A REVIEW ON: PHARMACOGENOMICS - DRIVEN DESIGN OF TARGETED DRUG DELIVERY SYSTEM

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Abstract

The integration of pharmacogenomics into targeted drug delivery systems (TDDS) marks a paradigm shift toward personalized medicine, offering the potential to optimize therapeutic outcomes while minimizing adverse effects. Pharmacogenomics examines the influence of genetic variations—particularly in drug-metabolizing enzymes, transporters, and drug targets—on individual responses to pharmacological agents. These genetic differences significantly contribute to variability in drug efficacy, toxicity, and dosing requirements. By leveraging this knowledge, researchers can design delivery systems that are customized to an individual's genomic profile, enhancing precision and predictability in treatment. Targeted drug delivery systems, including nanoparticles, liposomes, micelles, dendrimers, and antibody-drug conjugates, enable site-specific drug localization and controlled release. These systems, when informed by pharmacogenomic data, can be engineered to overcome drug resistance mechanisms, improve bioavailability, and reduce off-target toxicity. The synergy between pharmacogenomics and advanced drug carriers facilitates the development of "smart" therapeutics that respond to specific genetic or molecular cues, thereby refining disease management—especially in oncology, cardiovascular, and neurodegenerative disorders. This review explores the fundamental concepts of pharmacogenomics, key genetic polymorphisms affecting drug response, and the current landscape of targeted drug delivery platforms. It further discusses how integrating pharmacogenomic data into delivery system design can address existing therapeutic challenges and advance the field of precision medicine. Finally, the review highlights recent advances, clinical applications, and future perspectives in the co-evolution of genomics and drug delivery technologies, underscoring the need for interdisciplinary collaboration to realize the full potential of personalized therapeutics.

Key words: Pharmacogenomics, Personalized medicine, Targeted drug delivery systems (TDDS), Genetic polymorphisms, Nanocarriers

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1.Introduction:

Recent advances in clinical and genomic data collection have led to an unprecedented transformation in medicine, providing a shift from traditional "one-size-fits-all" therapeutics to precision medicine strategies tailored to the patient and his/her unique genomic, lifestyle, and environment. This shift is especially pronounced in the realms of pharmacogenomics and drug delivery where the two combined highlight the dynamic capabilities of customization of treatment strategies(1). Pharmacogenomics is the study of the influence of genetics on drug response. In general, this field is a combination of pharmacology (the science of drugs), and genomics (the study of genes and their functions) to improve drug efficacy and safety. Interindividual variability in drug response, such as suboptimal drug efficacy and adverse drug reactions (ADRs), can often be explained by genetic differences in drug-metabolizing enzymes, drug transporters, and drug targets(2). This knowledge of the presence and type of these genetic polymorphisms means that the most appropriate drug and dose can be selected, reducing trial-and-error prescribing and maximizing therapeutic efficacy. At the same time, Targeted Drug Delivery Systems (TDDS) focus on the localized administration of therapeutic agents at the precise site of action in the body while reducing drug exposure to normal healthy tissues. TDDS improve drug localization,

retention, and controlled release, thus promoting drug therapeutic index and lowering drugs systemic toxicity(3). In many cases, these systems utilize nanocarriers like liposomes, polymeric nanoparticles, micelles, dendrimers, and more recently, biomimetic or stimuli-responsive platforms for accurate delivery. An interesting trend in personalized medicine is the combination of pharmacogenomics with TDDS, creating a concept of pharmacogenomics-driven drug delivery. This strategy includes tailoring drug formulations or delivery vehicles to the genetic profile of the patient(4).

For example, controlled-release systems can be engineered to accommodate high or low metabolism in patients who are carriers of polymorphisms in drug-metabolizing enzymes, such as those in CYP2D6 and CYP2C9. Alternatively, delivery systems can be designed to specifically reach overexpressed receptors encoded by overactive or amplified genes, such as HER2 in breast cancer or EGFR in lung cancer(5,6).

Pharmacogenomics-driven design, which aligns genetic insights with advanced drug delivery technologies, presents multiple benefits:

1.Increased effectiveness by enabling the appropriate drug to find the appropriate target in the appropriate patient.

2.By passing through the genetic predilection to drug biotransformation or transport, it causes less toxicity or ADRs.

3.Patient compliance and outcomes were enhanced when compared to similar drugs due to decreased dosing frequency and improved therapeutic response.

4.Reducing failed treatments and adverse effects/hospitalizations = less expensive health care(7).

This review highlights the convergence of the fields of pharmacogenomics and targeted drug delivery. We start with the scientific underpinnings of pharmacogenomics and TDDS and then examine how genetic data can guide drug delivery design. We describe clinical applications, discuss technological innovations, and outline the hurdles and future directions for this emergent field. Incorporating genomic insights into the development and implementation of drug delivery systems brings us one step closer towards(8)

2.Essentials of Pharmacogenomics:

Pharmacogenomics, which includes pharmacokinetics (absorption, distribution, metabolism, and excretion) and pharmacodynamics (drug–receptor interactions and therapeutic effects), is the study of how the human genome affects drug response. Therapeutic results, medication safety, and the best dosage are all heavily influenced by genetic variations, especially single nucleotide polymorphisms (SNPs).

Drug response is governed by three main gene categories. Drug-metabolizing enzymes (DMEs) first classify people as poor, intermediate, extensive, or ultra-rapid metabolizers based on their metabolic activity, especially cytochrome P450 enzymes like CYP2D6, CYP2C9, and CYP3A4. For instance, CYP2C9 and VKORC1 polymorphisms have a major impact on the dosage requirements for warfarin. Second, the distribution and absorption of drugs are controlled by drug transporters like ABCB1 (P-glycoprotein) and SLCO1B1. These genes' variations may result in changed pharmacokinetics, which may exacerbate chemotherapy resistance or statin-induced myopathy. Third, HER2 and EGFR are two examples of therapeutic targets and receptors that frequently experience mutations or gene amplification, which significantly impacts the effectiveness of treatment, especially in oncology.

Technological developments in genotyping and sequencing have sped up the application of pharmacogenomics. Rapid identification of clinically significant variants is made possible by technologies like next-generation sequencing (NGS) and microarrays. The 1000 Genomes Project, CPIC (Clinical Pharmacogenetics Implementation Consortium), PharmGKB, and other public databases and consortia offer resources and guidelines to help apply these discoveries in clinical settings.

All things considered, pharmacogenomics is an essential first step toward customized treatment. It provides a scientific foundation for maximizing drug efficacy, reducing toxicity, and directing the creation of specialized therapeutic approaches by associating genetic variation with drug response. (9)

3.Polymorphisms in Drug Metabolism and Response:

Through modifications to drug metabolism, transport, and therapeutic targets, genetic polymorphisms have a substantial impact on individual variability in drug response. These variances frequently account for variations in the best dosage, toxicity, and efficacy between patients on the same medication regimen. Drug-metabolizing enzymes, drug transporters, and therapeutic targets are the three general gene classes that control drug response.

3.1Drug metabolizing enzymes (DMEs):

Cytochrome P450 (CYP) polymorphisms are significant interindividual causes of variability. Poor, intermediate, extensive, and ultra-rapid metabolizers are classified using enzymes like CYP2D6, CYP2C9, and CYP3A4. For instance, polymorphisms in CYP2C9 and VKORC1 have direct impacts on warfarin doses required, and poor metabolizers will require much lower doses to prevent bleeding complications. Polymorphisms in CYP2D6 have an impact on the pharmacokinetics of antidepressants, antipsychotics, and opioids and tend to result in an insufficient therapy or unwarranted side effects.(6)

3.2Transporters for drugs:

Absorption, distribution, and elimination of drugs are governed by transport proteins whose genetic variations could alter pharmacokinetics. For instance, polymorphisms in SLCO1B1 encoding liver transporter OATP1B1 have been related to low uptake of statins and subsequent statin-associated myopathy. Correspondingly, polymorphism in ABCB1 (p-glycoprotein) is responsible for affecting efflux of drugs such as anticancer agents and antiepileptics and causing chemotherapeutic resistance and variability in seizure treatment.

3.3Therapeutic targets/receptors:

Gene mutations or amplifications in genes coding for drug targets may significantly affect treatment outcomes. Oncologists recognize overexpression of HER2 in breast cancer to select patients responsive to therapy with trastuzumab and EGFR mutation in non-small cell lung cancer to identify patients responsive to EGFR kinase inhibitors like gefitinib. Conversely, patients harbouring no such genetic mutation may be refractory to therapy and hence require pre-therapy molecular profiling. Together, polymorphisms in drug-metabolizing enzymes, transporters, and therapeutic targets signify the incorporation of genetic testing into clinical practice. Insight into these differences lends a rational foundation to individualized therapy, reduction in adverse effects, enhancement in efficacy, and opening the portal to pharmacogenomics-based systems of drug delivery.(10)

4.Genomic Tools and Resources:

The emergence of genotyping and sequencing technologies like microarrays, and more recently next-generation sequencing (NGS), has enabled detection of clinically relevant variants. PharmGKB, CPIC (Clinical Pharmacogenetics Implementation Consortium), and 1000 Genomes Project are examples of public databases and consortia that offer information and recommendations on pharmacogenomic findings to assist in bringing them to the clinical setting(11).

5.Clinical Relevance:

Pharmacogenomics has transformed clinical decision-making by linking genetic variation and treatment outcomes. Traditional prescribing is at times trial-and-error and leads to suboptimal efficacy or ADRs. Tailoring drug therapy to patient genotype by pharmacogenomic data maximizes safety and efficacy. Another key benefit of pharmacogenomics is optimizing dosing of drugs. The polymorphisms in cytochrome P450 enzymes like CYP2D6, CYP2C9, and CYP2C19 directly affect the rate of drug metabolism and define whether a patient is an ultra-rapid or poor metabolizer. For instance, polymorphisms in CYP2C9 and VKORC1 considerably affect warfarin dosages required by a patient, and polymorphism in CYP2C19 affects the activation of clopidogrel and response to therapy.

This information helps in tailoring therapy to the individual patient and decreases risk of bleeding or thrombosis and failure of treatment. Pharmacogenomics plays an equal role in preventing life-threatening ADRs. One such established case is pre-treatment screening with HLA-B57:01 to prevent life-threatening hypersensitivity reactions with abacavir. Another is screening in Asian populations to prevent Stevens–Johnson syndrome induced by carbamazepine and associated with HLA-B15:02. Pharmacogenomic screening in predisposed individuals enhances patient safety and prevents avoidable complications. Aside from clinical safety, pharmacogenomics enhances patient compliance and outcomes in therapy. Patients with less side effects and favourable treatment response are likely to be compliant with therapy. This is best illustrated in psychiatry, where dosing of antipsychotics and antidepressants using CYP2D6 has enhanced response and tolerance rates. The same advantage is noted in oncology, where testing for HER2 or EGFR is used to direct therapy with agents like trastuzumab and gefitinib to patients best likely to derive their benefits. Another significant aspect is the economical effect. Pharmacogenomics saves health costs by evading futile treatment, reducing hospital admissions due to ADRs, and decreasing time to realize therapeutic efficacy. For long-standing illnesses like cancer, cardiovascular illness, and autoimmune diseases, pharmacogenomic-driven therapy besides enhancing the quality of life reduces the overall burden on healthcare systems as well (9).

6.Targeted Drug Delivery Systems (TDDS):

Targeted delivery systems of drugs (TDDS) are engineered to deliver therapeutic agents selectively to diseased cells or tissues in an effort to improve efficacy and reduce off-target effects. As opposed to traditional administration of drugs systemically through the whole body, TDDS are designed to deliver the drug selectively to the site of action and minimize unnecessary exposure to healthy tissues. This selective targeting elevates the therapeutic index, increases patient safety, and usually decreases dosing frequency.(12).

6.1Targeted Drug Delivery Principles:

The fundamentals of TDDS may be broadly classified as spatial targeting, temporal targeting, and stimulus-responsive release. Spatial targeting includes targeting drugs to organs, tissues, or cells by active or passive mechanisms. The temporal targeting ensures release of drugs in concordance with the progression of disease or biological rhythms so as to provide sustained and controlled action. Stimuli-

responsive delivery systems release their cargo in response to receipt of internal stimuli such as pH, redox status, or enzymes, or external stimuli such as temperature, light, ultrasound, or magnetic fields. These strategies enable site-specific delivery of drugs in accordance with the pathological microenvironment.(13).

6.2Targeting Strategies:

TDDS can be broadly classified based on their targeting approach into:

6.2.1Passive Targeting:

Passive targeting exploits the intrinsic physical and chemical properties of the drug and target tissue, letting the drug be guided to its target, using mechanisms such as:

6.2.1.1Enhanced Permeability and Retention (EPR) Effect: In tumor tissues, characterized by leaky blood vessels and poor lymphatic drainage, larger molecules like nanoparticles can accumulate adequately, increasing the amount of drug at the tumor site.

6.2.1.2Affinity-Based Targeting: In this, a ligand conjugated to the drug delivery system specifically attaches to specific receptors present on the target cell(14).

6.2.2Active Targeting:

6.2.2.1Receptor-Mediated Targeting: Drugs are concentrated at sites like tumors by binding drug carriers to overexpressed receptors on target cells. Ashish Ghera wrote: Antibody-Drug Conjugates: These combine monoclonal antibodies with cytotoxic drugs that act on specific cells, increasing precision and lowering toxicity. Peptide-Drug Conjugates (PDCs) — These peptides are conjugated to cytotoxic drugs to enable targeting and delivery to cell receptors. · Aptamers: These are single stranded oligonucleotides that bind with specific proteins to aid highly targeted delivery of drugs(13,14).

6.2.3Stimuli-Responsive Targeting:

Carriers can release the payload (drug or agent) by responding to an internal (pH, redox, enzymes) or external (temperature, ultrasound, magnetic fields) stimuli. Lastly we will discuss drug carrier systems, that are sensitive to certain stimulus(12).

6.3Carriers Used:

Some of the most common platforms of nanocarriers: Colloidal drug delivery systems are nanoscale vesicles that carry drugs to specific locations and release them, also altering their distribution. They are classified as, vesicular or microparticulate system**:** Novel vesicular drug delivery systems operate by delivering drugs at a predetermined rate and site (based on treatment). Nanosomes (liposomes, niosomes, transferosomes, and ethosomes) are novel vesicular carrier systems developed for targeted delivery. Vesicular characteristics, preparation therapeutic applications are each carrier generations(8).

6.3.1Liposomes : In this techniques, Storage and Liposome are nanoscale lipoidal vesicles with a bilayer membrane structure enclosing an aqueous core that can entrap hydrophilic and lipophilic drugs It is used in targeted oral, topical, and pulmonary delivery types They are made up of natural/synthetic phospholipid, cholesterol, and polymer-conjugated lipids that help to lower toxicity due to the presence of these physiological lipids(12).

6.3.2Niosomes: Niosomes are nanoscale drug delivery systems, consisting of a bilayer of non-ionic surfactants, further improving therapeutic properties by decreasing toxicity and targeting specific cells. Niosomes have similar physicochemical properties as liposomes but differ in composition (they are

composed of surfactants instead of phospholipids). Niosomes are more stable and do not require special preparation or storage conditions, which leads to lower production costs Liposomes and niosomes have limitations for transdermal delivery such as poor skin permeability, vesicle breakage, drug leakage, and aggregation(15).

6.3.3Transferosomes: Transferosomes is an ultra-flexible lipid vesicle that veils for a site while penetrating skin without disruption. It consists of an aqueous core and a lipid bilayer with edge-activators such as sodium cholate, span 80, and Tween 80 to improve deformability and skin penetration. These vesicles also cause a disorder on stratum contribulum intercellular lipids at membrane, promoting drug delivery. Where do you apply it to improve site specificity, drug safety, and for skin diseases, carrying proteins, peptides (insulin) and vaccines, reducing doses(13).

6.4Advantages of TDDS:

Enhanced therapeutic effectiveness: Local delivery allows for a higher concentration of the drug at the site of disease. Decreased systemic toxicity: Limit unwanted exposure of healthy tissues to cytotoxic drugs. It allows controlled and sustained release which ensures prolonged action and reduced frequency of dosing. Prolonged drug delivery systems offer extended, gradual release, eliminating frequent dosing and boosting patient adherence(14).

6.5Limitations and Challenges of TDDS:

THE PROMISE OF TDDS IS DIMMED BY THREE CHALLENGES: Biological barriers: blood-brain barrier (BBB) and tumour microenvironment. Nonspecific accumulation results in off-target effects. Manufacturing scalability and reproducibility. Stability and shelf-life during storage and use. Immunogenicity and clearance from the reticuloendothelial system (RES)(13).

7.Pharmacogenomics-Driven Design of TDDS:

Integration of pharmacogenomics into targeted drug delivery systems (TDDS) represents an important milestone in the evolution of precision medicine. Not only do genetic differences influence medication selection and dosing but also delivery method design so that therapy may be tailored to the individual patient's profile. Through the alignment of nanocarrier technology with pharmacogenomic data, therapy may be optimized for efficacy, safety, and patient acceptance.

7.1Individualization of Drug Formulation:

Not only do genetic polymorphisms guide drug choice and dose, but they also guide delivery strategies:

In contrast, extended-release systems can prevent accumulation in poor metabolizers. For ultra-rapid metabolizers, immediate-release formulations, or multiple doses per day, may be necessary. Nanocarriers may circumvent metabolism (e.g. CYP450) or alterations in drug transporters (es. P-gp) due to polymorphisms(10).

7.2Selection of Targets Based on Genotype:

Genetic profiling reveals overexpressed receptors or mutations that may serve as drug targets:

HER2 in breast cancer: Overexpression informs trastuzumab-labelled nanoparticles. Facilitated EGFR-targeted nanocarriers in NSCLC in view of EGFR mutations.

BCR-ABL fusion gene: Targeting success in chronic myeloid leukemia by delivering tyrosine kinase inhibitors(16).

7.3Overcoming Genetic Resistance:

Genomic variations often induce drug resistance: Avoiding recognition by efflux pumps (e.g. ABCB1), by using nanocarriers. Co-delivery of chemotherapeutic agents with gene-silencing tools (siRNA, antisense oligonucleotides) to knock down resistance genes. Nanoparticles targeting drug-resistant cancers that deliver paclitaxel and siRNA against MDR1 gene(17).

8.Clinical Applications:

Pharmacogenomic information integration with Targeted Drug Delivery Systems (TDDS) has been established to possess exceptional promise in many fields of therapy. Tailoring formulations in accordance with genetic differences and through nanocarrier technology enables therapeutic approaches to possess enhanced efficacy, lessened toxicity, and greater patient compliance. Top profile applications exist in oncology, cardiovascular therapy, neurology, infections, pain therapy, autoimmune disease, and organ transplantation.

8.1Oncology:

Oncology is the foremost developed field of pharmacogenomics-based TDDS. Various genetic markers like breast cancer HER2 amplification and lung cancer EGFR mutation have been effectively targeted by nanocarriers. For example, chemotherapeutics like doxorubicin or paclitaxel is directly transported to HER2-overexpressing cells by trastuzumab-conjugated nanoparticles, whereas EGFR-targeted liposomes improve gefitinib delivery in non-small cell lung cancer(18). Besides these, BRCA1/2 alterations direct PARP inhibitor application and are encapsulated in nanocarriers to be released in a tumor-specific manner. Co-delivery strategies using cytotoxic agents in combination with gene-silencing agents are in the process of being developed to circumvent drug resistance.(18).

8.2Cardiovascular diseases:

Pharmacogenomic variants in CYP2C9 and VKORC1 have disproportionate impacts on warfarin dosing in cardiovascular disease, while CYP2C19 polymorphisms influence clopidogrel response. Controlled release by using nanocarriers can achieve stable delivery of anticoagulants and reduce dosing variability and resultant risk in high-risk genotypes. This decreases bleeding or thrombosis complications and accomplishes more definitive therapeutics outcomes.(19)

8.3Psychiatry and Neurology:

Genotype-Guided Dosing Improves Response and Reduces Side Effects of Antidepressants and Antipsychotics. Polymorphisms in CYP2D6 are important in the metabolism of SSRIs, TCAs, and certain antipsychotics, such as risperidone. Nano formulations that enhance intranasal delivery or have systems to overcome the blood-brain barrier (BBB)(20)

8.4Infectious Diseases:

pharmacogenomics is implicated in individualizing antiviral therapy. For instance, pre-abacavir testing for HLA-B*57:01 avoids hypersensitivity reactions, and polymorphisms in UGT1A1 affect antiretroviral medication pharmacokinetics such as in cabotegravir. Adherence and side effects are enhanced and mitigated in HIV therapy by optimizing long-acting injectable formulations in accordance with these genetic polymorphisms and administered through nanocarriers.(21).

8.5Pain Management:

Codeine and CYP2D6: Codeine requires conversion to morphine but depends on CYP2D6 activity. Poor/ultra-rapid metabolizers have treatment failure or toxicity, respectively. Pharmacogenomics helps with alternative drug selection, while TDDS may be tailored to achieve optimized release and safer delivery(22).

8.6Autoimmune and Inflammatory Diseases:

The polymorphism of the MTHFR and ABCB1 genes modulates the response to methotrexate. Liposomal or folate-targeted nanoparticle formulations are designed to deliver methotrexate selectively to sites of inflammation to reduce systemic exposure and toxicity. Similarly, genotype-directed therapy is improving outcomes in rheumatology and dermatology.(23).

8.7Organ Transplantation:

Tacrolimus: Polymorphisms of CYP3A5 were thought to affect tacrolimus metabolism. Pharmacogenomic-guided dosing is in use. Such targeted delivery systems (e.g. lipid nanoparticles) are being investigated to increase bioavailability and reduce nephrotoxicity. Anticancer Immunotherapy(24)

8.8Immune checkpoint inhibitors (ICI): Polymorphisms related to PD-1/PD-L1 genes may affect response to ICIs. Pharmacogenomic screening can be combined with nanoparticle-based immunomodulators, which can improve the response rate and reduce immune-related adverse events(25).

9.Design Paradigms and Technology:

9.1Bioinformatics and Modelling: Also on the pharmacokinetics front, genetic data can be used in silico modelling to predict pharmacokinetics.AI/ML systems combine genotype, phenotype, and pharmacological information to suggest drug formulations. Examples: Rastering time lapse images of nanoparticle uptake to classify for different genetic backgrounds with deep learning algorithms(26).

9.2Theranostics:

Theranostic systems simultaneously relate to therapy and diagnostics: Nanocarriers modified with imaging agents (e.g., fluorescent the dyes, MRI contrast) for real-time tracing. It then proceeds to a smart delivery phase (release of drugs in response to biomarker expression (e.g., miRNA triggers)(27)

10.Conclusion:

Pharmacogenomics is a key aspect of personalized medicine for the rational construction of targeted drug delivery systems. Pharmacogenomics makes it possible to adjust therapeutic efficacy to avoid undesirable drug responses by combining an individual's genomic profile with drug formulation and delivery approaches(28). Such multi-Omics synergy can also be used to guide drug selection and dosing or inform the rational design of nanocarriers and biomaterials based on genetic biomarkers(27). Our recent advances have shown that the data pipeline can be used to improve the precision of therapy for cancers, cardiovascular disease, neurological disorders, and autoimmune diseases, particularly when used in conjunction with modernized drug delivery platforms, including liposomes, nanoparticles, and antibody-drug conjugates.(29) Genetics drives these technologies, enabling site-specific delivery, controlled release, and improved bioavailability of therapeutics(30).

ABBREVIATIONS:

1. ABCB1 – ATP Binding Cassette Subfamily B Member 1
2. ABL – Abelson Murine Leukaemia Viral Oncogene Homolog
3. ADRs – Adverse Drug Reactions
4. AI – Artificial Intelligence
5. AUC – Area Under the Curve
6. BCR – Breakpoint Cluster Region
7. BCRP – Breast Cancer Resistance Protein
8. BBB – Blood-Brain Barrier
9. CAR-T – Chimeric Antigen Receptor T-cell
10. CDSCO – Central Drugs Standard Control Organization
11. CNS – Central Nervous System
12. CPIC – Clinical Pharmacogenetics Implementation Consortium
13. CRISPR-Cas9 – Clustered Regularly Interspaced Short Palindromic Repeats-associated protein 9
14. CYP – Cytochrome P450
15. CYP450 – Cytochrome P450 Enzymes
16. DDS – Drug Delivery Systems
17. DPD – Dihydropyrimidine Dehydrogenase
18. DSMB – Data Safety Monitoring Board
19. EGFR – Epidermal Growth Factor Receptor
20. EMA – European Medicines Agency
21. EPR – Enhanced Permeability and Retention
22. FDA – Food and Drug Administration
23. G6PD – Glucose-6-Phosphate Dehydrogenase
24. GWAS – Genome-Wide Association Studies
25. HER2 – Human Epidermal Growth Factor Receptor 2
26. HLA – Human Leukocyte Antigen
27. ICI – Immune Checkpoint Inhibitor
28. ICD – International Classification of Diseases
29. IVIVC – In Vitro-In Vivo Correlation
30. LNPs – Lipid Nanoparticles

31. mAb – Monoclonal Antibody
32. MDR1 – Multidrug Resistance Protein 1
33. miRNA – MicroRNA
34. ML – Machine Learning
35. MRI – Magnetic Resonance Imaging
36. MRP – Multidrug Resistance-associated Protein
37. mRNA – Messenger RNA
38. MTHFR – Methylenetetrahydrofolate Reductase
39. MTX – Methotrexate
40. NCI – National Cancer Institute
41. NGS – Next-Generation Sequencing
42. NIR – Near Infrared
43. NPs – Nanoparticles
44. NSCLC – Non-Small Cell Lung Cancer
45. PAMAM – Poly(amidoamine)
46. PARP – Poly (ADP-ribose) Polymerase
47. PBPK – Physiologically Based Pharmacokinetic
48. PD – Pharmacodynamics
49. PDX – Patient-Derived Xenograft
50. PEG – Polyethylene Glycol
51. PK – Pharmacokinetics
52. PLGA – Poly (lactic-co-glycolic acid)
53. P-gp – P-glycoprotein
54. QSP – Quantitative Systems Pharmacology
55. QC – Quality Control
56. ROS – Reactive Oxygen Species
57. siRNA – Small Interfering RNA
58. SNPs – Single Nucleotide Polymorphisms
59. TDM – Therapeutic Drug Monitoring
60. TDDS – Targeted Drug Delivery System
61. TPMT – Thiopurine Methyltransferase

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The authors declare no competing interests.

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