Biomarker-Stratified Therapeutic Targeting: Machine Learning Frameworks for Precision Drug Development and Patient-Centric Dosing

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1. Introduction to Personalized Medicine in Drug Development

Personalized medicine tailors treatments to individual characteristics. This is typically done with genetic information but includes other factors such as environment, age, lifestyle, and concomitant medications. An important goal in developing individual patient treatment strategies is to maximize efficacy and minimize adverse effects. Among the aims of personalized drug therapy research is a better understanding of why patients may differ in their drug responses and to develop better information allowing a more rational use of both new and traditional medical compounds. There is a plethora of data on the large incidence of adverse effects in drug treatment. In a recent large study involving patients, the participants experienced a total of side effects. The vast majority of effects were inherited. Mining and integrating data on a patient-specific basis is thus an important tool in new drug research.

In this context, there is a paradigm shift in drug development, as companies are no longer adopting a one-size-fits-all approach. The paradigm is slowly shifting toward delivering more personalized medicines in order to satisfy various unmet needs such as striking a balance between safety and efficacy, ensuring that patients are likely to achieve positive clinical outcomes, and improving the adoption of novel products through better differentiation from existing therapies. Indeed, the individual qualities of patient groups with respect to genetic and other data must be integrated into the drug development processes. Big data is thus an essential aspect of this trend, as at least some patient-related environmental and individual biological data must be integrated into the drug development process. Artificial intelligence, and above all machine learning, is considered one of the foundations of this new therapeutic era, hence the birth of the concept of personalized medicine.

1.1. Overview of Personalized Medicine

1.1. Overview The goal of personalized medicine is to understand the individualized patient profile and provide healthcare to improve patient outcomes. The resulting personalization can be expected in a clinic by measuring a wide variety of 'omics', including genomics, proteomics, and metabolomics, and predicting and preventing various diseases considering lifestyles and environmental factors. One key area of personalization is pharmacology, including adverse drug reactions (ADRs), either on-target or off-target adverse effects of a drug, or failures of required therapeutic effects. Most drugs are moderately effective, and patient attributes are shown to influence the treatment process. Personalized drug discovery and development can increase the chances of successful outcomes as a patient-centric treatment process.

In history, many drugs were developed that showed variability in therapeutic as well as adverse effects in patients due to individual genetic variations. Accordingly, significant advances in molecular genetics, pharmacokinetics, and pharmacogenomics enable the identification and study of the relationships between various biological factors leading to variations in drug safety and efficacy. There is increasing evidence that genetic factors play a crucial role in variation in treatment outcomes. Personalization of a drug from the early phase of drug discovery has the potential for higher therapeutic efficiency, leading to increased patient compliance with decreased healthcare costs. A gene-drug interaction useful in the diagnostics and monitoring of adverse drug effects has already been approved for labeling information on therapeutic products. Overall, personalization in drug development and healthcare leads to optimized clinical decision-making, reduced healthcare costs, and ethical standards. Regulatory concern about clinical trials for personalized drugs leads to considerations on ethical and policy issues.

1.2. Importance of Personalization in Drug Development

The field of drug development, in the last two decades, is entering personalized medicine to ensure that drugs work best for a group of patients a priori. Personalized medicine is directed towards developing drugs that have the potential to deliver preventive, diagnostic, prognostic, and therapeutic value based on individual patient genomes without causing adverse effects. As opposed to the traditional 'one size fits all' principle, personalized medicine ensures minimum side effects and maximum efficacy for each individual, often resulting in savings of billions of dollars across healthcare institutions on an annual basis by reducing drug side effects.

Compared to the standard approach to cancer treatment regimens, the personalized medicine approach showed a 30% increase in efficacy against lung cancer, 50% against breast cancer patients, and a 100% increase in remissions among those undergoing treatment for chronic myeloproliferative disorders. It is a revolutionary approach that has the potential to change the course of clinical drug development. At the system level, the economic benefits of personalized medicine are important; it has the potential to dramatically reduce the cost of healthcare for a nation as treatment decisions are driven by the clinical efficacy of the dosage, which amounts to fewer occurrences and reoccurrences of diseases in the population and thus a reduced number of visits to hospitals. Some of the bottlenecks that a personalized approach faces in clinical settings are off-target activity of the drugs, tumor heterogeneity, and optimum doses administered in the initial hospital visits. The personalization of cancer therapies should ensure the identification of potential biomarkers that would lead to patient stratification and also definitely enhance the development of pharmaceutical agents.

2. Fundamentals of Machine Learning in Healthcare

Healthcare and medicine have experienced a digital and data-driven transformation during the last decade. Modern machine learning techniques allow us to infer from data actionable information that can automatically change system behavior. Despite its great potential, machine learning applied to healthcare and medicine presents multiple specific challenges, including the need for interpretability and causality, as well as ethical concerns. It is necessary to provide guidelines to develop and evaluate new algorithms, as well as protocols, frameworks, and benchmarks that standardize and compare the potential and limitations of these algorithms. We introduce the second part that includes the next chapters. Let us start with a general introduction to the topic: the fundamentals of machine learning in healthcare.

Machine learning (ML) is a scientific field that aims to develop predictive algorithms. Its applications in healthcare settings are numerous, including optimizing diagnostic accuracy, early prediction, disease prevention, patient stratification, and drug development. Supervised and unsupervised learning are the branches of ML that can be applied to the medical field depending on the tasks. Several algorithms have been developed, depending on the complexity of the input samples, data distribution, and privacy. The optimization approach can be either linear or non-linear, data-driven or hypothesis-driven, and supervised or unsupervised. The algorithms typically used can be grouped according to their approach: decision tree learning, association rule learning, artificial neural networks, clustering, decision networks, genetic algorithms, deep learning, etc. Data are essential and are the starting point of the algorithm training. Data storage and protection, as well as dataset non-stationarity, are topics of interest in the field. Ethical issues including healthcare, consent, responsibility, rights of AI, and human control are fundamental when approaching this new paradigm.

2.1. Basic Concepts of Machine Learning

In the world of AI-based solutions, it is crucial to understand the basic concepts of machine learning. Generally, there are two different paradigms for solving problems: programming (traditional approach) and machine learning (novel approach). In the traditional approach, the trend for the solution is coded, whereas in machine learning, solutions are programmed to learn from the data and make predictions or decisions. The most pivotal word for understanding machine learning is "learn," which makes a dataset available for the machines to learn. Machine learning is adaptable and adjusts its parameters based on the feedback from external data.

Machine learning can be trained in various ways; these are described below: • Supervised learning: Input and output available • Unsupervised learning: Only input available • Semi-supervised learning: Partially input and output available • Reinforcement learning: Based on the branching reward

Machine learning is entirely dependent on big data. It can only be trained with large amounts of data. Large amounts of data are used to do tasks that cannot be coded explicitly. It involves a lot of preprocessing steps, including data cleansing. Commonly, models can be assessed based on metrics like precision, recall, accuracy, F1-score, confusion matrix, and area under the curve. Examples of machine learning include diagnostics, predictive modeling, and language translators. Accuracy ranges from 1 to 100 percent. The mismatch in results from two or more models to the same problem is due to inherent noise in the data. Usually, machine learning data should be checked for missing values, class imbalance, and outliers.

Despite the exponential increase in the power of computational hardware, their application on healthcare data for drug discovery and development has not been substantial. Machine learning-based healthcare solutions exist in diagnostics and image recognition, curating medical text-based knowledge discovery and predictive solutions. In diagnostics, a supervised learning model uses brain magnets to segment the heart to identify and localize calcium clusters. The human accuracy is predicted with the machine learning model, with 91% sensitivity and 99% specificity.

2.2. Applications of Machine Learning in Healthcare

With an increasing amount of available healthcare data, there are a number of practical applications of machine learning algorithms in healthcare. Machine learning is increasingly used in disease prediction and early diagnosis. With an increasing ability to analyze large, richly structured patient data, machine learning algorithms can facilitate personalized, data-driven treatment recommendations. Such approaches have already reported very promising results. Machine learning algorithms for image recognition have the potential to transform the use of radiology in healthcare. Machine learning has also been used to analyze patient data in order to minimize the risk and complications in acute medical care by predicting the worsening of patient conditions within the first 24 hours of admission to the hospital. Indeed, the integration of machine learning models into operational settings may result in considerable efficiency increases.

Machine learning can accelerate the synthesis and analysis of evidence via text mining for information extraction and literature surveillance. Indeed, machine learning algorithms can predict structured outcome data using unstructured data and predict treatment effect using related patient data if treatment-control assignments are not random. The application of machine learning to larger and richer available datasets is expected to generate even more advanced and precise models for personalized treatment recommendations. Researchers and practitioners are increasingly aware of the issues related to the use of black-box algorithms, including ethical concerns about the distribution of benefits, data privacy and transparency requirements, and the public and regulatory need for interpretable, justifiable decisions and algorithmic suggestions. In fact, machine learning is expected to greatly accelerate and enrich clinical practice through novel disease and patient management algorithms. The value of the disruptive potential arising from machine learning in healthcare should reflect improvements in clinical outcomes.

3. Integration of AI in Drug Development

AI is currently augmenting the drug development process at various stages and bringing more efficiency and reproducibility to these steps. The first notable process during drug development is drug discovery, where developers work to identify candidate objects using prior evidence of the working drug. Researchers at this stage have to analyze large datasets, including the molecular properties of the drugs along with their therapeutic usefulness through different parameters. These tasks are almost impossible to perform independently when done manually or using traditional computational methods. Moreover, the researchers perform these analyses and keep in mind the compatibility of these drug molecules with the existing drugs to avoid any toxicological effects.

In such instances, AI plays a significant role through its ability to integrate a large amount of public data and provide researchers with meaningful insights. AI and pharmaceutical researchers are collaborating to work out the design of personalized drugs suitable for a wide range of patients. In this context, Clinical Decision Support AI tools were developed to churn a large database of pharmaceutical knowledge that could be used to design new active pharmaceutical drug molecules. AI also has a vital role in revolutionizing the design of various clinical trials by identifying various patient subgroups according to disease burden as well as standard therapy. During the drug development process, AI is also allowed to identify the right candidate drug molecules using machine learning models and deep learning platforms. Through these models, a company developed tardigrades or water bear-related TGF-beta and B-cell lymphoma-2 antagonist peptide and other inhibitors that have shown promising results.

3.1. AI in Drug Discovery

The role of medicine in society has continued to advance as we better understand the intricacies of human biology. Nonetheless, many drugs fail during development in phases 2 or 3, effectively costing hundreds of millions of dollars. In early-phase research, one builds compounds to modulate activity within the body in hopes that a certain chemical interaction may lead to effective drugs or therapies. One of the potential roles of AI systems is to predict which compounds are more likely to be good drugs. This area specifically focuses on finding compounds that are effective at treating a disease, although it is one of many areas where AI can have an impact. Common techniques for drug discovery include virtual screening, molecular modeling, and compound library comparison. In particular, huge strides have been made in recent years with the application of machine learning. The increased reliance on AI and machine learning to assist drug discovery goes into the many challenges and opportunities in their application. AI models require a diverse training set of drug-like compounds in order to not rely on correlation alone, hindering the application in populations represented only sparsely in the training data.

The application of AI to drug discovery provides a clear case of a successfully completed project that was made possible by machine learning and virtual screening to accelerate the drug optimization process. While the cynical nature one should take towards a discovery in marketing was discussed, consider it to be a counterpoint to the economic implications of the successful application of AI in the creation of a blockbuster drug candidate. In the study, patent disclosures and defined "usual procedures" were followed to a point before employing computational research, directly against established and trusted procedures, to zero in on a project rescue previously not yet considered. The application of AI could be applied to quickly narrow in on potential compounds to effectively suppress mutated parasites, accelerating the drug discovery process significantly.

3.2. AI in Clinical Trials

In clinical development, AI is predominantly utilized in the clinical trial phase, although increased application in early phases is expected in the future. In clinical trials, AI plays a role in patient selection, trial design, and in the statistical analysis of data. Real-time data analysis can be used to detect patient outliers that exhibit a different response than the bulk in the trial and either exclude or include these patients in different treatment arms. In addition, AI can be used to continuously assess long-term safety and effectiveness beyond the controlled environment of the randomized controlled trial. AI is also used for adaptive trial designs, which can increase the efficiency of trials and may, in some cases, make them feasible. When used in combination with AI-based data analysis and patient selection, adaptive trials can also reduce the time needed to run trials and the overall costs of development.

Careful data management is necessary to apply AI smartly in the clinical development phase. For those data sets that AI uses to pattern-match or to train, it is vital to ensure these are well documented and comprehensive. For trial data, bias reduction methods may be needed. This includes the requirement to widen the patient profiles to ensure a diverse set of trial participants, including children and pregnant or breastfeeding women. However, looking at success stories in clinical trials, most of them face challenges in managing relevant data. In one trial, AI was used for streamlining sub-study recruitment while considering evidence generated from sub-study interest. In another trial, insights were generated using machine learning to assess patient heterogeneity in molecular aspects associated with clinical trials. Cell-centered models were used to predict responses to different immunosuppressive medications. Model-predicted responders were identified, which allowed support in streamlining enrollment for the trial. In addition, a platform was used to identify an additional sub-study that could help improve the chances of observing an effect in this trial.

4. Utilizing Patient Genetic Data in Drug Personalization

Over the past decade, technological progress has enabled public health researchers to develop an increasingly detailed picture of genetic variation, revealing the rapid emergence and diffusion of certain traits from analyses of DNA sequence data. This has revealed new genes and genomic loci that contribute to specifically fine-tuned phenotypic information, such as personality traits or individual responses to drugs. Several pharmacological strategies have already been proposed based on genetic data, including the development of new drugs that might be useful only for subjects with particular genetic progress. This kind of novel approach to drug development can capitalize on existing techniques to at least partially overcome the problem of different genetic backgrounds affecting the response of study participants. Few genomic drug development methods have been conducted. A total of 270 niches related to natural products and 90 connected to genes and genetics are present. Additional concepts related to genomics, including genetic medicine, personal genomes, proteomes, and environmental genomes, have also appeared, but not productive genes or genetic targets required for developing new drugs have been discovered.

With the advent of whole-genome sequencing and personal genomics, personalized therapies for genetic disorders, either based on replacing or silencing defective genes through different delivery methods, have been successfully translated into clinical practice. It is now well accepted that virtually all drugs approved by the U.S. Food and Drug Administration have the potential to exhibit a distinct effect in a specific subpopulation, driven not only by environmental risk factors but also by the genetic background of the individual. This is also reflected in the extensive research performed in the specific field of adverse drug reactions, which occur due to an individual patient's genetics. However, few examples of such studies are mentioned. Clearly, ethical issues of genetic tests need to be discussed much more in detail. Furthermore, it is always important to respect individuals' privacy, because revealing genetic information can no longer be considered anonymous. They regret to learn how a common genetic variation in the drug transporters influences not only the individual user's response and metabolism of the drug but also the actual active compound in the form of a prodrug. Also, the implications on the pharmacological properties of the prodrug active form are noteworthy, which can be affected by another common polymorphism in the endogenous enzyme responsible for drug metabolism. Pharmacogenomics has led to the development of a small number of companion diagnostics, which are tests that report when a patient has a certain genotype that informs on which dosage lower than normal should be provided to the patient with the right genotype. This is based on the genotype of the primary target of the drugs and not on genotype data about the complete pharmacokinetics or pharmacodynamics of the drug therapy. Some novel psychopharmacological medicines have been coupled with a qualifying test to direct the selection (e.g., by two CYP2D6 isoenzyme variants, extensive metabolizer represented by ultrarapid metabolizers and poor metabolizers). For example, approximately 16 medications should be given to the ultra-rapid metabolizers and not to the poor metabolizers. This list includes those for leukemia, psychiatric disorders, seizures, respiratory infections, and other conditions. However, this is far from the ethical goals of pharmacogenomics, as drug doses based on the genotype can allow for the improvement of drug therapy. In addition, genotyping is seen as giving an early preventive warning about influential environmental hazards, pediatric problems, metabolic diseases, aging, susceptibility to infectious agents, side effects of drugs, and other relevant issues that affect society over time. Determining the specific genotype of patients can result in better drug outcomes to ensure less expensive and more efficient therapy.

4.1. Genomic Data Analysis

In personalized drug development, genomic data are abundantly used for model personalization. Hence, genomic data analysis plays a major role in drug personalization. It involves the collection, processing, interpretation, and most significantly, the use of genomic data to predict how cells will respond to drugs. Multiple techniques can be used to collect genomic information, of which a popular one is next-generation sequencing. This high-throughput sequencing technology is capable of sequencing millions of short reads of DNA or RNA and their modifications on RNA simultaneously. As a result, genomics refers to the genetic material, the DNA of an organism, here referring to human beings, which includes the whole genome and other genetic molecules such as mRNA, microRNA, and tRNA.

The results from the analysis of the genome sequence can predict a drug's response. Variants generated through the transcription of expressed genes that persist in the mature mRNA, proteins, and other functional parts of cells are collectively referred to as oncogenic mutations. Thus, the identification and interpretation of these variants are of crucial value in personalizing drugs used to treat patients. These kinds of variants are the desired outcomes of oncogenomic databases. Techniques from bioinformatics are frequently used to make sense of large, complex genomic datasets. A database is a system that stores and manages data for easy search or retrieval. Several genomic databases store different types of genomic data. Some identify mutations that change the resulting protein product, some find structural changes that result from chromosome rearrangements, and some hold data including general gene expression information, where mRNA expression is the nucleotide sequence from within the transcription pipeline but after modification.

In personalized cancer therapy, cancer-relevant patients' genomic data are integrated to make clinical decisions, abbreviating the gap between scientific achievements and practical utility. Working with complex data integrated from many sources and produced by many different techniques is a main challenge in cancer research. Data heterogeneity is a potential source of misinterpretation. Notably, data produced by next-generation sequencing for clinical purposes should be of the highest possible accuracy as it is a guiding parameter between life and death and can determine the choice of treatment with new personalized therapeutics. Genomic data analysis has been established as the first step in developing systems to personalize drug development and design. In precision oncology, pharmacogenomics aims to identify genetic variations in response to drugs and adverse drug reactions. Genomic data are fundamental and provide valuable information that can be used in drug development and personalized approach strategies. The field of drug personalization utilizes molecular information to envisage and understand the potential impact of disease on patients. Central to the utility of personalized predictions is the subsequent potential impact of different treatment options with an empirically directed biomarker. In the last decade, there have been 'biomarker-focused' predictions within this area. Although genomics and biomarkers are new in the area of personalization, research in this field has been undertaken to discover new personalized treatments for diseases.

4.2. Pharmacogenomics

Various reviews and guidelines have strived to identify and summarize drug-related gene variants and provide drug-ADRs associations into the pharmacogenomics-pharmacovigilance pipeline. Since the establishment of the concept of the "right drug for the right patient at the right dose," a "vision" that is often associated with Sir Archibald Cochrane or the late 20th century, medical fields have been proposing different practical clinical approaches to using pharmacogenetic information in therapy. Pharmacogenomics evaluates the relationship between genes and drug treatment effectiveness or drug susceptibility. Such genetic information may assist in selecting safe and effective medicines, as well as deciding appropriate dosing regimens and analyzing reasons for therapy failure. One of the outstanding healthcare cases of preventing adverse drug reactions through pharmacogenomics remains irinotecan-induced severe neutropenia in patients with UGT1A1 polymorphisms. Key candidates for pharmacogenomic testing have included warfarin, clopidogrel, HLA-B, abacavir, and thiopurine/TPMT.

Notably, some patients are likely to require higher doses of the curing agents since gene variations lead to more rapid drug elimination, as observed for the majority of elderly people. Consequently, genetic screening helps treatment adjustment if a side effect happens. As more genes and relationships are discovered, monogenic and polygenic pharmacogenetics may evolve therapeutic areas in the coming years. The aim, as indicated by personalized therapy, is to make informed conclusions based on the genetic makeup of the patient. Personalized therapy seeks to optimize care and circumvent side effects associated with current treatment failure. Pharmacogenomics promotes this through the identification of genetic variations. For most patients, therapies with the greatest effectiveness and therapeutic index are now chosen. Pharmacogenomics has the potential to reduce the incidence of adverse drug reactions by allowing only those at risk to have reactions. The reduction of adverse effects and the potential avoidance of treatment failure are important aspects of drug personalization. Challenges to implementation include the high cost of genetic testing, availability, reimbursement and regulatory issues, adherence to the use of human rights, and ethical issues. Pharmacogenomics of drug metabolizing enzymes and transporters is likely to be one of the starting points for drug personalization.

5. Utilizing Patient Phenotypic Data in Drug Personalization

Patient Phenotypic Data for Personalization Personalization of drug treatments has an increasing interest in helping find optimal treatments for patients. Phenotypes refer to properties of organisms that can be observed or measured, including modulated responses to social, environmental, and genetic factors, and can include genetics, metabolomics, proteomics, epigenetics, immunophenotyping, structural, functional, and behavioral characterizations. Treatments can have differential effects due to these properties; they can identify patient variability in the response to a given drug, based on factors such as prior treatments, race, gender, age, presence of comorbidities, concomitant medication use, or more general differences in genotype and lifestyle. Phenotypic data can be collected in the clinic, using electronic patient questionnaires, and where necessary, lab tests, imaging, and other biological sample analyses. Such information is recorded in the patient's health record. The use of existing patient data, especially data recorded in electronic health records, offers the convenience of large databases with a history of treatments, repeated measures, and patient outcomes. The recorded data can be used to stratify patients into subpopulations and predict treatment outcomes, including predictivity for hypothesis-testing trials and general representative outcomes observed in medical practice. One challenge with the utility of such data is when the information is very incomplete. Another challenge in using phenotype information is the variability in how the phenotypes are recorded, since it varies between countries, clinics, and healthcare providers. Nonetheless, personality measures can help identify subtype characteristics measurable in the clinic or in a clinical trial, overcoming these limitations. In addition, the phenotypic information collected can be used to inform the personalization of in silico models, looking at personalized neural models, machine learning models, or providing further information for the personalization of large population pharmacokinetic or pharmacodynamic models. Gaining affordable access to such phenotype data will be beneficial, not only in guiding drug personalization strategies but also in facilitating the optimization of drug development.

5.1. Clinical Data Analysis

Clinical data, which originate mostly from electronic health records concerning extremely heterogeneous factors (from gender and age to pathology severity and possible associated pathologies or treatments), are especially useful for providing the reasoning behind various aspects of personalized medicine. Given the increasing population trends and the consequent increasing number of admissions to health facilities, significant amounts of this type of data are available, which has partly contributed to clinical data analysis being closer to validating commercial products. This data analysis largely uses statistical methodologies that generally describe the trend between responses and factors such as a one-factor-at-a-time analysis approach where the confounding effect of covariates is handled, and the multiple testing correction is used to reduce false discoveries. The techniques also improve clinical data analysis with methods from machine learning to transform them into predictive tools for patient responses to drugs in the hope of facilitating clinical decision-making.

In practice, determining the best treatment is not attainable in most cases, but this target can be achieved by grouping the analyzed patients, among those defined as "similar" on the basis of their clinical features, so that we can get responses inside them, similar enough to be considered equivalent. There are some case studies where the collection of drug response data together with existing health records allowed us to determine whether the patient would most likely benefit from the treatment. Many issues are related to the clinical data analysis, including data quality and the possibility of integrating data from multiple sources, since different institutions or healthcare providers may use different software to collect and process patients' data. In the willingness to reduce these problems, many types of research are now based on the analysis of large and detailed sources of information, which can provide valuable insights on how one can predict and best individualize drug treatment based on a patient's clinical data profile.

5.2. Biomarker Identification

Biomarkers are defined as biological parameters that can be measured and evaluated objectively to indicate the physiological state of a person. Understanding biomarker levels in each individual patient is fundamental to predicting drug efficacy and side effects because variations in gene expression, protein levels, and drug metabolizing enzyme activities affect drug effects. Thanks to technological advances, several methods can be used to identify biomarkers at the genomic, proteomic, and metabolomic levels. The integration of genomics and proteomics is considered an essential approach in drug discovery and drug development. The integration of data should enhance the efficiency in providing new potential biomarkers at an early stage in drug development. Affinity proteomic techniques can be used in systematic assays that span several orders of magnitudes of protein concentrations. Such protein profiling offers a convenient platform for large-scale disease or drug proteomics to identify disease markers, drug targets, and potential predictive biomarkers.

Several examples of biomarker-driven therapies exist. In all cases, genetic diagnostics are used to predict the outcome of therapy. Other biomarkers may reflect the activities of certain targets in the body. There are several specific challenges associated with the validation of gene expression markers. Some of these relate to the measurement of the expression of disease-associated genes and the sensitivity needed to show their connection to the disease state. Equally important is measuring the large dynamic range of gene expression in a variety of tissues. Currently, genes showing the best expression profiles are detected in tissues relevant to the manifestation of the specific disease. This is generally feasible in cancer and in chronic diseases where tissue biopsies are available from the affected organs. Efforts to measure gene expression patterns in noninvasive means, such as blood sampling, urine excretion, and exhaled air, are also being developed. Furthermore, the need to standardize assay conditions and statistical methods for measuring mRNA changes is crucial. Development of technologies based on gene expression measurements will require further integration with the drug metabolizing enzyme and transporter profiles because these molecules also affect the concentrations of the active drug. These challenges require a multidisciplinary approach, where industry, regulators, and academic initiatives can be joined. Like in many other fields today, international collaboration is required to validate and standardize validated biomarkers in drug development. According to current trends, biomarkers will be integrated as part of genomics and proteomics in the future so that personalized medicine has the power to become a routine practice in clinical activities.

6. Future Direction

Personalized medicine is an exciting and rapidly evolving field, and ultimately is about delivering the right drug to the right patient at the right time. The sheer volume and variety of data generated across the lifecycle of a product demands robust data analytics to make sense of what the data tell us about the safety, efficacy, dose, timing, and sequencing of therapeutics. We predict that in the future, data analysis will increasingly occur in real-time, supported by learning systems running advanced algorithms. One of the simplest future directions is to invest in developing the technologies that underpin real-time data analysis. As more companies collect more data and investments in healthcare and life sciences continue to grow, the world is getting more and more complex and more and more able to be analyzed and algorithmically acted upon. The technology is changing fast, and as developments in quantum computing, multi-modal data enablement, and embedding these technologies in edge-computing devices become mainstream, data-driven learning approaches to analyzing healthcare data will have a far broader impact on patient health.

In terms of the analyses of today, although AI can undoubtedly do amazing things, it does have limitations, and we should be careful about expecting it to do everything. More research efforts are also required to ensure seamless avenues to resolving ethical concerns, patient acceptance, integration into regulatory pathways, and also addressing the issues of funding this level of personalization. It is widely acknowledged that there is a need for bigger and better datasets and algorithms, improved conduct, and better measurement systems to make sure that we are developing safe, efficacious, well-tolerated, albeit often expensive drugs. With the unprecedented convergence of technological advancements in omics technologies and digital health, coupled with breakthroughs in computer science, it is highly plausible that we are approaching a perfect storm of research that will drive such personalized medicine approaches to improve and extend human life. We should welcome the wave of investment that is and will transform the digital and biological revolution and drive the future targeted treatments for patients.

7. Conclusion

Improvements in personalized medicine can increase the efficacy of treatments and reduce unnecessary side-effects, eventually enhancing patient outcomes. The use of innovative AI technology such as DNNs, transfer learning, and advanced representations of raw data, are essential to individualize therapies and advance drug development. The large amounts of data now available, platforms, infrastructures, and algorithms are playing a crucial role here. The systematic integration of diverse datatypes in AI models, including RNA as well as single-cell RNA expression, genomics, proteomics, and glycomics data or imaging data is also likely to become increasingly critical. Being able to initially care for patients on a more personalized basis and better comprehend and optimise treatments, at scale, is also likely to have substantial positive impacts on patients of the future.

We will see innovative AI solutions that can bring great benefits to the drug design process if the challenges are addressed. These solutions will be data-driven, use unprecedented amounts of diverse data, and will integrate different data types. They will be able to learn from and be deployed across a wide range of potential therapies and gather crucial insights, not only to optimize/drive the development to the corresponding compounds, but also to identify relevant biomarkers and future personalized combination therapies. To date, the use of AI in drug development shows both the potential advantages and currently unresolved challenges of using an AI approach. This chapter describes recent research on personalized therapies and further strategies for developing them. This presentation focuses on innovative methods, including AI, which, based on various patient and patient sample data, integrate 'omics' data, multi-omics' sets, as well as imaging data, to develop new therapies, including innovative combination therapy, and to diagnose in a personalized manner. Both methods are particularly suitable for treating immune-mediated diseases, however, their use can be extended to non-immune diseases, expanding their impact.

The current fields of research involve extensive collaborations, which bring together not only academic researchers from diverse fields, but also company-based researchers, NGO participants, patient advocates and regulators from the healthcare and social sectors. In the future, both collaborative forums or consortia and investment opportunities will bring new ideas, data sets, and analyses forward; support research and development for identifying new targets and ingenious methodologies; and allow for the application and validation of AI and other computational strategies used in the development and implementation of personalized therapies. As a research community, ongoing collaboration and broader sector integration are essential to developing improved strategies and ensuring the successful use of innovative personalized technology in medicine. Biomedical researchers are rapidly appreciating the need to develop biomedical research based on the convergence of novel approaches and strategies from a variety of scientific disciplines including big data, AI and sensing technologies. AI approaches that are powerful, have sometimes been developed in isolation, don't rely upon a deep understanding of biology, thus limiting their tangible impact. As a result, more comprehensive AI-driven conceptual approaches are being developed, which can integrate multi-omics and multi-parameter patient data and molecular images with data on patient history and ongoing patient pathways. Re-identifying patients from initial diagnosis through trial enrolling to patient follow-up will be possible with these approaches. As well as discovering new innovative trial paths. They will change the very way trials are run and standard practice in the healthcare systems. The fields of AI and multi-omics-driven approaches are growing rapidly, and this constantly evolving aspect is still in its very early days.