but it did not include studies that were not directly related to pharmacological applications. An organized key word approach was utilized based on a combination of terms such as single-cell omics, single-cell RNA sequencing, multi-omics, spatial omics, pharmacology, drug response, drug resistance, therapeutic targets, biomarkers, and precision medicine. Studies that were retrieved were initially filtered using titles and abstracts and then full-text filtered to establish relevance. Themes in eligible studies were then tabulated based on cellular heterogeneity, drug-response profiling, resistance mechanisms, target and biomarker discovery, multi-omics and spatial integration, and emerging translational applications. The results were relatively summarized to discover similar tendencies, key trends, and gaps in the research. The general flow of the review process is presented in Figure 1 and it consists of literature identification, screening, thematic classification and evidence synthesis.

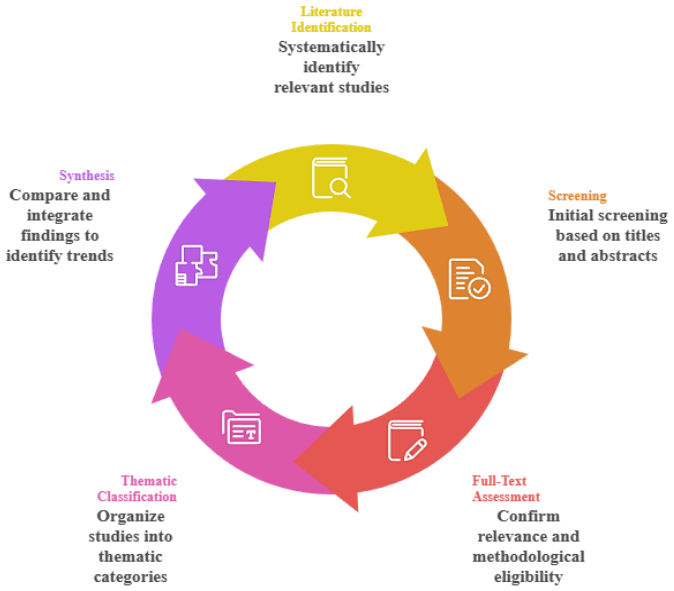

Figure 1. Overview of the Comprehensive Review Process

3. Results

The systematic survey revealed six key themes that reveal the manner in which single-cell omics is being implemented in pharmacological studies. These areas were cellular heterogeneity, drug response variability, therapeutic resistance mechanisms, discovering therapeutic targets and

International Journal for Research in Biology & Pharmacy
(ISSN: 2208- 2093)
Vol. 12, Issue 03, August 2026
DOI: 10.65327/bp.v12i3.2530

biomarkers, integrating multi-omics and spatial technologies, and new translational uses. Combined, the results indicate that single-cell methods offer a more comprehensive insight into the process of pharmacology through the resolution of molecular and functional disparities between single cell populations.

3.1 Single-Cell Omics and Cellular Heterogeneity

Single-cell omics has shown a great heterogeneity of cells of the same tissue or disease with variations in transcriptional, clonal, epigenetic, protein expression, cellular plasticity, and microenvironmental responses. The significance of these differences is pharmacological in that the individual cell populations can be characterized by varying degrees of drug sensitivity and resistance. Table 1 provides a summary of the key applications of single-cell in the characterization of cellular heterogeneity.

Table 1. Applications of Single-Cell Omics in Characterizing Cellular Heterogeneity

Single-Cell Approach	Heterogeneity Identified	Pharmacological Relevance	References
Single-cell RNA sequencing	Transcriptionally distinct cell states	Identifies drug-sensitive and resistant populations	Baerthel et al. (2023); Feng et al. (2024); Van de Sande et al. (2023)
Single-cell genomics	Genetic and clonal diversity	Reveals treatment-associated subclones	Li et al. (2021); Rosati & Giordano (2022)
Single-cell epigenomics	Regulatory and chromatin-state differences	Explains cellular plasticity and adaptive states	Aziz (2024); Kim et al. (2026)
Single-cell proteomics	Protein-level heterogeneity	Supports functional characterization of cellular states	Baysoy et al. (2023); Guan & Quek (2025)
Single-cell multi-omics	Integrated molecular heterogeneity	Improves identification of therapeutic vulnerabilities	Inayatullah et al. (2025); Le et al. (2025)
Spatial single-cell profiling	Location-dependent cellular variation	Links cellular states with local therapeutic response	Che et al. (2024); Tang et al. (2023)

3.2 Single-Cell Profiling of Drug Response and Therapeutic Vulnerability

Profiling of single cells has revealed that the pharmacological activity may differ significantly in cell groups treated with the same drug. It is possible to differentiate drug-sensitive, partly responsive, and drug-resistant populations and understand heterogeneous therapeutic responses and early therapeutic adaptation (Cheng et al., 2025; Van de Sande et al., 2023). It is also possible to identify clone-specific vulnerabilities, which can be used to uncover selective therapeutic opportunities that could not be observed with bulk analyses (Suphavilai et al., 2021). Moreover, cell-state-specific variations may affect the drug sensitivity and enable the creation of state-specific treatment plans and rational combination treatments (Huang et al., 2024; Guan and Quek, 2025). Spatial drug-response profiling can also be used to determine regional variations in therapeutic sensitivity in tissues, and repeated single-cell evaluation post-treatment can be used to demonstrate dynamic alterations in cellular populations and initial therapy adaptation (Tang et al., 2023; Zhang et al., 2024).

Single-cell profiling can be used to identify heterogenous responses to therapy by differentiating between drug-sensitive, partially responding and drug-resistant cell groups. It is also useful in pointing out clone-specific weaknesses, cell-state-dependent reactions, spatial variations in drug sensitivity, and adaptive therapy to early treatment. The overall process is illustrated in Figure 2.

International Journal for Research in Biology & Pharmacy
(ISSN: 2208- 2093)
Vol. 12, Issue 03, August 2026
DOI: 10.65327/bp.v12i3.2530

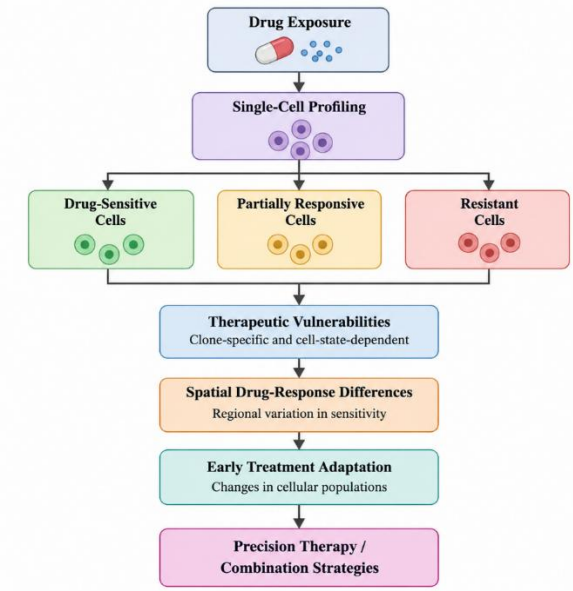

Figure 2. Single-Cell Profiling of Drug Response and Therapeutic Vulnerability

Single-cell analysis coupled with drug exposure, as depicted in Figure 2, has the potential to connect cellular responses to drug exposure and uncover therapeutic weaknesses that can guide precision treatment and rational combination approaches.

3.3 Single-Cell Mechanisms of Drug Resistance

The theme of drug resistance became prominent in single-cell pharmacology, and it was demonstrated that both pre-existing resistant clones and adaptive responses during treatment could develop resistance. Cellular plasticity, remodeling of epigenetic, metabolic, immune interactions, and spatial heterogeneity can all play a role in diminished therapeutic sensitivity. Table 2 lists the major resistance mechanisms that have been discovered using single-cell methods.

Table 2. Major Drug-Resistance Mechanisms Revealed by Single-Cell Omics

Resistance Mechanism	Single-Cell Observation	Pharmacological Consequence	References
Pre-existing resistant subclones	Resistant populations present before treatment	Selection and expansion during therapy	Rosati & Giordano (2022); Da et al. (2026)
Cellular plasticity	Transition into resistant cellular states	Adaptive treatment resistance	Aziz (2024); Cheng et al. (2025)
Epigenetic reprogramming	Changes in regulatory and chromatin states	Reduced therapeutic sensitivity	Kim et al. (2026)
Microenvironment-mediated resistance	Stromal, immune, and tumor-cell interactions	Protection from therapy	Chen et al. (2025); Sabit et al. (2025)
Metabolic adaptation	Altered metabolic pathways	Survival under treatment pressure	Zhang et al. (2023)
Immune-mediated resistance	Altered tumor–immune interactions	Reduced immunotherapy response	Le et al. (2025)
Spatial heterogeneity	Regional differences in resistant populations	Uneven therapeutic response	Che et al. (2024); Tang et al. (2023)

3.4 Therapeutic Target and Biomarker Discovery

Single-cell technologies have reinforced therapeutic target and biomarker discovery to find molecular

International Journal for Research in Biology & Pharmacy
(ISSN: 2208- 2093)
Vol. 12, Issue 03, August 2026
DOI: 10.65327/bp.v12i3.2530

abnormalities and vulnerabilities that are unique to specific disease-related cell populations. The methods can aid selective drug development by uncovering cell-specific molecular characteristics and pharmacologically pertinent pathways (Du et al., 2024; Loscalzo, 2024). Single-cell profiling can also be used to determine drug-response signatures, which could be used to predict sensitivity to treatment and biomarkers of resistance to treatment (Nassar et al., 2021; Sahu et al., 2026; Cheng et al., 2025). Moreover, the study of perturbed molecular networks can provide new points of intervention to be pharmacologically targeted, and variations between molecularly different populations can help to stratify patients and select treatment more accurately (Guan & Quek, 2025). Combining these findings with network-based strategies can also help bridge several pathways and therapeutic targets to aid the creation of multi-target treatment strategies (Thombre et al., 2026).

Single-cell omics aids in therapeutic target and biomarker identification, showing cell-specific molecular weaknesses, drug-response phenotypes, resistance-related signatures, altered pathways and molecularly different patient groups. These key applications are summarized in Figure 3.

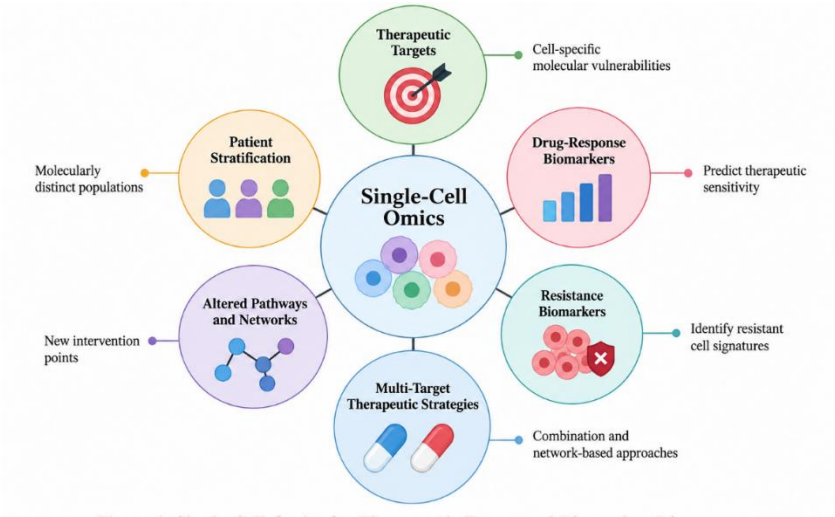

Figure 3. Single-Cell Omics for Therapeutic Target and Biomarker Discovery

Single-cell analysis can be used to associate molecular characteristics and therapeutic targets, patient stratification, and multi-target treatment strategies, as illustrated in Figure 3, which will aid in making more accurate pharmacological decisions.

3.5 Integration of Single-Cell Multi-Omics and Spatial Omics in Precision Pharmacology

Combining various single-cell omics layers can offer a more comprehensive view of pharmacological processes than any single platform can. Integration of genomic, transcriptomic, epigenomic, proteomic, metabolomic and spatial data aids in relating molecular changes to cell conditions, drug response, as well as drug resistance. Spatial omics also maintains the context of the tissue and explains how the local microenvironment affects the therapeutic outcome. The key combined strategies are outlined in Table 3.

Table 3. Integration of Single-Cell and Spatial Omics in Pharmacological Research

Omics Integration	Information Generated	Pharmacological Application	References
Transcriptome + genome	Genotype–phenotype relationships	Drug-response and resistance characterization	Li et al. (2021); Baysoy et al. (2023)
Transcriptome + epigenome	Regulatory cellular states	Identification of adaptive resistance mechanisms	Kim et al. (2026)

International Journal for Research in Biology & Pharmacy
(ISSN: 2208- 2093)
Vol. 12, Issue 03, August 2026
DOI: 10.65327/bp.v12i3.2530

Transcriptome + proteome	Molecular expression and functional signaling	Therapeutic target validation	Baysoy et al. (2023); Guan & Quek (2025)
Transcriptome + metabolome	Cell-specific metabolic programs	Identification of metabolic vulnerabilities	Zhang et al. (2023)
Single-cell + spatial omics	Molecular states within tissue architecture	Spatial drug-response mapping	Che et al. (2024); Tang et al. (2023)
Integrated multi-omics	Combined molecular characterization	Precision pharmacology and treatment stratification	Inayatullah et al. (2025); Le et al. (2025)

3.6 Emerging Trends and Translational Applications in Single-Cell Pharmacology

Recent advances show that single-cell pharmacology is leaving descriptive profiling to more integrated and clinically useful applications. Other important trends are spatial pharmacology, high-dimensional multi-omics, single-cell systems pharmacology, longitudinal treatment monitoring, precision oncology, immunotherapy studies, and non-cancer expansion. These novel directions and their pharmacological significance are summarized in Table 4.

Table 4. Emerging Trends and Translational Applications in Single-Cell Pharmacology

Emerging Trend/Application	Pharmacological Relevance	References
Spatial pharmacology	Maps location-specific drug response and resistance	Che et al. (2024); Tang et al. (2023)
Multi-omics integration	Improves understanding of therapeutic mechanisms	Baysoy et al. (2023); Guan & Quek (2025)
Systems pharmacology	Supports drug-response and combination therapy analysis	Huang et al. (2024)
Longitudinal profiling	Detects treatment-induced adaptation and resistance	Cheng et al. (2025); Da et al. (2026)
Precision cancer pharmacology	Supports cell-specific therapeutic strategies	Baerthel et al. (2023); Xiong et al. (2024)
Immunotherapy applications	Clarifies immune response and resistance mechanisms	Le et al. (2025)
Non-cancer applications	Extends single-cell pharmacology beyond oncology	Wang et al. (2026); Wu et al. (2025)

4. Discussion

The results of this review, which are based on a large overview of single-cell omics research, suggest that this type of technology is changing the paradigm of pharmacological studies by showing the degree of cellular complexity that is not sufficiently represented by your standard bulk techniques. Throughout the evidence reviewed, cellular heterogeneity turned out to be one of the key determinants of drug sensitivity, treatment response, and resistance. It implies that pharmacological results cannot be explained only by the level of tissue or population since the reaction of separate cellular subpopulations to the identical therapeutic intervention might be different. The possibility of discovering uncommon clones, specific transcriptional positions and microenvironmental interactions thus offers a more accurate foundation of explanation of the variation in response to treatment in the same illness.

These results are in line with the past studies on prostate cancer that indicate that single-cell omics can be used to differentiate between heterogeneous malignant and non-malignant groups and also describe the interactions within the tumor microenvironment. These observations confirm the finding of the current review that the composition and functional condition of individual cellular populations

International Journal for Research in Biology & Pharmacy
(ISSN: 2208- 2093)
Vol. 12, Issue 03, August 2026
DOI: 10.65327/bp.v12i3.2530

are highly associated with therapeutic response but not tumor cells per se (Yu et al., 2023). Endothelial Tumor endothelial biology has also shown similar evidence of significant functional diversity in endothelial subpopulations, which further suggests that stromal and vascular elements of the disease microenvironment can modify pharmacological response (Zeng et al., 2023). Collectively, these studies support the idea that the average molecular profiles should not be used in the assessment of the mechanism of treatment anymore.

The other significant discovery was the usefulness of single-cell technologies in determining therapeutic vulnerabilities, biomarkers, and drug targets. Cell-resolved molecular profiling is able to indicate pathways that are selectively activated in clinically relevant subpopulations, which means targets can be prioritized that would otherwise not have been detected. This understanding aligns with the past studies that have identified the increased importance of single-cell technologies in drug discovery and development, such as in target identification, pharmacological screening, mechanism-of-action analysis, and response monitoring (Zhang et al., 2024). What this suggests is that single-cell methods can enhance early-stage pharmaceutical testing in addition to the choice of more personalized treatment methods. Drug resistance was also demonstrated to be a multifactorial and dynamic process which included clonal selection, cellular plasticity, metabolic adaptation, epigenetic reprogramming and microenvironmental influences. Metabolomic studies have also shown that resistant cancer cells can experience significant changes in the metabolism and that combining bulk, single-cell, and spatial metabolomics can enhance the insights into the failure of treatment (Zhang et al., 2023). These results indicate that resistance must be researched as a dynamic cellular procedure as opposed to a steady cellular molecular trait. This method can enhance the detection of early signs of resistance and contribute to the creation of combination treatments targeting various resistant conditions.

The ability to integrate genomic, transcriptomic, proteomic, epigenomic, metabolomic and spatial data is another significant implication of the review. The bulk and single-cell molecular profiling have proven beneficial in breast cancer studies to offer more comprehensive insights into tumor heterogeneity and potentially enhance the ability to identify clinically significant molecular subtypes and vulnerabilities (Zhu et al., 2023). This is in line with the increasing significance of multi-omics integration in precision pharmacology. These are the benefits, but there are a number of drawbacks. Single-cell researches can be costly, complicated, and susceptible to sample-processing biases, batch effects, sparseness of data, and variability in analysis. The comparison of studies across the studies is also challenging since the platforms, preprocessing techniques, populations of diseases, and the endpoints are not uniform. Moreover, most of the discoveries are still exploratory and have to be clinically and functionally validated before they can be used as therapeutic agents.

Standardized workflows in analysis, larger and more heterogenous cohorts of patients, longitudinal pre- and post-treatment sampling, and single-cell data combined with spatial and functional pharmacological measurements should be the focus of future studies. More focus should also be on the validation of identified biomarkers and therapeutic targets in clinically relevant models. Such advances have the potential to make single-cell omics translation to practical precision pharmacology and personalized treatment decisions.

5. Conclusion

Single-cell omics has become a powerful method of pushing forward the pharmacological studies by giving a detailed understanding of cellular heterogeneity, drug response, therapeutic resistance, and target discovery. In contrast to traditional bulk methods, single-cell methods provide insights into molecular and functional variations in individual cells enabling the researcher to detect rare populations, resistant clones and treatment responsive cellular states that would otherwise be undetectable. The results of this review reveal that these technologies are becoming more and more involved in the process of discovering biomarkers, therapeutic vulnerabilities, and mechanisms of the varying treatment outcomes. They are further enhanced with integration with genomics, transcriptomics, epigenomics, proteomics, metabolomics, and spatial profiling and can now be used

to comprehend complex pharmacological mechanisms in intact tissue settings. Regardless of this potential, issues with cost, technical complexity, data integration, analytical variability, and limited clinical validation remain to limit widespread use. Future studies ought to be directed towards the standardization of workflows, longitudinal treatment monitoring, greater and more diverse study populations, and more robust functional validation of single-cell-derived targets and biomarkers. A more thorough incorporation of spatial, multi-omics, and pharmacological data can also enhance prediction of therapeutic response and resistance. Altogether, single-cell omics offers a valuable basis of precision pharmacology and has great potential to aid more individualized, mechanism-based, and effective treatment approaches.

References

1. Aziz, M. A. (2024). Multiomics approach towards characterization of tumor cell plasticity and its significance in precision and personalized medicine. Cancer and Metastasis Reviews, 43(4), 1549-1559.
2. Baerthel, S., Falcomata, C., Rad, R., Theis, F. J., & Saur, D. (2023). Single-cell profiling to explore pancreatic cancer heterogeneity, plasticity and response to therapy. Nature cancer, 4(4), 454-467.
3. Baysoy, A., Bai, Z., Satija, R., & Fan, R. (2023). The technological landscape and applications of single-cell multi-omics. Nature Reviews Molecular Cell Biology, 24(10), 695-713.
4. Che, G., Yin, J., Wang, W., Luo, Y., Chen, Y., Yu, X., ... & Liu, J. (2024). Circumventing drug resistance in gastric cancer: A spatial multi-omics exploration of chemo and immuno-therapeutic response dynamics. Drug Resistance Updates, 74, 101080.
5. Chen, F., Fu, Y., Bai, G., Qiu, J., & Hua, K. (2025). Multi-omics dissection of tumor microenvironment-mediated drug resistance: mechanisms and therapeutic reprogramming. Frontiers in Pharmacology, 16, 1634413.
6. Cheng, X., Peng, T., Chu, T., Yang, Y., Liu, J., Gao, Q., ... & Wei, J. (2025). Application of single-cell and spatial omics in deciphering cellular hallmarks of cancer drug response and resistance. Journal of Hematology & Oncology, 18(1), 70.
7. Da, E., Zhu, R., Xi, B., Zhang, L., & Tang, G. (2026). Tumor heterogeneity as a driver of drug resistance and its implications for personalized therapy. Cancer Drug Resistance, 9, 16.
8. Du, P., Fan, R., Zhang, N., Wu, C., & Zhang, Y. (2024). Advances in integrated multi-omics analysis for drug-target identification. Biomolecules, 14(6), 692.
9. Feng, D. C., Zhu, W. Z., Wang, J., Li, D. X., Shi, X., Xiong, Q., ... & Yang, L. (2024). The implications of single-cell RNA-seq analysis in prostate cancer: unraveling tumor heterogeneity, therapeutic implications and pathways towards personalized therapy. Military Medical Research, 11(1), 21.
10. Guan, A., & Quek, C. (2025). Single-cell multi-omics: insights into therapeutic innovations to advance treatment in cancer. International journal of molecular sciences, 26(6), 2447.
11. He, G. Q., He, S. J., Jing, X. Y., Dai, Y. L., Guo, X., Gao, J., & Zhang, W. (2026). Dissecting neuroblastoma heterogeneity through single-cell multi-omics: insights into development, immunity, and therapeutic resistance. Oncogene, 45(2), 123-139.
12. Huang, X., Li, Y., Zhang, J., Yan, L., Zhao, H., Ding, L., ... & Yang, J. J. (2024). Single-cell systems pharmacology identifies development-driven drug response and combination therapy in B cell acute lymphoblastic leukemia. Cancer cell, 42(4), 552-567.
13. Ibekwe, P. M. R., Akintayo, E. A., Okuku, C. N., Muhammed, I., Jeje, F. M., Oseghale, O., ... & Onwuemelem, L. A. (2025). Decoding tumor heterogeneity through multi omics: Insights into cancer evolution, microenvironment and therapy resistance. Journal of Cancer and Tumor International, 15(3), 91-112.
14. Inayatullah, M., Dwivedi, A. K., & Tiwari, V. K. (2025). Advances in single-cell omics: Transformative applications in basic and clinical research. Current Opinion in Cell Biology, 95, 102548.

15. Kim, H. J., Lee, H., Hong, J., & Park, D. (2026). Epigenetic heterogeneity and plasticity in therapy-induced tumor states through single-cell multi-omics. Molecular Oncology.
16. Le, J., Dian, Y., Zhao, D., Guo, Z., Luo, Z., Chen, X., ... & Deng, G. (2025). Single-cell multi-omics in cancer immunotherapy: from tumor heterogeneity to personalized precision treatment. Molecular Cancer, 24(1), 221.
17. Li, Y., Ma, L., Wu, D., & Chen, G. (2021). Advances in bulk and single-cell multi-omics approaches for systems biology and precision medicine. Briefings in bioinformatics, 22(5), bbab024.
18. Loscalzo, J. (2024). Multi-omics and single-cell omics: new tools in drug target discovery. Arteriosclerosis, thrombosis, and vascular biology, 44(4), 759-762.
19. Nassar, S. F., Raddassi, K., & Wu, T. (2021). Single-cell multiomics analysis for drug discovery. Metabolites, 11(11), 729.
20. Rajendran, L. K. K. (2024). Genomic Profiling: Utilizing multi-omics data to identify potential therapeutic targets and resistance markers. Power System Protection and Control, 52(4), 159-166.
21. Rosati, D., & Giordano, A. (2022). Single-cell RNA sequencing and bioinformatics as tools to decipher cancer heterogenicity and mechanisms of drug resistance. Biochemical pharmacology, 195, 114811.
22. Sabit, H., Arneth, B., Pawlik, T. M., Abdel-Ghany, S., Ghazy, A., Abdelazeem, R. M., ... & Hashash, A. (2025). Leveraging single-cell multi-omics to decode tumor microenvironment diversity and therapeutic resistance. Pharmaceuticals, 18(1), 75.
23. Sahu, P., Satapathy, A., Satapathy, A., & Satapathy, T. (2026). Single-cell multi-omics for biomarker discovery: Technologies, molecular mechanisms, applications and translational challenges. Letters in Drug Design & Discovery, 100286.
24. Suphavilai, C., Chia, S., Sharma, A., Tu, L., Da Silva, R. P., Mongia, A., ... & Nagarajan, N. (2021). Predicting heterogeneity in clone-specific therapeutic vulnerabilities using single-cell transcriptomic signatures. Genome Medicine, 13(1), 189.
25. Tang, N., Li, J., Gu, A., Li, M., & Liu, Y. (2025). Single-cell multi-omics in biliary tract cancers: decoding heterogeneity, microenvironment, and treatment strategies. Molecular Biomedicine, 6(1), 82.
26. Tang, Z., Liu, X., Li, Z., Zhang, T., Yang, B., Su, J., & Song, Q. (2023). SpaRx: elucidate single-cell spatial heterogeneity of drug responses for personalized treatment. Briefings in Bioinformatics, 24(6), bbad338.
27. Thombre, K. R., Gabhane, V., Gupta, K. R., & Umekar, M. J. (2026). Network pharmacology in the multi-omics era: uncovering novel therapeutic strategies. Discover Chemistry, 3(1), 111.
28. Van de Sande, B., Lee, J. S., Mutasa-Gottgens, E., Naughton, B., Bacon, W., Manning, J., ... & Ferran, E. (2023). Applications of single-cell RNA sequencing in drug discovery and development. Nature reviews Drug discovery, 22(6), 496-520.
29. Wang, X., Wang, L., Su, H., Yuan, N., & Wang, T. (2026). Integration of single-cell sequencing and multi-omics approaches with pharmacological analysis to unveil biomarkers and mechanisms of traditional Chinese medicine in treating heart diseases. Letters in Drug Design & Discovery, 100223.
30. Wu, L., Wu, Q., Du, X., Ling, M., & Tong, H. (2025). Revolutionizing pharmacological research of traditional Chinese medicine with single-cell omics technologies. Fitoterapia, 106846.
31. Wu, Z., Lawrence, P. J., Ma, A., Zhu, J., Xu, D., & Ma, Q. (2020). Single-cell techniques and deep learning in predicting drug response. Trends in Pharmacological Sciences, 41(12), 1050-1065.
32. Xiong, X., Wang, X., Liu, C. C., Shao, Z. M., & Yu, K. D. (2024). Deciphering breast cancer dynamics: insights from single-cell and spatial profiling in the multi-omics era. Biomarker research, 12(1), 107.
33. Yan, L., Su, P., & Sun, X. (2025). Role of multi-omics in advancing the understanding and

treatment of prostate cancer. Molecular Medicine Reports, 31(5), 130.

34. Yu, X., Liu, R., Gao, W., Wang, X., & Zhang, Y. (2023). Single-cell omics traces the heterogeneity of prostate cancer cells and the tumor microenvironment. Cellular & Molecular Biology Letters, 28(1), 38.
35. Zeng, Q., Mousa, M., Nadukkandy, A. S., Franssens, L., Alnaqbi, H., Alshamsi, F. Y., ... & Carmeliet, P. (2023). Understanding tumour endothelial cell heterogeneity and function from single-cell omics. Nature Reviews Cancer, 23(8), 544-564.
36. Zhang, A., Zou, J., Xi, Y., Gao, L., Deng, F., Liu, Y., ... & Hao, J. (2024). Single-cell technology for drug discovery and development. Frontiers in Drug Discovery, 4, 1459962.
37. Zhang, Z., Bao, C., Jiang, L., Wang, S., Wang, K., Lu, C., & Fang, H. (2023). When cancer drug resistance meets metabolomics (bulk, single-cell and/or spatial): Progress, potential, and perspective. Frontiers in Oncology, 12, 1054233.
38. Zhu, Z., Jiang, L., & Ding, X. (2023). Advancing breast cancer heterogeneity analysis: insights from genomics, transcriptomics and proteomics at bulk and single-cell levels. Cancers, 15(16), 4164.