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Advances in Targeted Drug Discovery: A Path Towards Precision Medicine

ARHAM ALI[1], SUFYAN ARIF[2], ISRAR AHMAD[3], SHABBIR HUSSAIN[3], AZHAR SHABIR[4], AQSA AFZAL[5], ARSLAN RASOOL[2], MUHAMMAD TJAMMAL REHMAN[*6]

[1]Faculty of Veterinary Medicine, Universitat Autònoma de Barcelona, Cerdanyola del Vallès, Spain
[2]Department of Biochemistry, University of Agriculture, Faisalabad, Pakistan
[3]Institute of Chemistry, Khwaja Fareed University of Engineering and Information Technology, Rahim Yar Khan, Pakistan
[4]Institute of Biochemistry and Biotechnology, PMAS Arid Agriculture University, Rawalpindi
[5]Department of Chemistry, University of Agriculture, Faisalabad, Pakistan
[6]Department of Biochemistry and Biotechnology, The University of Faisalabad, Faisalabad, Pakistan
[*]Corresponding author: tjammalrehman.bio@tuf.edu.pk

ABSTRACT: Customized medical treatments for each patient, taking into consideration their distinct genetic, biochemical, environmental, and lifestyle factors, is the goal of the new field of precision medicine. The aim of targeted drug development, a key component of precision medicine, is to create therapies that specifically alter particular molecular targets linked to diseases. Significant progress towards the cure of autoimmune diseases and cancer has been made as a result of recent developments in the fields of genomics, proteomics, artificial intelligence, and nanomedicine. It has made it possible to find genetic variants associated with illnesses and create biomarkers for prognosis, diagnosis, and treatment choice. The field of precision medicine relies heavily on pharmacogenomics, which is the investigation of how genetic variations affect drug responses. It makes it possible to create targeted medications with decreased toxicity and increased specificity. Case studies demonstrate the effectiveness of genomic-guided treatments, such as imatinib for chronic myeloid leukemia and trastuzumab for HER2-positive breast cancer. The creation of medications that are specific to particular disease subtypes is dictated by genomic information, as shown by these medicines. The field of drug discovery has been transformed by advanced technologies such as genome sequencing, proteomics, metabolomics, high-throughput screening, structural biology, and rational drug design. They give the means to find targets, develop medications, and improve therapy. Precision medicine still confronts obstacles despite these developments, such as implementation costs, ethical issues, data security, and discriminatory risks. The field becomes much more complex due to drug resistance mechanisms and the requirement for improved integration of drug development. Precision medicine has many advantages, but in order to fully realize its potential and guarantee that everyone has access to individualized healthcare, these issues must be resolved.

Keywords: Drug Discovery, precision medicine, breast cancer, Genomic Revolution, resistance

INTRODUCTION

Precision medicine is a novel and cutting-edge field that aims to tailor medical interventions for specific individuals or patient groups according to their distinct molecular, genetic, environmental, and lifestyle features (Joyner and Paneth, 2019). Because it recognizes and considers the inherent diversity and complexity of human biology as well as the pathophysiology of illnesses, this approach has enormous promise to improve disease prevention, diagnosis, and treatment (Duan et al., 2024). Targeted drug discovery is a key component of precision medicine, as it is essential to the identification and development of novel therapeutic medicines that can selectively alter certain molecular targets or pathways that contribute to the development or progression of diseases (Pan et al., 2023). Compared to conventional pharmaceuticals, targeted therapies have many benefits, such as increased efficacy, less toxicity, fewer side effects, and improved patient adherence to treatment plans (Ahmad, 2020).

Numerous innovative techniques and technologies, including genomics, proteomics, artificial intelligence, and nanomedicine, have contributed to the development of focused drug discovery (Ho et al., 2019). The progress gained in cancer treatment is one example of how these developments have resulted in important discoveries in the context of various illnesses. However, the sector still faces a number of challenges and possibilities, especially in the area of enhancing target validation and identification (Quazi, 2022). With a focus on the most promising targets, technologies, and methodologies that have surfaced in the previous five years, the article offers a comprehensive examination of the most recent developments in precision medicine targeted drug discovery (Louie et al., 2021). We also explore the current difficulties and potential opportunities, stressing the need for patient-centered approaches, interdisciplinary collaboration, easy data integration, artificial intelligence integration, and complete biomarker validation (Hartl et al., 2021).

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HISTORICAL PERSPECTIVE

Numerous scientific disciplines have contributed to the lengthy and intricate history of drug discovery. The first medications were from natural sources, including plants, animals, and minerals, and were frequently used in experimentation without a thorough understanding of how they worked. Throughout the 19th and 20th centuries, advances in modern chemistry and pharmacology made it possible to synthesize and characterize novel compounds with specific biological activities, as well as the elucidation of their molecular targets and modes of action (Drews, 2000). However, most of these drugs were still designed based on trial-and-error approaches, with limited selectivity and specificity for their intended targets, resulting in suboptimal efficacy and undesirable side effects (Hughes et al., 2011).

The emergence of precision medicine as a paradigm shift in drug discovery was driven by the advances in molecular biology, genomics, proteomics, and bioinformatics in the late 20th and early 21st centuries. These technologies enabled the identification and characterization of the molecular alterations that underlie various diseases, especially cancer, and the development of drugs that target these alterations specifically (Collins and Varmus, 2015). Precision medicine aims to tailor the treatment to the individual patient's genetic and molecular profile, thereby increasing the likelihood of therapeutic response and minimizing toxicity (Jameson and Longo, 2015). Precision medicine also encompasses the use of biomarkers to stratify patients into subgroups based on their predicted response or resistance to a given drug, as well as to monitor the efficacy and safety of the treatment (Colburn, 2003).

Targeted drug discovery is a key component of precision medicine, as it focuses on designing drugs that interact with specific molecular targets that are involved in the pathogenesis or progression of a disease. Targeted drugs can be classified into two main categories: small molecules and biologics. Small molecules are low-molecular-weight organic compounds that can bind to the active sites or allosteric sites of enzymes, receptors, or other proteins, modulating their activity or function. Biologics are large-molecular-weight molecules that are derived from living organisms or cells, such as antibodies, cytokines, growth factors, or vaccines, that can bind to extracellular targets or elicit immune responses (Reichert et al., 2005). Targeted drug discovery involves several key steps, including preclinical testing, clinical trials, regulatory approval, target discovery and validation, and lead identification and optimization (Hughes et al., 2011).

Targeted drug discovery has achieved remarkable success in various therapeutic areas, including oncology, immunology, infectious diseases, cardiovascular diseases, and neurodegenerative diseases. Some examples of targeted drugs that have revolutionized the treatment of these diseases are imatinib for chronic myeloid leukemia (Druker et al., 2006), trastuzumab for HER2-positive breast cancer, rituximab for non-Hodgkin's lymphoma, sofosbuvir for hepatitis C virus infection, ivabradine for chronic heart failure, and aducanumab for Alzheimer's disease (Hochhaus et al., 2009). However, many challenges and limitations hinder the development and application of targeted drugs, such as target redundancy and heterogeneity, drug resistance and toxicity, pharmacokinetic and pharmacodynamic variability, biomarker validation and implementation, ethical and regulatory issues, and cost-effectiveness and accessibility (Workman et al., 2017). Therefore, further research and innovation are needed to overcome these challenges and to realize the full potential of targeted drug discovery for precision medicine (Fayad et al., 2013).

TARGET IDENTIFICATION AND VALIDATION

Target identification and validation are crucial steps in the development of targeted therapies for precision medicine. Target identification refers to the process of discovering and characterizing the molecular targets that are involved in the pathogenesis of a disease or a phenotype. Target validation refers to the process of demonstrating the causal relationship between the target and the disease or the phenotype, and assessing the potential therapeutic benefits and risks of modulating the target (Ross et al., 2016). Several technologies and approaches have been employed for target identification and validation, such as genomics, proteomics, and bioinformatics. Genomics is the study of the structure, function, and evolution of genomes, which are the complete set of genetic information in an organism. Genomics can reveal the genetic variations and mutations that are associated with diseases or phenotypes such as insertions, deletions, translocations, copy number changes, and single nucleotide polymorphisms (SNPs) (Stratton et al., 2009). Proteomics is the study of the structure, function, and interactions of proteins, which are the main effectors of biological processes. Proteomics can identify the proteins that are differentially expressed or modified in diseases or phenotypes, such as enzymes, receptors, signaling molecules, and transcription factors (Nakagawa et al., 2015). Bioinformatics is the application of computational methods to analyze and integrate biological data, such as genomic, proteomic, transcriptomic, and metabolomic data. Bioinformatics can provide insights into the molecular mechanisms and pathways that underlie diseases or phenotypes, and identify potential targets for intervention (Shuken, 2023).

Biomarker discovery is another important aspect of target identification and validation for precision medicine. Biomarkers are measurable indicators of biological processes or states, such as gene expression, protein levels, metabolites, or physiological parameters. Biomarkers can be used for various purposes, such as diagnosis, prognosis, prediction of response or resistance to therapy, monitoring of disease progression or treatment efficacy, and stratification of patients into subgroups based on their molecular profiles (Samal et al., 2021). Biomarker discovery involves the identification and validation of biomarkers that are relevant for a specific disease or phenotype, using various techniques such as genomics, proteomics, metabolomics, imaging, or biosensors (Sarwar et al., 2016).

Preclinical models are essential tools for target identification and validation for precision medicine. Preclinical models are experimental systems that mimic the

biological features and behaviors of human diseases or phenotypes *in vitro* or *in vivo* (Darzentas, 2010). Preclinical models can be used to test the effects of modulating potential targets on disease or phenotype outcomes, such as cell viability, proliferation, differentiation, migration, invasion, apoptosis, angiogenesis, inflammation, immune response, metastasis, or tumorigenesis (Long and Tian, 2019). Preclinical models can also be used to evaluate the pharmacokinetics, pharmacodynamics, safety, toxicity, and efficacy of candidate drugs that target specific molecules or pathways (Hartl et al., 2021). Preclinical models can be derived from various sources, such as cell lines, primary cells, organoids, tissues, animals (e.g., rodents), or humanized models (e.g., xenografts) (Hidalgo et al., 2014).

THE GENOMIC REVOLUTION

The advent of high-throughput technologies for sequencing and analyzing the human genome has ushered in a new era of biomedical research and drug discovery (Adachi and Lieber, 2002). The ability to identify the genetic variations that underlie human diseases and drug responses has opened up new avenues for developing more effective and personalized therapies. Human genome sequencing has also enabled the identification of biomarkers, which are molecular indicators of disease states or drug responses. Pharmacogenomics aims to optimize drug therapy by taking into account the individual's genetic makeup, as well as other factors such as age, gender, lifestyle, and environment. This review summarizes the current state and prospects of targeted drug discovery based on the principles of pharmacogenomics and precision medicine (Daly et al., 2001).

Human genome sequencing and its impact

The Human Genome Project, completed in 2003, was a landmark achievement that provided the first comprehensive map of the human genome, consisting of about 3 billion base pairs of DNA (Liao et al., 2005). Since then, advances in sequencing technologies have enabled rapid and cost-effective generation of genomic data for individuals and populations. These data have revealed the extent and nature of genetic diversity among humans, as well as the genomic alterations that cause or contribute to various diseases (Pavlopoulos et al., 2013). Biomarkers can be used for diagnosis, prognosis, prediction, and monitoring of diseases and therapies. For example, biomarkers can help to stratify patients into subgroups based on their molecular profiles, and to select the most appropriate drugs or doses for each subgroup (Khoury et al., 2007).

Pharmacogenomics and individualized treatment

Pharmacogenomics is the study of how genetic variations affect drug responses, such as efficacy, safety, and toxicity. Pharmacogenomics can facilitate the development of targeted drugs, which are designed to modulate specific molecular targets that are involved in disease pathogenesis or drug action. Targeted drugs can offer several advantages over conventional drugs, such as higher specificity, lower toxicity, and reduced drug resistance. However, targeted drugs may also have limitations, such as heterogeneity, complexity, and redundancy of molecular pathways, as well as inter- and intra-tumor variability. Therefore, targeted drugs need to be combined with appropriate biomarkers to ensure their optimal use and benefit (Roses, 2000).

Case studies highlighting genomic-guided therapies

Several examples of successful genomic-guided therapies have emerged in recent years, especially in the field of oncology. For instance, trastuzumab is a monoclonal antibody that targets the human epidermal growth factor receptor 2 (HER2), which is overexpressed in about 20% of breast cancers (Dancey and Chen, 2006). Trastuzumab has been shown to improve survival and reduce recurrence in patients with HER2-positive breast cancer when used in combination with chemotherapy. The selection of patients for trastuzumab treatment is based on the detection of HER2 amplification or overexpression by immunohistochemistry or fluorescence *in situ* hybridization (Sawyers, 2008).

Another example is imatinib, a small molecule inhibitor of the BCR-ABL tyrosine kinase, which is a fusion protein resulting from a chromosomal translocation in chronic myeloid leukemia (CML). Imatinib has been shown to induce complete remission and prolong survival in patients with CML when used as a first-line therapy. The diagnosis of CML and the monitoring of imatinib treatment are based on the detection of the BCR-ABL fusion gene by polymerase chain reaction or cytogenetic analysis (Slamon et al., 2001). These case studies demonstrate how focused medication development and use for particular disease subtypes can be guided by genetic information. Nonetheless, there are still a lot of obstacles to overcome and chances for this profession to advance and innovate. Finding new targets and biomarkers, creating innovative medication delivery systems and combination strategies, combining multi-omics data and computational techniques, conducting clinical trials and empirical evidence studies are a few of the current research objectives (Romond et al., 2005).

TECHNIQUES AND TECHNOLOGIES

Rapid technological advancements are enabling the creation of new treatments and broadening the toolkit available for precision medicine. Developments in liquid biopsies, which examine blood-derived cells, proteins, DNA, RNA, or vesicles, have drawn special attention for their potential to provide insights into the biology of tumors and their metastases (Seyhan and Carini 2019). Personalized medicines based on genetic differences are becoming a reality because to advances in DNA sequencing that have combined previously unheard-of accuracy with low cost. In order to further promote tailored treatments, remarkable progress has been made in the creation of biological medicines. The development of biological therapeutic therapies that will aid in the advancement of precision medicine is making use of a variety of innovative technologies (Maggi et al., 2016).

High-throughput screening

One of the most current techniques in drug design is high-throughput screening (HTS), which can be applied in the

chemical and biological sciences. Due to the application of robots in this approach, Numerous chemical compound studies can be completed quickly with the use of detectors and computer programs that manage the entire process. It can identify 100,000 chemicals every day. More often, the HTS approach is used in combination with analytical methods like NMR or linked methods like LC-MS/MS. It makes it possible to determine the toxicity of such structures and to examine the rate of affinity for targets or the level of toxicity with regard to the conjugation of nanoparticles with pharmaceuticals. The downsizing of all systems enables the possibility of measuring cytotoxicity in this way, thus greatly advancing precision medicine (Szymański et al., 2011).

Genomic sequencing and profiling

Preclinical and clinical elements of drug development, target discovery, and advancement can be aided by genetic and genomic knowledge. Prioritizing therapeutic targets is based on the importance of bulk and single-cell gene expression data for determining a target's biological relevance, the contribution of population genomics to target discovery, and genome-wide CRISPR editing (Cardon and Harris, 2016). In genomics, exome and whole genome sequencing can be compared using genotyping arrays. Additionally, transcriptomics can be utilized to handle data from biomarker selection and pharmacological perturbation. Furthermore, target identification, mechanism of action, and the idea of gene-to-drug mapping can all be accomplished with CRISPR screens. The likelihood that a medicine will be developed and approved is increased when genetic assistance is utilized (Spreafico et al., 2020).

Proteomics and metabolomics

By examining its constituents in the context of immunohistochemistry, biochemistry, metabolomics, and proteomics, an effort is being made to address the advantages of contemporary biomedical methodologies in order to improve therapeutic efficacy and lessen the negative effects of conventional medicine (Lill et al., 2021). In this sense, by targeting several sites, the DGR combination has a more potent therapeutic impact. Therefore, DGR has a synergistic/additive effect, regulates molecular networks through target proteins, intensifies dynamic changes in metabolic biomarkers, and activates both intrinsic and extrinsic pathways (Yang et al., 2023).

Structural biology and rational drug design

A crucial technique for quicker and more economical medication design is structure-based drug design. In contrast to the conventional strategy, which has yielded hundreds of new targets and potential for further drug discovery. The need to manage the "big data" produced by combinatorial chemistry presents a significant challenge in this scenario. Deep learning and artificial intelligence (AI) are vital for the statistical machine learning method's analysis and systemization of bigger data sets (Lee et al., 2018). The process of finding new drugs, including medicinal chemistry, is greatly impacted by advanced AI-based machine learning techniques. Virtual screening and de novo drug design are currently available techniques and algorithms for structure-based drug design, with a focus on AI and deep learning-based approaches for drug discovery (Batool et al., 2019).

APPLICATIONS IN PRECISION MEDICINE

Oncology

Targeted therapies have shown remarkable success in cancer treatment. Monoclonal antibodies and tyrosine kinase inhibitors (TKIs) for chronic myeloid leukemia are two examples against HER2 in breast cancer. Biomarker-driven patient stratification has improved treatment efficacy and survival outcomes (Centanni et al., 2025).

Neurological disorders

In neurodegenerative conditions like Parkinson's and Alzheimer's, attempts are being made target misfolded proteins, aggregation pathways, and neurotransmitter imbalances. Precision approaches hold promise for reducing off-target effects and improving patient quality of life (Gbaraba et al., 2025).

Rare and genetic diseases

Development of rare illness diseases, often driven by single-gene mutations, has been revolutionized by gene therapy and antisense oligonucleotides. Personalized interventions are increasingly feasible due to the growing understanding of genotype–phenotype relationships (El-Tanani et al., 2025).

CASE STUDIES

Successful examples of targeted therapies

Advances in precision medicine have changed the landscape of cancer treatment. Modern drug delivery materials and techniques enable the modification of a drug's pharmacological characteristics without sacrificing the intended impact on molecular targets (Patra et al., 2018). They can specifically alter a medication's pharmacokinetics, stability, absorption, and exposure to both healthy tissues and cancers. They can also make it easier to administer drug combinations that work well together. Opportunities to improve the therapeutic index of cancer medications are identified by this factor (Manzari et al., 2021).

Impact on patient outcomes

Both excitement and skepticism have been raised by the use of genetics in medication development and discovery. Although several new pharmacological targets were successfully identified by previous attempts, the overall clinical efficacy of created medications has remained underwhelming, largely due to the many causes of disease (Quinn et al., 2021). Nonetheless, recent developments in genomics technology and analysis have made it feasible to quickly determine and decipher the genetic variation causing a single patient's illness (Dugger et al., 2018).

Challenges and limitations

Medical practice has changed significantly as a result of precision medicine. It is also being used to treat chronic and infectious disorders such as connective tissue disease and asthma. Medical practice has changed significantly as a result of precision medicine. Infectious and chronic disorders like obesity, diabetes, cardiovascular disease, connective tissue diseases, and asthma are also being managed with it. Humanity has advanced greatly with this new age of medicine, and it is hoped that in the near future, patients and caregivers will reap even greater benefits (Hollingsworth and Biankin, 2015). However, the future of precision medicine still faces several obstacles, including the expense, morality, security of big data, combining different platforms to combine data, and finding qualified personnel to handle the data and algorithms (Naithani et al., 2021).

Resistance mechanisms

The issue facing clinical oncologists is that not all of the genetic changes and changes in the tumor microenvironment that trigger the spread of cancer cells are understood, nor are the changes that are likely to encourage metastases. Driver mutations encourage the growth and spread of cancer. The activity of the mutant protein can be stopped by pharmacological treatment, although drug resistance almost always results. Numerous different mechanisms are linked to drug resistance in cancer. Drug resistance mutations can arise in parallel routes or in the same pathway, avoiding the signal that was intercepted, and in the same protein or in distinct proteins (Bhullar et al., 2021). The problem facing clinical oncologists is that not all of the genomic changes and changes in the tumor microenvironment that cause cancer cells to proliferate are known, nor are the changes that are likely to encourage metastasis. A few molecular processes underlie drug resistance. There are some molecular mechanisms underlying drug resistance. It is rare that cancers with a shared driver mutation will develop a common mechanism of drug resistance, and it is possible to forecast the likely mechanisms that the tumor cells will develop. In order to satisfy its infinite demands, this necessitates the selection and prioritization of target combinations with the aid of the rising huge compute power that makes artificial intelligence possible as well as increasing data collection (Nussinov et al., 2021).

Cost and accessibility

Science has made tremendous strides in comprehending the molecular causes of illness and rapidly developing novel, sensitive, and efficient remedies. Paradoxically, the success of science is making it more difficult to afford universal health care. Both the importance of science in healthcare and the seemingly unavoidable conflict between health and the economy are highlighted by the COVID-19 pandemic (Henderson et al., 2023). The growing costs of treatment are mostly due to drug development in ever-smaller target populations. Drug development has historically and structurally been ineffective and inadequately integrated within the public and private sectors. For this end, it is hypothesized that there is an alternate and integrated paradigm wherein business and governments share the advantages and risks of medication development. It requires millions to implement a novel multi-stakeholder public-private partnership approach for sustainable precision oncology, which integrates clinical trials into the standard of care and speeds up biomarker-dependent medication development (Lu et al., 2023).

ETHICAL CONCERNS

Through an awareness of variations in genetics, lifestyle, and environment, precision medicine seeks to personalize therapy. This technique shows promise in two areas: pharmacogenomics and cancer genetics. Due to genetic variations in how each person reacts to numerous medications, pharmacogenomics testing may be able to guide medication prescriptions to improve safety and efficacy. Likewise, testing to determine a person's genetic susceptibility to cancer can direct prevention. A few tests for each have been used in clinical settings, and others are being developed. Lack of data from a variety of populations and the small body of evidence to support clinical use are obstacles to implementation. Therefore, methods that improve the reliability of clinical practice standards and develop decision support for patients and clinicians that meet their requirements and allow for flexibility when making morally challenging decisions should be given top priority in future research (Korngiebel et al., 2017).

However, a number of moral dilemmas and possible hazards could arise from the use of precision medicine. Professional groups and practitioners are aware of its advantages and possible drawbacks, but little is known about how patients feel about these possible ethical hazards. From the perspective of the patients, eight major themes about the hazards and ethical issues of precision medicine are emerging: Patient data security and privacy, the financial impact on patients, possible drawbacks of precision medicine, including psychological harm, the possibility of discrimination against particular groups, risks during the informed consent process, mistrust of the provider and medical research, and issues with the diagnostic accuracy of precision medicine and modifications to the doctor-patient association. Regarding the use of precision medicine, patients should be aware of ethical concerns and potential hazards. Patient education, focused research, and formal regulations are necessary to address these challenges. In order for doctors to comprehend and treat patients' problems in clinical practice, more research is required to validate the results (Ahmed et al., 2023).

CONCLUSION

Precision medicine is a novel method that has the potential to transform illness prevention, diagnosis, and treatment by customizing medical interventions for each patient according to their distinct genetic, molecular, environmental, and lifestyle traits. A key element of precision medicine, targeted drug discovery has sparked a new wave of therapeutic innovation by making it possible to create medications that specifically target particular biochemical pathways linked to illnesses. The integration of cutting-edge technologies such as genomics, proteomics, artificial intelligence, and advanced drug delivery systems has significantly advanced the field,

leading to remarkable breakthroughs in various therapeutic areas, particularly in oncology. Nevertheless, precision medicine faces several challenges and limitations. These encompass the high cost of genetic and molecular profiling, ethical concerns related to data privacy and discrimination, the need for robust biomarker validation, and ensuring equitable access to these advanced therapies. Additionally, understanding and addressing the intricate mechanisms of drug resistance remains a significant hurdle. The ethical implications surrounding patient data, informed consent, and the doctor-patient relationship are vital considerations in the implementation of precision medicine. Patients express concerns about privacy, economic impacts, and the potential psychosocial consequences. To realize the full potential of precision medicine, these ethical challenges must be addressed through patient education, research, and well-defined policies. In the ever-evolving landscape of precision medicine, interdisciplinary collaboration, the integration of artificial intelligence, and a patient-centred approach are paramount. The future of targeted drug discovery and precision medicine holds great promise, and addressing the current challenges will be pivotal in delivering the benefits of this transformative approach to a broader population.

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