



CANCER TYPE–SPECIFIC PATTERNS OF ANTICANCER DRUG SENSITIVITY AND TARGET PATHWAY ASSOCIATIONS IN GDSC2 CELL LINES

Manjusha W A¹, Dr Wali Tariq², Reshmi Krishna A³, Rajni Agarwal⁴, Ould Brahim⁵

¹Assistant Professor and Head, Department of Biotechnology, Malankara Catholic College Mariagiri, Kailakkavilai
manjuaruljose@gmail.com

²Associate Professor, KM Medical College & Hospital, MATHURA, drstwali@gmail.com

³Research Scholar, Vinayaka Missions college of Pharmacy, Vinayaka Missions research foundation (Deemed University) Salem, Email ID: krishnareshmi953@gmail.com

⁴Prof. and Head, Department of OBG and Gynae, Rajshree Medical Research Institute, Bareilly (UP), India
goelrajni9@gmail.com

⁵Lecturer, University of Science and Technology Houari Boumediene, Email id : ouldbrahimpubli@gmail.com

*Corresponding Author: Manjusha W A

*Email: manjuaruljose@gmail.com

Received date: 06-05-2026

Revised date: 27-07-2026

Accepted date: 02-09-2026

Published date: 21-09-2026

Abstract

Anticancer drug response varies substantially across cancer types because of differences in molecular characteristics, therapeutic targets, and pathway dependencies. Large-scale pharmacogenomic resources such as GDSC2 provide an opportunity to examine these variations systematically across diverse cancer cell lines and compounds. This study aimed to compare anticancer drug sensitivity across cancer types and evaluate target pathway–specific response patterns using GDSC2 cell-line data. A secondary-data analysis was conducted using 242,036 drug–response observations from 969 cancer cell lines. Drug sensitivity was assessed using LN_{IC50}, AUC, and Z-score. Cancer-specific and pathway-specific response patterns were summarized using descriptive statistics, median sensitivity measures, Kruskal–Wallis tests, and Spearman correlation. Drug sensitivity differed significantly across cancer types and target pathways. Hematological malignancies generally showed lower LN_{IC50} values than many solid tumors. Mitosis, protein stability and degradation, cell-cycle regulation, and apoptosis were associated with comparatively greater sensitivity. Significant heterogeneity was observed across cancer categories and pathways, while LN_{IC50} and AUC showed a strong positive association. GDSC2 revealed distinct cancer type–specific and pathway-specific patterns of anticancer drug response. These findings support the value of integrated pharmacogenomic screening for identifying therapeutic vulnerabilities and guiding future precision-oncology research.

Keywords: GDSC2, drug sensitivity, cancer cell lines, target pathways, precision oncology.

1. Introduction

The treatment of cancer is still a problem since the process of treatment shows significant differences among tumors, even within the same diagnostic category. The variation in gene expression, signaling, molecular background, and cellular context might impact the efficacy of anticancer agents and cause resistance. The goal of pharmacogenomic methods is thus to bridge the gap between tumor biology and drug-response phenotypes in order to facilitate more personalized therapeutic approaches. The models of cancer cell-lines continue to be useful preclinical models due to the ability to systematically test various compounds in different molecular backgrounds (Kardamiliotis et al., 2022). Molecular profiles have been demonstrated to capture significant determinants of drug sensitivity, which can be implemented using gene-expression and network-based studies. Transcriptomic signatures have been applied to infer response in cancer cell lines and biomarkers in cell-line models have demonstrated promise in predicting tumor response (Chawla et al., 2022; Li et al., 2021). The recent studies of breast cancer have also shown that explainable deep-learn and network-based methods can be useful in finding patterns of drug-response and better predicting treatment (Anushya et al., 2026; Huang et al., 2021).

The Genomics of Drug Sensitivity in Cancer resource offers a vast pharmacogenomic framework that can be used to study the variation in anticancer drug response among cancer cell lines. GDSC2 has the ability to compare a variety of compounds, cancer types, and measures of response, allowing it to be used to perform wide sensitivity profiling. Macro GDSC data analyses have shown a high response heterogeneity and the value of combined pharmacogenomic data sets in revealing cancer specific therapeutic vulnerabilities (Rajendran, 2026). Some of the commonly used measures of drug response include half-maximal inhibitory concentration and area under the dose-response curve. Such metrics offer complementary data and can have different predictive behavior based on the context of the analysis (Chiu et al., 2026). GDSC has also been integrated with other molecular resources to aid better drug-sensitivity modeling and interpretation of targets (Mergen et al., 2026). Multi-omics methods have also revealed that the integration of various molecular layers can be used to uncover the mechanisms that underlie drug response variation (Kusch & Schuppert, 2020).

Anticancer medications have molecular targets that regulate cell proliferation, cell apoptosis, cell genome maintenance, cell metabolism, and cell signaling. The association of pharmacological response with target information can hence explain why a drug can be more effective in one cancer setting compared to the other. Combination of pharmacological screening with CRISPR-based functional genomics has demonstrated that a combination of these data can enhance the process of finding drug mechanisms and therapeutic dependencies (Goncalves et al., 2020). Pathway-level analysis is especially beneficial since the response of drugs frequently is coordinated molecular processes and not lone genes. Pathway-enrichment models provide interpretations to sensitivity predictions, which have been enhanced through explainable models (Tang & Gottlieb, 2021). The relevance of genome-integrity mechanisms can also be motivated as the therapeutic susceptibility can be influenced by the changes in the DNA-maintenance program, which was demonstrated in the pan-cancer analysis of DNA2-related pathways (Pandit et al., 2026). Corresponding research has also found that there are metabolic, immune, and signaling programs linked with treatment sensitivity in pancreatic and endometrial cancers (Demirtas Korkmaz et al., 2026; Hu et al., 2026).

Past research has tended to concentrate on single types of cancer, or a single drug, or a single biomarker or a specific predictive algorithm as opposed to directly comparing the patterns of sensitivity of a large number of types of cancer in parallel with their therapeutic pathways. The analysis of drug-response on heterogeneous tumor populations has been extended to single-cell studies (Pellecchia et al., 2023), whereas heterogeneous drug-cell-gene networks have enhanced interpretation of gene contributions to response (Inoue et al., 2025). Other studies have been aimed at looking at specific resistance mechanisms, such as cisplatin resistance in non-small cell lung cancer (Li et al., 2025), or programmed cell-death genes and drug sensitivity in gastric cancer (Qu et al., 2025).

These results substantiate the necessity of combined analyses comparing pharmacological responses in different cancer groups with taking into account the molecular target pathways. This analysis can display broader trends which could not be found in disease-specific analyses. Hence, this current research utilized GDSC2 cell-line information to determine the sensitivity of anticancer drugs to cancer types, contrasting cancer-drug response scenario, and how key target pathways were connected with variations in pharmacological response among different malignancies.

Objectives of the study

- 1.To compare anticancer drug sensitivity across cancer types and identify major cancer–drug response patterns.
- 2.To evaluate target pathway–specific sensitivity and the relationship between LN_IC50 and AUC3.

2. Methodology

2.1 Study Design

A secondary-data analytical design was used in this study to examine the cancer type-specific patterns of anticancer drug sensitivity and the associations between these patterns and molecular target pathways. The previously obtained data on pharmacological screening of GDSC2 cancer cell lines was analyzed without the direct data collection or manipulations. The comparison was made on variations in drug-response measures between cancer groups, per compound, and annotated therapeutic pathways. Statistical methods based on comparison and association were used to discover the trends of relative drug sensitivity and pathway-associated response differences across the cancer cell lines included.

2.2 Data Source

The data were obtained from the publicly available Kaggle repository containing the Genomics of Drug Sensitivity in Cancer (GDSC) dataset (Alipour, 2024). The main analysis file contained 242,036 drug-response data of 969 cancer cell

lines, 295 drug identifiers of 286 distinct compounds. There was also information on cancer classification, putative molecular targets, and target pathways. The key measures of the pharmacological response were LN_IC50, area under the dose-response curve, and standardized Z-score.

2.3 Cell-Line and Cancer-Type Classification

Cancer cell lines were identified using COSMIC_ID and CELL_LINE_NAME. The classification of cancer types was determined using the TCGA_DESC variable that categorized cell lines into specific malignancy types. The records that were tagged as UNCLASSIFIED, OTHER or had no information about cancer were not subject to cancer-specific comparisons. After filtering, 195,099 responses of drugs in 781 classified cell lines that represented 30 cancer groups were retained. These data were later applied to compare the variations in drug-response distributions and pattern of sensitivity differences between the different types of cancers in the screened anticancer compounds.

2.4 Drug and Target Pathway Classification

The most frequent use of DRUG_ID was to identify anticancer compounds, whereas DRUG_NAME was stored in case of reporting and interpretation. The PUTATIVE_TARGET variable provided putative molecular targets and the PATHWAY_NAME provided the pathway classifications. Significant categories of therapeutic targets were PI3K/MTOR signaling, DNA replication, ERK MAPK signaling, cell cycle, apoptosis regulation, RTK signaling, EGFR signaling, WNT signaling, genome integrity, and related pathways. Unclassified, Other, or Other categories were not a subject of focused comparison of pathways to enhance biological interpretability.

2.5 Drug-Sensitivity Measures

Sensitivity to drugs was measured by LN IC50, AUC and Z score. LN_IC50 was assumed to be the main response parameter since it was the logarithmically transformed concentration that was needed to obtain half-maximal inhibition. The values that were lower than LN_IC50 were considered to be more sensitive to the drug and the values that were higher meant that the sensitivity was relatively less. The complementary measure of overall drug response was AUC and the standardized response behavior was Z-score. The three variables were represented in numerical form and analyzed by looking into their completeness, distribution and consistency prior to statistical analysis.

2.6 Data Cleaning and Preprocessing

Missing values, duplicates, inconsistent identifiers and missing cancer or pathway classification were screened out of the data and analyzed. There were no clear duplicate rows. Drug-response variables were transformed to numeric and records with invalid cancer-type classifications were excluded in cancer-specific comparisons. Focused pathway analyses were eliminated of non-specific pathway categories. Observations of drug response were then clustered based on type of cancer, drug identifier and target pathway and median response values were calculated where necessary in order to minimize the effect of extreme observations.

2.7 Statistical Analysis

Categorical variables were summarized by frequencies and counts, whereas continuous measures of drugs-response were summarized by mean, SD, median, interquartile range, minimum and maximum. Cancer-drug and cancer-pathway comparisons were done using median values of LN_IC50. The Kruskal-Wallis test was used to determine differences in LN_IC50 between cancer types and target pathways. To determine the relationship between LN_IC50 and AUC, Spearman rank correlation was used. A p value of $p < 0.05$ was taken to be statistically significant.

3. Results

3.1 Study Sample and Analytical Characteristics

The sample size used in the analysis consisted of 242,036 observations of drug-response in 969 distinct cancer cell lines. All in all, there were 295 drug identifiers (286 unique compounds) 185 putative molecular targets and 24 target-pathway categories. No precise matches were identified and LN_IC50, AUC and Z-score were not missing. Cancer-type filtering resulted in a retention of 195,099 observations of 781 cell lines representing 30 classified cancer groups, and 143,782 observations in particular pathway analyses (Table 1).

Table 1. Overall characteristics of the study sample

Characteristic	Value
Total drug-response observations	242,036
Unique cell lines	969
TCGA cancer categories	32
Unique drug IDs	295

Unique drug names	286
Unique putative targets	185
Target-pathway categories	24
Classified observations	195,099
Classified cell lines	781
Cancer types analyzed	30
Specific-pathway observations	143,782

3.2 Overall Patterns of Drug Sensitivity

The measurements of drug-response showed that there is a significant variability in the entire analysis. LN_IC50 was distributed widely with a median value of 3.237 and interquartile range of 3.192 suggesting that the drug sensitivity varies significantly across cancer cell lines and compounds. The average of the AUC values was mostly concentrated on the higher range, and the standardized Z-scores tended to be focused on zero. Table 2 shows the descriptive profile that determines the central tendency, dispersion, and observed ranges of the three largest measures of responses.

Table 2. Descriptive statistics of anticancer drug-response measures

Variable	N	Mean ± SD	Median	Q1	Q3	IQR	Minimum	Maximum
LN_IC50	242,036	2.817 ± 2.762	3.237	1.508	4.700	3.192	−8.748	13.820
AUC	242,036	0.883 ± 0.147	0.944	0.849	0.975	0.126	0.006	0.999
Z-score	242,036	0.000 ± 0.999	0.011	−0.657	0.656	1.313	−8.255	7.979

Figure 1 shows the relative distribution of the main drug-response measures.

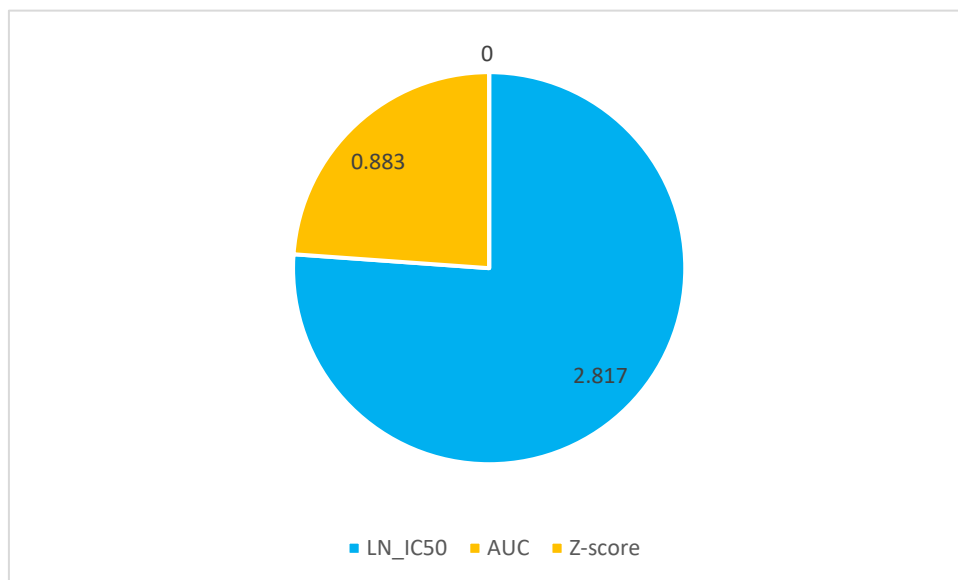


Figure 1. Overall Drug-Response Profile

The graph shows definite variations in the relative size of the three drug-response values. LN_IC50 had the highest proportion, then AUC and the standardized Z-score was relatively small, indicating that it was centrally distributed in the overall pharmacological response profile.

3.3 Cancer Type-Specific Drug Sensitivity

The sensitivity of drugs to different types of cancer was different. The median LNIC50 values of hematological malignancies tended to be lower than most solid tumors, and this is a sign of a relatively high sensitivity of the screened compounds. Other groups that had low values included chronic lymphocytic leukemia, acute myeloid leukemia, diffuse large B-cell lymphoma, acute lymphoblastic leukemia, and chronic myeloid leukemia. Conversely, pancreatic adenocarcinoma, mesothelioma, lung adenocarcinoma, and various other solid tumors had larger median LN_IC50 distributions which are summarized in Table 3.

Table 3. Drug-sensitivity patterns across selected cancer types

Cancer type	Cell lines	Observations	Median LN_IC50	Median AUC	Median Z-score
CLL	2	550	1.728	0.855	-1.163
LAML	26	6,209	2.051	0.925	-0.854
DLBC	34	7,978	2.105	0.928	-0.919
ALL	26	6,795	2.113	0.931	-0.906
LCML	10	2,611	2.169	0.919	-0.861
MM	17	4,598	2.473	0.945	-0.665
NB	32	7,469	2.888	0.939	-0.254
SCLC	59	13,570	3.280	0.954	-0.018
BRCA	51	13,106	3.493	0.952	0.188
LUAD	62	15,653	3.769	0.944	0.387
MESO	21	5,561	3.949	0.946	0.580
PAAD	29	7,513	4.177	0.947	0.679

The total difference in LN_IC50 between cancer groups was statistically significant based on KruskalWallis test ($H = 10,549.02$, $p = 0.001$). This established the fact that the distributions of drug-responses varied significantly between cancer types and validated the fact that there were cancer-specific sensitivity patterns.

Figure 2 shows the comparative median LNIC50 and AUC value of the chosen types of cancers.

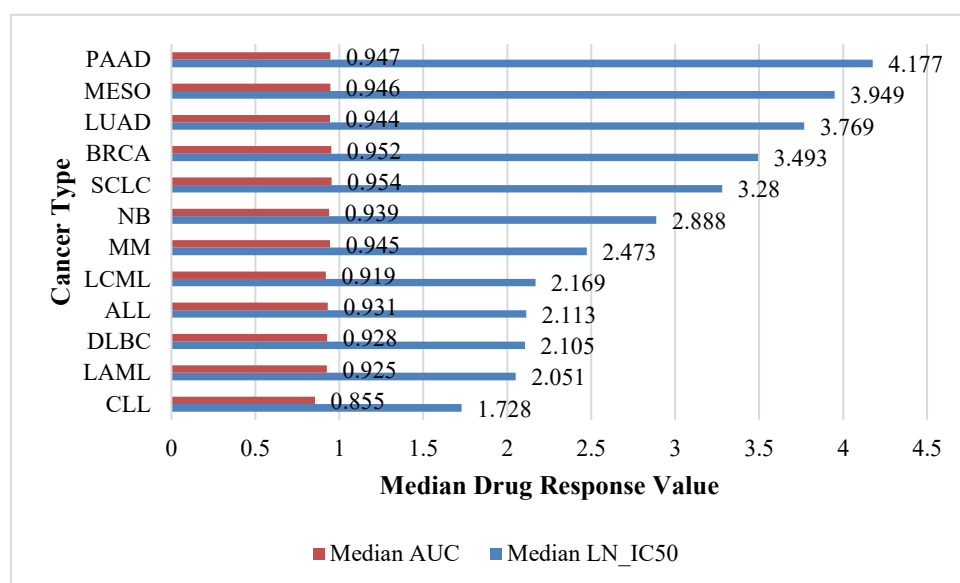


Figure 2. Cancer Type–Specific Drug Response Profile

In the figure, a distinct difference in the pattern of drug-response across cancer types can be seen. The median LN_IC50 values in pancreatic adenocarcinoma, mesothelioma, and lung adenocarcinoma were relatively higher, and hematological malignancies tended to have lower median LN_IC50 values, which is indicative of overall increased sensitivity of the studied anticancer compounds.

3.4 Cancer–Drug Sensitivity Patterns

There was also marked heterogeneity on an individual level of cancer-drug. Dasatinib was shown to be highly sensitive to chronic myeloid leukemia and SN-38 to be low in LNIC50 of daporinad and SN-38 in acute lymphoblastic leukemia. Diffuse large B-cell lymphoma was also relatively sensitive to dactinomycin, romidepsin, docetaxel and vinblastine. Conversely, various groups of solid tumors had high LN_IC50 values of ascorbate, which implied low relative sensitivity. Table 4 shows representative contrasting combinations.

Table 4. Representative cancer–drug combinations with greater or lower sensitivity

Cancer type	Drug	Putative target	Target pathway	Median LN_IC50	Median AUC	Pattern
LCML	Dasatinib	ABL, SRC, Ephrins, PDGFR, KIT	Other, kinases	−7.024	0.074	Greater sensitivity
ALL	Daporinad	NAMPT	Metabolism	−6.807	0.358	Greater sensitivity
DLBC	Dactinomycin	RNA polymerase	Other	−6.512	0.144	Greater sensitivity
ALL	SN-38	TOP1	DNA replication	−6.124	0.749	Greater sensitivity
DLBC	Romidepsin	HDAC1, HDAC2, HDAC3,	Chromatin histone	−5.996	0.769	Greater sensitivity

		HDAC8	acetylation			
LAML	Vinblastine	Microtubule destabiliser	Mitosis	-5.981	0.469	Greater sensitivity
DLBC	Docetaxel	Microtubule stabiliser	Mitosis	-5.948	0.748	Greater sensitivity
PRAD	Ascorbate	Anti-oxidant proteins	Other	11.305	0.980	Lower sensitivity
PAAD	Ascorbate	Anti-oxidant proteins	Other	11.272	0.968	Lower sensitivity
LUAD	Ascorbate	Anti-oxidant proteins	Other	11.133	0.977	Lower sensitivity
MESO	N-acetyl cysteine	Metabolism	Metabolism	10.866	0.965	Lower sensitivity

3.5 Target Pathway-Specific Sensitivity

Target-pathway analysis showed that there were strong drug response variations. Drugs that target mitosis exhibited the lowest median LN_IC50, with drugs that target protein stability and degradation, cell-cycle regulation, and apoptosis coming next. There were intermediate sensitivity patterns of EGFR, DNA replication, PI3K/MTOR, RTK, and ERK MAPK pathways. On the other hand, WNT signaling, genome integrity, hormone-related pathways, p53 signaling, metabolism, and JNK/p38 signaling were found to have relatively larger median LN_IC50 values. Table 5 shows detailed pattern of responses at a pathway level.

Table 5. Anticancer drug sensitivity according to target pathway

Target pathway	Drugs	Observations	Median LN_IC50	Median AUC
Mitosis	8	5,204	-1.930	0.848
Protein stability and degradation	9	5,705	0.371	0.881
Cell cycle	13	9,362	1.810	0.856
Apoptosis regulation	13	8,724	2.273	0.885
EGFR signaling	7	5,427	2.651	0.953
DNA replication	21	14,242	2.690	0.915
PI3K/MTOR signaling	27	18,333	2.777	0.921
RTK signaling	12	8,524	2.879	0.939

ERK MAPK signaling	15	10,759	3.088	0.931
Chromatin histone acetylation	10	6,576	3.429	0.952
WNT signaling	9	6,143	4.037	0.962
Genome integrity	13	9,844	4.109	0.949
p53 pathway	4	3,045	4.729	0.965
Metabolism	6	3,870	4.835	0.962
JNK and p38 signaling	2	1,534	5.135	0.977

Statistical significance in the differences of LN_IC50 among target-pathway groups was significant (Kruskal -Wallis $H = 21,659.27$, $p = 0.001$). This showed that the compounds that were targeted to various therapeutic pathways had vastly different sensitivity patterns across the cancer cell lines studied.

Figure 3 shows the distribution of unique anticancer drugs in the major target-pathway categories.

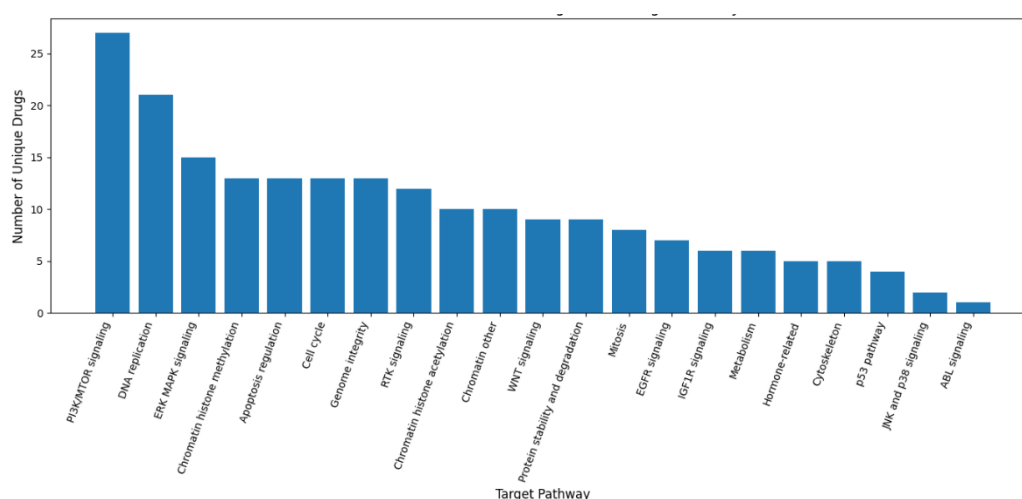


Figure 3. Distribution of Anticancer Drugs Across Target Pathways

The figure indicates that PI3K/MTOR signaling and DNA replication had the highest number of unique anticancer drugs and then ERK MAPK signaling and a number of chromatin- and cell-cycle-related pathways. Conversely, fewer compounds were found to represent JNK/p38 and ABL signaling.

3.6 Association Between Drug-Response Measures

There was a positive monotonic correlation between LNIC50 and AUC which was strong. The analysis using Spearman correlation showed that the coefficient of 0.757 was significant, thus showing that the greater the LNIC50 values; the greater the AUC values. The correlation was statistically significant with $p < 0.001$. These findings coupled with the notable cancer-type and pathway-level differences showed stable differences in pharmacological response between different analytical dimensions. Table 6 summarizes the key inferential statistical results.

Table 6. Summary of inferential statistical analyses

Statistical analysis	Statistic	p-value
Spearman correlation between LN_IC50 and AUC	$\rho = 0.757$	<0.001
Kruskal–Wallis test across cancer types	$H = 10,549.02$	<0.001
Kruskal–Wallis test across target pathways	$H = 21,659.27$	<0.001

4. Discussion

The current study illustrated that anticancer drug sensitivity in GDSC2 cancer cell lines is highly heterogeneous, at the cancer-type level and across molecular target pathways. Several hematological malignancies had a lower median LN50 LNIC50 measurement, whereas a number of solid tumors were more comparable, suggesting that there is less consistency

Volume 01 Issue 03 September 2026

in the sensitivity of the screened compounds. The trend indicates the idea that the response to drugs is highly context-dependent and indicates the biological heterogeneity of cancer models. Extensive pharmacogenomic experiments have also pointed to the fact that the variability in responses in cell lines is very high and that the interpretation of drug-screening data should be done cautiously to be used in translation (Tran and Klau, 2025).

Analysis of cancer/drug showed further significant differences in particular response combinations. Compounds like dasatinib, dapirinad, dactinomycin, romidepsin, docetaxel, vinblastine and SN-38 were found to have strong sensitivity in the chosen hematological malignancies. These results are in line with more comprehensive evidence that clinically-relevant proteins and pathway dependencies can have a strong impact on drug response in cancer cell lines. Zhao et al. (2020) demonstrated that the large-scale characterization of clinically relevant protein targets can provide clear sensitivity trends and enhance the knowledge of therapeutic vulnerabilities. Equally, it was shown by Wang et al. (2022) that the essentiality of genes signatures can assist in explaining drug action mechanisms and determining biologically significant response determinants.

There were also interesting pathway level findings. Mitosis-targeting compounds had the lowest median LN_{IC50}, closely followed by those that targeted protein stability and degradation, cell-cycle regulation and apoptosis. Such findings indicate that the pathways that regulate cell division and survival can serve as widely sensitive areas of therapy in a variety of cancer-related settings. This biological fact is biologically possible since destabilization of mitotic control is capable of causing potent antiproliferative effects in rapidly dividing tumor cells. Yin et al. (2022) also emphasized the therapeutic value of G2/M checkpoint inhibition in esophageal squamous cell carcinoma and exemplified the significance of mitotic control as a vulnerability that is vulnerable to drugs.

On the other hand, WNT signaling, genome integrity, p53 signaling, metabolism and JNK/p38 signaling pathways had relatively high median LN_{IC50} value. These patterns can be indicators of increased complexity of pathways, compensatory signaling or non-uniform reliance among tumor types. Response variation could also be due to epigenetic state. Vural et al. (2021) found correlations between epigenetic molecular factors, DNA methylation, and sensitivity to chemotherapy, showing that drug response can not be determined only based on pathway labels without taking into account the wide scope of molecular control. This is especially so with pathways of genome integrity and chromatin-related processes.

The AUC and LN_{IC50} revealed a strong positive relationship, which meant that the two measures had similar effects on the pharmacological response, and thus the internal consistency of the sensitivity analysis was supported. Nevertheless, these metrics can still be viewed as complementary as opposed to interchangeable. Predictive studies done recently have started to employ integrated genomic and transcriptomic models to enhance drug-response models and mechanistic interpretations. Yu and Fan (2025) found that deep learning can be used to supplement response prediction and biological understanding, whereas Zhou et al. (2024) found that a combination of single-cell sequencing and drug-sensitivity profiling can enhance prognostic and therapeutic interpretation in liver cancer.

These results have implications on precision oncology as they indicate that cancer type and context of therapeutic pathway can affect drug sensitivity. The findings can be used to prioritize candidate drug classes to be evaluated further via experimental means and provide pathway-directed hypothesis generation. Nevertheless, there are a number of limitations to consider. This was analyzed using cell lines in vitro and, thus, might not recapitulate tumor microenvironment effects, patient heterogeneity, pharmacokinetics, or clinical treatment response. Moreover, disproportional representation of drugs and types of cancer can affect comparative trends.

Future research must incorporate GDSC2 drug-response measurements with gene expression, mutation, epigenetic and single-cell measures to enhance biological resolution. Translational relevance would also be reinforced with external validation on patient-derived models, organoids, xenografts or clinical cohorts. More complex multivariate and pathway-sensitive models might further elucidate whether patterns of observed sensitivities are still strong when molecular confounding factors and tumor-specific genomic features are taken into consideration.

5. Conclusion

This study has shown that there is significant sensitivity variability in anticancer drug sensitivity among GDSC2 cancer cell lines, drug combinations and molecular target pathways. The hematological malignancies typically had low LN_{IC50} values compared with most solid tumors, and therefore, were relatively more sensitive to the screened compounds. A number of combinations of cancer and drugs were especially sensitive in response, whereas others were significantly less sensitive. Mitosis, protein stability and degradation, cell-cycle regulation and apoptosis were related with lower median LN_{IC50} values, and pathways such as p53 signaling, metabolism, genome integrity, and JNK/p38 signaling were relatively higher. The high positive correlation between LN_{IC50} and AUC also added to the consistency of the patterns of pharmacological responses. These dramatic variations in the cancer types and target pathways underscored that it is important to remember both the tumor context and therapeutic mechanism in the interpretation of anticancer drug sensitivity. The findings demonstrate the utility of GDSC2 as a large-scale pharmacogenomic tool to determine cancer-specific and pathway-specific response patterns that can be used to inform future hypothesis generation in precision oncology. Yet, due to the in vitro cell-line models used in the analysis, clinical interpretation must be approached with a great deal of care. Further research that incorporates genomic, transcriptomic, epigenetic, and patient-derived datasets may enhance a biological resolution and help prove the existence of the identified therapeutic patterns in more clinically relevant systems.

References

1. Alipour, S. (2024). Genomics of drug sensitivity in cancer (GDSC) [Data set]. Kaggle. <https://www.kaggle.com/datasets/samiraalipour/genomics-of-drug-sensitivity-in-cancer-gdsc>

2. Anushya, A., Alreshidi, A., Varshini, N. H., Venkatachalam, K., Yoo, S., & Cho, J. (2026). Novel explainable deep learning based drug sensitivity prediction for early treatment of breast cancer. *Scientific Reports*, 16(1), 14833.
3. Chawla, S., Rockstroh, A., Lehman, M., Ratther, E., Jain, A., Anand, A., ... & Sengupta, D. (2022). Gene expression based inference of cancer drug sensitivity. *Nature communications*, 13(1), 5680.
4. Chiu, Y. J., Wu, P. Q., & Huang, Y. H. (2026). Comparative Evaluation of Drug Response Metrics for Predicting Cancer Sensitivity Using Transcriptomic Profiles. In *BIO Web of Conferences* (Vol. 232, p. 01001). EDP Sciences.
5. Demirtas Korkmaz, F., Sevim, Y., Duzgun, Z., & Deveci Ozkan, A. (2026). The Metabolic Rheostat Index Uncovers Pathway-Level Coordination, Immunosuppressive Microenvironment Remodeling, and Therapeutic Co-Vulnerabilities in Pancreatic Ductal Adenocarcinoma. *Current Issues in Molecular Biology*, 48(8), 820.
6. Gonçalves, E., Segura-Cabrera, A., Pacini, C., Picco, G., Behan, F. M., Jaaks, P., ... & Garnett, M. J. (2020). Drug mechanism-of-action discovery through the integration of pharmacological and CRISPR screens. *Molecular Systems Biology*, 16(7), MSB199405.
7. Hu, J., Shang, A., Wang, H., Han, L., Geng, L., Miao, Y., & Lu, C. (2026). Investigating the Role of ALPK2 in Endometrial Cancer Progression: From Biological Function to Clinical Translation. *Reproductive Sciences*, 1-16.
8. Huang, S., Hu, P., & Lakowski, T. M. (2021). Predicting breast cancer drug response using a multiple-layer cell line drug response network model. *BMC cancer*, 21(1), 648.
9. Inoue, Y., Lee, H., Fu, T., & Luna, A. (2025). drGT: Attention-guided gene assessment of drug response utilizing a drug-cell-gene heterogeneous network. *ArXiv*, arXiv-2405.
10. Kardamiliotis, K., Karanatsiou, E., Aslanidou, I., Stergiou, E., Vizirianakis, I. S., & Malousi, A. (2022). Unraveling drug response from pharmacogenomic data to advance systems pharmacology decisions in tumor therapeutics. *Future Pharmacology*, 2(1), 31-44.
11. Kusch, N., & Schuppert, A. (2020). Two-step multi-omics modelling of drug sensitivity in cancer cell lines to identify driving mechanisms. *PloS one*, 15(11), e0238961.
12. Li, H., Zhang, R., Tao, W., Cheng, Y., Lin, X., Zhang, J., ... & Zhou, J. (2025). Predictive modeling and functional characterization of the ceRNA regulatory network in cisplatin resistance of non-small cell lung cancer. *Molecular Pharmacology*, 100087.
13. Li, Y., Umbach, D. M., Krahm, J. M., Shats, I., Li, X., & Li, L. (2021). Predicting tumor response to drugs based on gene-expression biomarkers of sensitivity learned from cancer cell lines. *BMC genomics*, 22(1), 272.
14. Mergen, B., Coban, M., Ozkan, S. S., Basaran, O. F., & Ozcan, G. (2026). Drug Sensitivity Prediction Using Machine Learning on Integrated COSMIC, DGIdb, and GDSC Data. *IEEE Access*.
15. Pandit, D., Dhillon, A., Chakrabarty, S., & Bilachi, R. S. (2026). Multi-omics analysis positions DNA2 at the interface of genome integrity programs and tumor behavior in pan-cancer. *Functional & Integrative Genomics*, 26(1), 147.
16. Pellecchia, S., Viscido, G., Franchini, M., & Gambardella, G. (2023). Predicting drug response from single-cell expression profiles of tumours. *BMC medicine*, 21(1), 476.
17. Qu, H., Zhou, P., Yang, Z., Wang, H., Deng, K., Wang, N., ... & Xia, J. (2025). Comprehensive analysis of prognosis and drug sensitivity of programmed cell death pattern-related genes in gastric cancer patients. *Scientific reports*, 15(1), 22535.
18. Rajendran, L. K. K. (2026). Integrative Pharmacogenomic Analysis of Drug Response Heterogeneity Across Cancer Cell Lines: Insights From Large-Scale GDSC Data. *Scientific Culture*, 12(4), 7537-7546.
19. Tang, Y. C., & Gottlieb, A. (2021). Explainable drug sensitivity prediction through cancer pathway enrichment. *Scientific reports*, 11(1), 3128.
20. Tran, N. K., & Klau, G. W. (2025). Drug response prediction: a critical systematic review of current datasets and methods. *Pattern Recognition Letters*.
21. Vural, S., Palmisano, A., Reinhold, W. C., Pommier, Y., Teicher, B. A., & Krushkal, J. (2021). Association of expression of epigenetic molecular factors with DNA methylation and sensitivity to chemotherapeutic agents in cancer cell lines. *Clinical Epigenetics*, 13(1), 49.
22. Wang, W., Bao, J., Zheng, S., Huang, S., Aldahdooh, J., Wang, Y., ... & Tang, J. (2022). A gene essentiality signature for studying the mechanism of action of drugs. *bioRxiv*, 2022-11.
23. Yin, Y., Yu, X., Feng, R., Li, Y., Zhao, Y., & Liu, Z. (2022). Drug Repurposing Applications to Overcome Male Predominance via Targeting G2/M Checkpoint in Human Esophageal Squamous Cell Carcinoma. *Cancers*, 14(23), 5854.
24. Yu, G., & Fan, Q. (2025). Deep learning-driven drug response prediction and mechanistic insights in cancer genomics. *Scientific Reports*, 15(1), 20824.
25. Zhao, W., Li, J., Chen, M. J. M., Luo, Y., Ju, Z., Nesser, N. K., ... & Liang, H. (2020). Large-scale characterization of drug responses of clinically relevant proteins in cancer cell lines. *Cancer cell*, 38(6), 829-843.
26. Zhou, Q., Wu, J., Bei, J., Zhai, Z., Chen, X., Liang, W., ... & Liu, M. (2024). Integration of single-cell sequencing and drug sensitivity profiling reveals an 11-gene prognostic model for liver cancer. *Human Genomics*, 18(1), 132.