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REVIEW

Smarter stem cells: how AI is supercharging iPSC technology

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Abstract
Integrated with artificial intelligence (AI), induced pluripotent stem cell (iPSC) technology could enhance disease modeling, cellular biology, regenerative medicine, and pharmaceutical development. AI has enhanced iPSC differentiation, cultural conditions, and speed of disease-specific model development. Furthermore, AI-based massive omics database analysis exposes hidden biological tendencies, enhancing customized treatment. Investigating new AI algorithms will enable one to solve problems, including interpretability and data quality, resulting from AI's interaction with iPSC technology. These advances fundamentally alter stem cell research and therapeutic applications, therefore facilitating the emergence of regenerative medicine and precision healthcare. AI has evolved in biomedical research into a transformational technology unique in great data analysis, predictive modeling, and automation capacity. AI integration increases the development of patient-specific cell types for disease modeling, pharmacological research, and regenerative medicine by substantially improving IPSC-based technologies. Emphasizing changes in disease models, alternative methodologies, and cellular reprogramming, this work examines current advancements in the use of AI in iPSC technology. The argument on significant obstacles and possibilities reveals how AI could alter the objectives of iPSC research and implementation.

Keywords AI · Induced pluripotent stem cells (iPSCs) · Cellular reprogramming · ML(ML) · Differentiation protocols · Disease modeling · Drug discovery · Multi-omics · Predictive modeling · Regenerative medicine · High-content imaging · Transcriptomics · DL · Reinforcement learning · Personalized medicine

Introduction

Integrating induced pluripotent stem cell (iPSC) technology with AI could transform cellular biology, disease modeling, regenerative medicine, and drug development. AI has improved iPSC differentiation, raised cultural standards, and accelerated the generation of disease-specific models. Furthermore, studying massive omics databases using AI reveals hidden biological patterns, enhancing customized treatment. Further research of AI algorithms will help to solve challenges, including interpretability and data quality resulting from the interaction of AI with iPSC technology. These findings considerably transform stem cell research and therapeutic uses, advancing precision and regenerative medicine. In biomedical research, AI has developed into a transforming tool unique in scope for predictive modeling, automated capabilities, and thorough data analysis. By dramatically boosting IPSC-based technologies, AI greatly enhances the manufacturing of patient-specific cell types for disease modeling, pharmacological research, and regenerative medicine. Emphasizing changes in disease models, differentiation strategies, and cellular reprogramming, this study addresses present innovations in the application of AI in iPSC technology. Discussing meaningful opportunities and difficulties shows AI is ability to change iPSC research and application goals (Atmaramani et al. 2024; Grafton et al. 2021; Joshi-Barr and Wampole 2024; Kreir et al. 2024; Kusumoto et al. 2022; Ragunton et al. 2023).

Emphasizing its transformational ability to improve reprogramming, differentiation, and quality control systems, this rigorous study examines the growing integration of AI in iPSC technology over the past decade. AI has sped developments in disease modeling, pharmacological discovery, and tailored regenerative therapies using vast omics data and therapeutic outcome prediction. To fully maximize AI's potential in improving iPSC-based technologies and clinical

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applications, strong frameworks and multidisciplinary cooperation remain indispensable even if data standardization, model interpretability, and ethical concerns have made significant progress (Coronnello and Francipane 2022; Vo et al. 2024).

AI accelerates medication development and improves stem cell research through optimal reprogramming, differentiation, and quality assurance applied via predictive modeling and high-throughput screening. Large-scale omics data analysis driven by AI has helped to define new therapeutic targets and improve knowledge of disease dynamics. AI could tailor pharmaceuticals, simplify research processes, and change clinical translation. They highlight the need for multidisciplinary approaches that skillfully exploit AI capabilities (Kim and Hong 2024). This work examines how AI and ML might be introduced into iPSC research to improve iPSC differentiation, reprogramming, and quality control processes. Among other subjects, the article addresses the part AI and ML technologies play in personalized medicine and drug discovery, their contribution to large-scale data analysis, and their improvement of the safety, scalability, and repeatability of iPSC manufacturing. It shows how AI might enable regenerative medicine and clinical translation to surpass obstacles. Still, it also emphasizes how ethical, computational, and data-related issues must be addressed if we truly enjoy their benefits.

Cellular reprogramming improvements driven by AI

Using ML methods and other AI-driven approaches, progress in reprogramming, delivery method optimization, and essential transcription factor discoveries are expected. For example, new combinations of variables that increase reprogramming efficiency have been found using DL models educated on omics data. From somatic cells, the reprogramming process generates iPSCs, which are developed into mesenchymal, cardiac, hematopoietic, and neural stem cells. AI-driven technologies included in the iPSC process improve applications and research capability. Using ML algorithms to decode the fundamental molecular mechanisms guiding stem cell behavior, gene regulatory networks (GRNs) and protein interaction networks (PINs) are modeled; genomic analysis helps identify significant transcriptional and epigenomic changes during the reprogramming and differentiation process; and the integration of AI technologies accelerates advances in regenerative medicine, drug discovery, and disease modeling. Techniques and methods of proteomic analysis provide an understanding of post-translational modifications and protein expression. Using OCT4, SOX2, KLF4, and c-MYC, among other vital components, reprogramming somatic cells produces iPSCs. This triploblastic, self-renewing cell type transforms scientific inquiry. Production of patient-specific cell types helps to simulate diseases, screen drugs, and enable regenerative therapies. Additionally, iPSCs help gene therapy by fixing genetic flaws and assessing toxicity. They can forward translational and basic research, opening the path for creative therapies (Fig. 1).

AI enhances iPSC colony quality assessment using multi-source data, including colony shape, gene expression patterns, and epigenetic markers. By examining these criteria, ML approaches forecast iPSC pluripotency, genetic stability, and functionality, thus facilitating the choice of premium iPSCs for research and medicine. This AI-driven approach enhances consistency and repeatability in iPSC-based research, optimizing quality control mechanisms for maximum efficiency and accuracy (Yue et al. 2021). Improving reprogramming techniques and settings for producing iPSCs, big data analysis, and AI increases efficiency in researching age-related diseases. AI-driven models identify essential elements influencing iPSC generation, including the cultural environment and reprogramming variables. AI finds biological pathways and biomarkers linked with age-related diseases using multi-omics data. This enhances reprogramming methods, accelerates the discovery of treatments for age-related disorders, and improves the accuracy of disease models in iPSC-based research (Esteves et al. 2023). Through reprogramming, AI boosts human iPSC production prediction and optimization. Convolutional neural networks (CNNs) track and visualize changes in cell shape over time by analyzing time-lapse bright-field microscopy pictures. Training AI detects important morphological features linked to effective reprogramming, simplifying real-time observation, and early iPSC-generating identification. This approach simplifies processes, increases the accuracy of reprogramming outcome predictions, and improves the general iPSC development (Chu et al. 2023) uniformity and efficiency.

By evaluating large datasets to find ideal parameters, AI and predictive modeling improve reprogramming efficiency in iPSC technology. AI-driven models reduce trial-and-error, provide repeatability, and help develop protocols. Combining multi-omics data, AI finds critical biological pathways and biomarkers linked with successful reprogramming. ML-enabled real-time monitoring improves general success rates and maximizes iPSC creation through constant feedback and modifications throughout the process (Vo et al. 2024). Using ML approaches, optimal circumstances, parameters, and reprogramming techniques are investigated and projected, thereby improving the efficiency of cell engineering. Using large-scale experimental data analysis, AI models find essential elements influencing the success of cellular reprogramming, including timing, ambient circumstances, and particular transcription factors. These results reduce variability and improve iPSC generation, hence producing more effective and consistent reprogramming techniques. Furthermore,

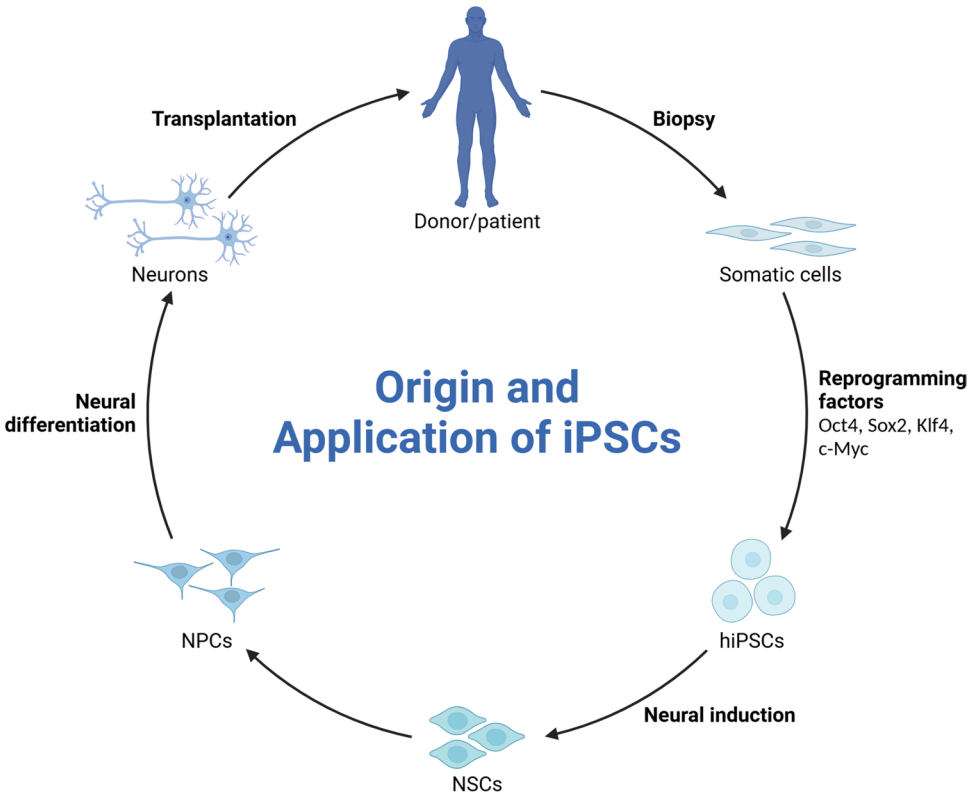

Fig. 1 Origin and application of iPSCs. Reprogramming somatic cells generates induced pluripotent stem cells (iPSCs) using essential factors such as OCT4, SOX2, KLF4, and c-MYC; these cells can be self-renewed and differentiate into multiple cell types. iPSCs enable drug testing, disease research, and the creation of patient-specific cells for medicinal applications through disease modeling, drug screening, and regenerative therapies, which have revolutionized biomedical research—all of which benefit from their use. Moreover, supporting gene therapy by correcting genetic defects and assessing toxicity is facilitated by iPSCs. Additionally, iPSCs have significant potential to generate new drugs and propel translational and basic research

using reprogramming, real-time changes enabled by AI-driven feedback systems improve accuracy and efficiency in cellular engineering activities (Capponi and Wang 2024). Extensive dataset analysis indicates important factors affecting stem cell reprogramming efficiency for ovarian aging treatment, improving AI performance. AI systems improve cultural circumstances and change reprogramming components to improve the consistency and efficiency of produced stem cells. Integrating AI with multi-omics data helps enhance control of stem cell fate and differentiation by pointing up molecular markers linked with successful reprogramming. This data-driven strategy speeds up the development of tailored stem cell therapies for ovarian aging, improving the probability of positive clinical results (Wang et al. 2024).

One has to be sure about the pluripotency and quality of iPSC lines. AI can assess colony form, spot genetic abnormalities, and project differentiation possibilities. Among these tools are image analysis techniques and predictive models. Precision classification of iPSC colonies using AI-enabled automated imaging technologies eliminates the need for human examination. DL methods identify and classify cell shape, architecture, and viability from high-resolution images of grown cardiomyocytes. This AI-driven method helps to find essential features like structural defects or beating cells and enables real-time evaluation of cardiomyocyte differentiation and quality feasibility. The method improves quality control in iPSC-derived cardiomyocyte cultures by increasing scalability, speed, and accuracy, supporting regenerative medicine, drug testing, and disease modeling (Orita et al. 2019). Human pluripotent stem cells (hPSCs) are maximized counting and quality assessment using fast, in-line, label-free technology, AI (AI). The authors evaluate the quality of hPSC colonies by using DL algorithms to assess real-time imaging data, including phase contrast and bright-field microscopy images, enabling automatic identification and quantification of the colonies. Based on morphological characteristics, an AI-powered system can distinguish between healthy and aberrant colonies, providing a scalable, non-invasive, effective quality control mechanism. Eliminating the requirement for manual counting or labeling speeds up monitoring and provides a more accurate and reliable assessment of stem cell cultures for both scientific and medicinal use (Ragunton et al. 2023).

Following and evaluating the printing process with ML and DL techniques help to maximize quality control in 3D bioprinting. Real-time imaging, temperature, and pressure sensors are used in AI models to evaluate data, ensuring the precise deposition of biomaterials and preserving structural integrity over printing. These AI-driven techniques enable quick corrective action by helping to identify flaws, inconsistencies, or deviations from the intended design. This increases the precision, efficiency, and repeatability of 3D bioprinting methods, enhancing their dependability for tissue engineering, regenerative medicine, and the creation of

new biomaterials (Kathirvel and Gobinath 2024; Zia et al. 2024). By automating the search for cellular abnormalities, functional characteristic evaluation, and therapy predictions, using ML systems improves the accuracy and efficacy of quality control. Time-lapse images of developing PSCs were analyzed to detect important morphological traits and cellular activity associated with positive differentiation results. AI models can foresee and monitor several courses in real time by being taught to identify these trends and improve protocols and cultural environments. This approach reduces experiment variability, accelerates the creation of standardized iPSC-based models for therapy and research, and improves the consistency of differentiation results (Yang et al. 2023).

AI and iPSC differentiation protocols

Sometimes, differentiating iPSCs into several cell types requires iterative modification. Research and therapy of neurodegenerative diseases benefit from brain organoids generated from induced pluripotent stem cells (iPSCs). From a healthy donor, lentiviral transduction—Sendai virus, retrovirus, or transposons—removes fibroblasts and other somatic cells and reprograms them into iPSCs. These iPSCs develop into three-dimensional brain organoids reflecting some aspects of human brain development and operation throughout incubation. Complying with cell phenotypic characterization, the iPSC-derived brain organoids are fully described to help one understand the cellular and molecular changes related to neurodegenerative diseases. Using these organoids in disease modeling facilitates research on pathogenic processes and new therapeutic medication screening. Moreover, they provide a platform for designing customized treatments and encouraging the development of drugs to improve patient outcomes (Fig. 2).

By analyzing high-dimensional data, AI-based technologies—including reinforcement learning—have been developed differentiating techniques. These models project the ideal mixes of time, cultural settings, and development nutrients to get the intended results. Molecular architecture and its connection to acceptable differentiation results were investigated using ML methods. The AI model can identify the ideal molecular alternatives for initiating heart development from pluripotent stem cells by focusing on form aspects, including geometric features and molecular configurations. This method helps identify pertinent molecules that can affect differentiation even with limited information. It increases the accuracy and efficiency of creating therapeutic strategies for cardiac regeneration (Etezadi et al. 2024a). Design studies utilizing AI enable the automatic development of a multicellular heart model for high-throughput screening. Projected ideal conditions for growing and producing various cell types inside a heart model using ML algorithms helped to maximize experimental settings. AI-driven design of experiments (DoE) techniques are used to examine the complex interactions between multiple cell types, media, and culture conditions, thereby enabling the identification of ideal combinations for accurate modeling of heart function. This automation increases the efficiency and scalability of screening activities in a multicellular environment, facilitating the rapid evaluation of possible drug candidates and therapeutic actions (Raniga et al. 2023). Utilizing data-driven methods, the maturity degree of cardiomyocytes produced from human pluripotent stem cells (hPSCs) utilizing AI was assessed. Using ML techniques, various data sources—including gene expression profiles, cellular shape, and electrophysiological features—were investigated to quantify the degree of cardiomyocyte development. AI models trained to recognize known markers of mature cardiomyocytes offer a precise assessment of maturation phases during the differentiating process. Their use in disease modeling, drug testing, and regenerative therapies depends on their consistency and precision in determining cardiomyocyte maturity; hence, this data-driven assessment improves these aspects (Hong et al. 2024).

It is underlined how patients' iPSCs should be used to replicate and cure neurogenetic disorders. Somatic cells from patients and healthy donors are converted into induced pluripotent stem cells (iPSCs) and then develop into suitable brain cell types. While healthy donor–derived iPSCs generate control neurons, patient-derived iPSCs produce neurons with mutations; CRISPR/Cas9 technology enables the creation of isogenic control neurons for comparison. By comparing patient and control neurons, disease phenotypes are identified through immunocytochemistry, gene expression analysis, and electrophysiological evaluation, thereby exposing information on the cellular and molecular basis of the disease. Personalized drugs and disease trait rescue are produced using therapeutic approaches that incorporate in vivo validation and high-throughput drug screening (Fig. 3). This method emphasizes how precision medicine and neurogenetic disease research could benefit iPSC-based technologies (Barral and Kurian 2016).

AI systems follow differentiation processes in real-time using multi-modal data, including transcriptomic, proteomic, and imaging datasets. Forecasting differential success with predictive models allows early intervention and change of approach. Using ML, stem cell differentiation and proliferation phases were investigated from electrical impedance spectroscopy (EIS) data. EIS signal analysis guided the construction of predictive models to precisely separate numerous phases of stem cell growth and differentiation. This non-invasive method offers a fast and reasonably cost-effective solution for conventional biochemical tests by real-time monitoring of biological parameters. Combining ML

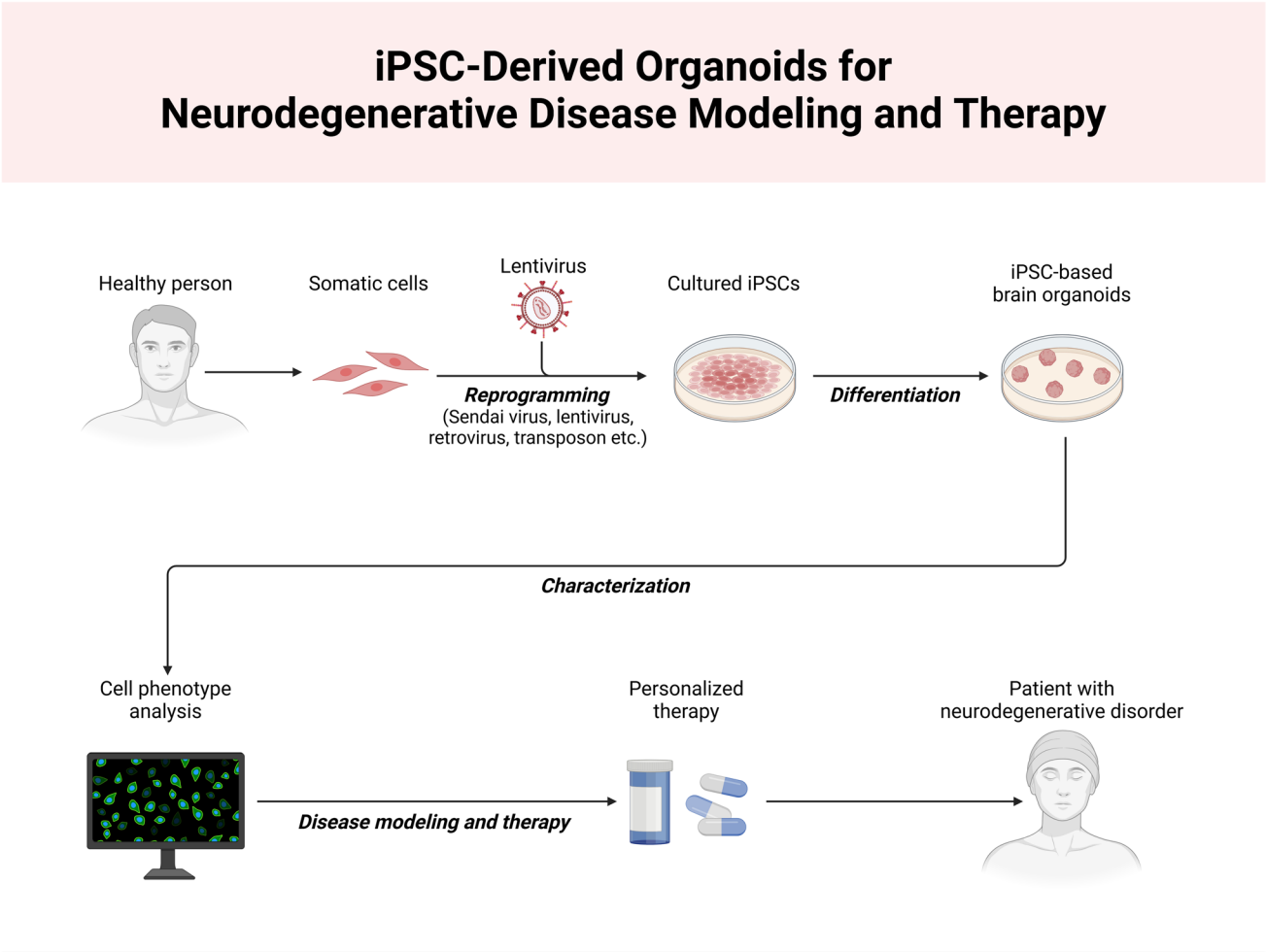

Fig. 2 IPSC-derived organoids for neurodegenerative disease modeling and therapy. This graph illustrates the benefits of studying and treating neurodegenerative diseases using brain organoids generated from induced pluripotent stem cells (iPSCs). Somatic cells—such as fibroblasts—are converted into induced pluripotent stem cells (iPSCs) using various methods and then cultivated to produce 3D brain organoids that mimic human brain features. These organoids aid in investigating molecular and cellular changes associated with neurodegenerative diseases. Individualized therapy development, research into pathogenic mechanisms, disease modeling, and screening of medicinal substances all contribute to improving patient outcomes (Jusop et al. 2023)

with EIS increases the accuracy and efficiency of stem cell characterization (Cunha et al. 2019).

ML and DL approaches were used to evaluate the degree of variation of retinal pigment epithelial (RPE) cells obtained from human iPSCs. Using robust algorithms to assess images and molecular data, notable features revealed the maturity and uniqueness status of RPE cells. The paper presents an automatic and exact method for evaluating different outcomes using convolutional neural networks (CNNs) and other ML methods. This approach enhances the precision and scalability of evaluation, allowing for the use of iPSC-derived RPE cells in pharmacological screening, disease modeling, and regenerative therapy for retinal diseases (Lien et al. 2023).

We investigated the variation in induced pluripotent stem cell growth systems using a live-cell imaging-based ML approach. ML algorithms extracted the necessary morphological and dynamic traits from real-time imaging data of several PSC cultures, which predict different outcomes. This approach increases consistency and efficiency in testing by identifying these essential traits and allowing real-time control and regulation of differentiation processes. Reducing heterogeneity in iPSC differentiation helps to enable the continuous creation of particular cell types for therapeutic use, disease modeling, and research (Yang et al. 2023).

AI-driven automation utilizing human pluripotent stem cells (hPSCs) facilitates differentiation. Using ML and DL approaches, the study uses high-content imaging and omics data to ascertain cell morphology, marker expression, and functional properties. Designed to identify cell states and track differentiation results, AI models provide a consistent, high-throughput, and scalable method for cell

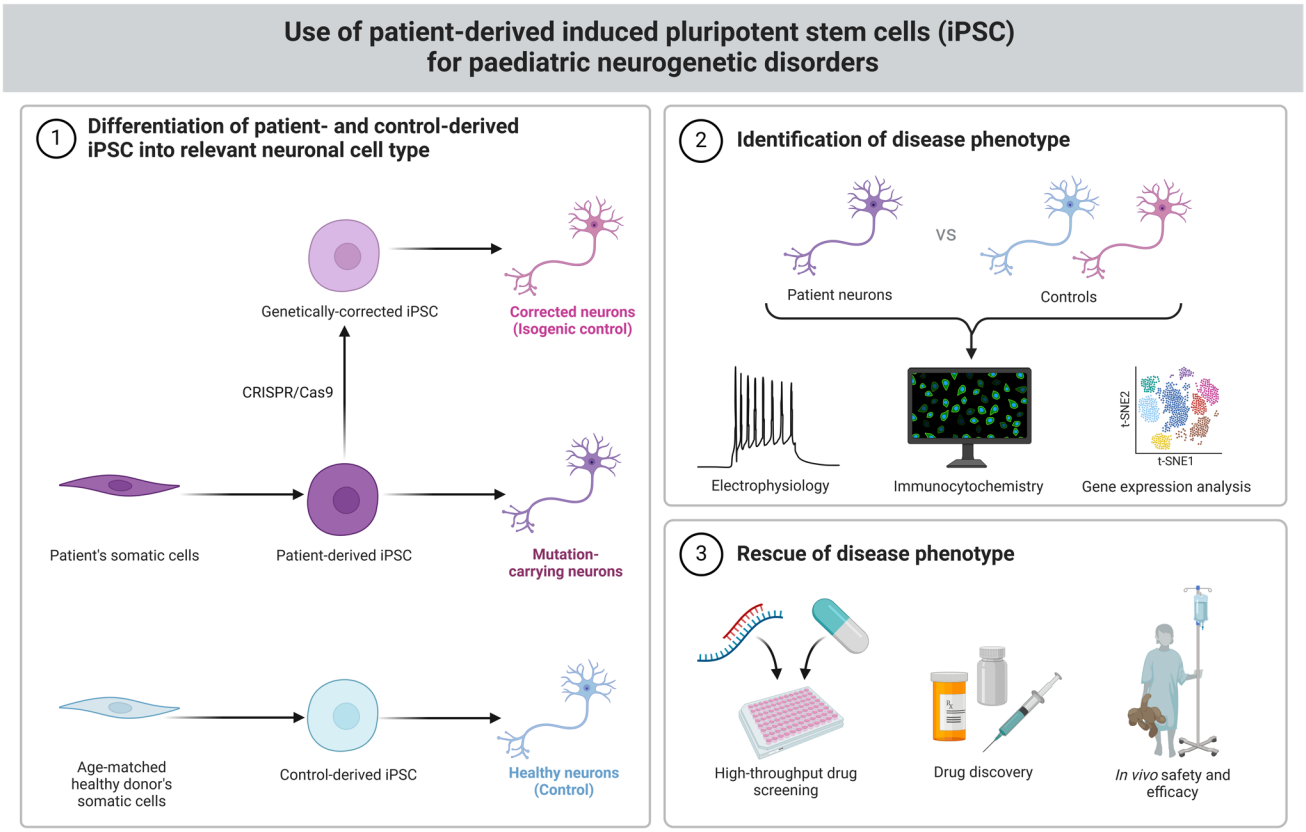

Fig. 3 IPSC-based disease modeling of childhood neurogenetic disorders. This procedure outlines how patient-derived induced pluripotent stem cells (iPSCs) are used to simulate and potentially cure young neurogenetic diseases. Somatic cells from both patients and healthy donors are reprogrammed into iPSCs, which are then differentiated into neural cell types. By utilizing CRISPR/Cas9 technology, isogenic control neurons are produced, thereby fixing disease-causing mutations. However, patient-derived iPSCs with disease-causing mutations still produce mutant neurons. Comparative analysis of patient and control neurons, using immunocytochemistry, gene expression analysis, and electrophysiology, reveals disease-specific characteristics. While high-throughput drug screening identifies potential therapeutic compounds, in vivo evaluation evaluates safety, therapy efficacy, and research quality, this approach highlights the adaptability of iPSC-based technologies in understanding disease circuits and producing targeted therapeutics for young neurogenetic diseases

characterization. This automated method lowers human error and enhances consistency, improving the assessment of hPSC-derived cells for drug discovery, disease modeling, and regenerative medicine (Marzec-Schmidt et al. 2023).

Convolutional neural networks (CNNs) were used to evaluate high-resolution imaging data on kidney organoids produced from human iPSCs. The morphological and structural traits linked with effective kidney organoid development and differentiation were clarified. Prediction models facilitate the early identification of organoids with great differentiation potential, thereby optimizing culture conditions and procedures. This approach enhances the scalability, repeatability, and efficacy of kidney organoids in disease modeling, pharmacological screening, and regenerative medicine (Park et al. 2022).

The application of multivariable process modeling ML techniques helped to clarify the cardiac development of human iPSCs. Consolidating and analyzing several factors influencing differentiation, including gene expression patterns, cell culture conditions, and time-lapse imaging data, ML techniques help the model precisely predict cardiac lineage commitment and differential efficiency by using essential parameters and their interaction. This approach reduces variability, improves repeatability, and optimizes differentiation processes to enable the generation of iPSC-derived cardiac cells for therapeutic and research uses (Williams et al. 2020).

Emphasizing the need to integrate AI with organoid technologies to enhance in vitro models, the concept of "organoid intelligence" was proposed. It became precise how AI-driven analysis of imaging, omics, and functional data may enable organoids to develop. ML techniques would allow researchers to track real-time performance, project developmental paths, and optimize organoid growth conditions. Furthermore, applications of this mix are achievable in disease modeling, tailored therapy, and high-throughput drug

screening. Emphasizing the possibility of combining AI with organoid technology to surpass present limits in scalability, repeatability, and interpretability, we entered a new century in exact in vitro modeling (Shi et al. 2024a). Through realistic multicellular modeling inside a controlled setting, AI/ML improves the repeatability and efficiency of preclinical research. Forecasting and optimizing iPSC differences, the ML approach also identifies ideal external parameters, such as the interplay between co-culture conditions and growth media. This helps identify setups that enhance the accuracy and physiological relevance of disease simulations.

AI, iPSC in drug discovery and disease modeling

Since they help to investigate disease mechanisms at the cellular level, patient-derived iPSCs offer a potent tool for studying genetic markers and disease-related traits. Since it dramatically improves efficiency and creativity, AI is vital for the creation of drugs. By using large datasets to maximize manufacturing parameters, AI-driven algorithms help to improve consistency, yield, and waste control. Utilizing the predictive maintenance capabilities of AI, drug development monitors real-time equipment performance to prevent downtime and associated expenses. Moreover, ML techniques ensure strict quality control, identifying flaws and maintaining high standards in drug development. AI enables the availability of raw materials and finished products, optimizes stock levels, and streamlines supply chain management. This adaptability facilitates the broad development of patient-specific drugs, leading to more effective and customized therapies. These developments enable AI to accelerate pharmaceutical manufacturing and drug discovery, thereby enhancing cost efficiency, quality, and accessibility, and ushering in a new era of patient-centered healthcare innovation (Fig. 4).

Convolutional neural networks (CNNs) have been investigated using high-content imaging data; for example, results have shown that ill and healthy cells show different morphologies. AI was used to differentiate between genetic heart diseases through sophisticated biomedical data analysis, which leveraged AI approaches. By means of ML algorithms, the integration of several datasets—including genetic sequences, ECG patterns, and clinical symptoms—helps to identify disease-specific biomarkers and phenotypes. This AI-driven approach improves the design of personalized therapy options for genetic heart disease, prognosis prediction of disease progression, and diagnostic accuracy (Juhola et al. 2019).

Using AI, stem cell technology, three-dimensional and four-dimensional printing, one can provide breakthrough tools for tailored cardiovascular treatment. Proposed to be able to improve stem cell differentiation, forecast therapy outcomes catered to individual patients, and hasten the manufacturing of printed cardiovascular components is AI. Analyzing complex data using ML and DL helps researchers maximize biomaterial choice for printing, guarantee functional integration of stem cell-derived tissues, and customize treatments to fit specific patient demands. By addressing scalability, repeatability, and customization in cardiovascular medications, this multidisciplinary approach holds great promise for promoting precision medicine (Bax et al. 2023).

By utilizing organoid models, organoid intelligence combines AI, neurological research, and biological computing, thereby enabling advanced analysis and modeling of organoid data, including neural activity, developmental patterns, and functional responses. This approach simplifies organoids as biological computer systems, therefore allowing the study of complex neurological processes and the assessment of therapeutic interventions. While addressing scalability, repeatability, and ethical issues, the authors underline the possibilities of AI-driven organoids for clarifying brain function, disease processes, and individualized treatment (Ballav et al. 2024).

DeepNEU is a computational model for infantile-onset Pompe disease (IOPD) based on simulations of artificially produced stem cells and differentiated skeletal muscle cells. Using AI, technology replicates disease-specific biological environments to find new biomarkers and therapeutic targets. DeepNEU accelerates the drug discovery process and enhances the understanding of the pathophysiology of IOPD through the integration of multi-omics data and modeling of metabolic and molecular pathways. This approach shows how tailored treatment and the development of drugs for uncommon genetic diseases could be improved by AI-driven simulations (Esmail and Danter 2019).

Using induced pluripotent stem cells (iPSCs), omics technologies, and ML, the interaction among race, genes, and congenital heart disease (CHD) was investigated. Derived from many racial backgrounds, induced pluripotent stem cells (iPSCs) imitate CHD and probe the genetic changes linked with the condition. Combining omics data—such as transcriptomics, proteomics, and genomics—enables the identification of essential biomarkers and molecular mechanisms associated with coronary heart disease in various populations. Then, large-scale databases are examined using ML techniques to project disease paths and probable therapies. The work uses AI and omics to show how tailored medicine could increase understanding of ethnic inequalities in coronary heart disease. (Mullen et al. 2021) and better accuracy of therapies.

Using multimodal data fusion and ML integration, pathphenotypic features of iPSC dilated cardiomyopathy (DCM) models were identified. The integration of functional readouts, cellular shape, and gene expression profiles generated

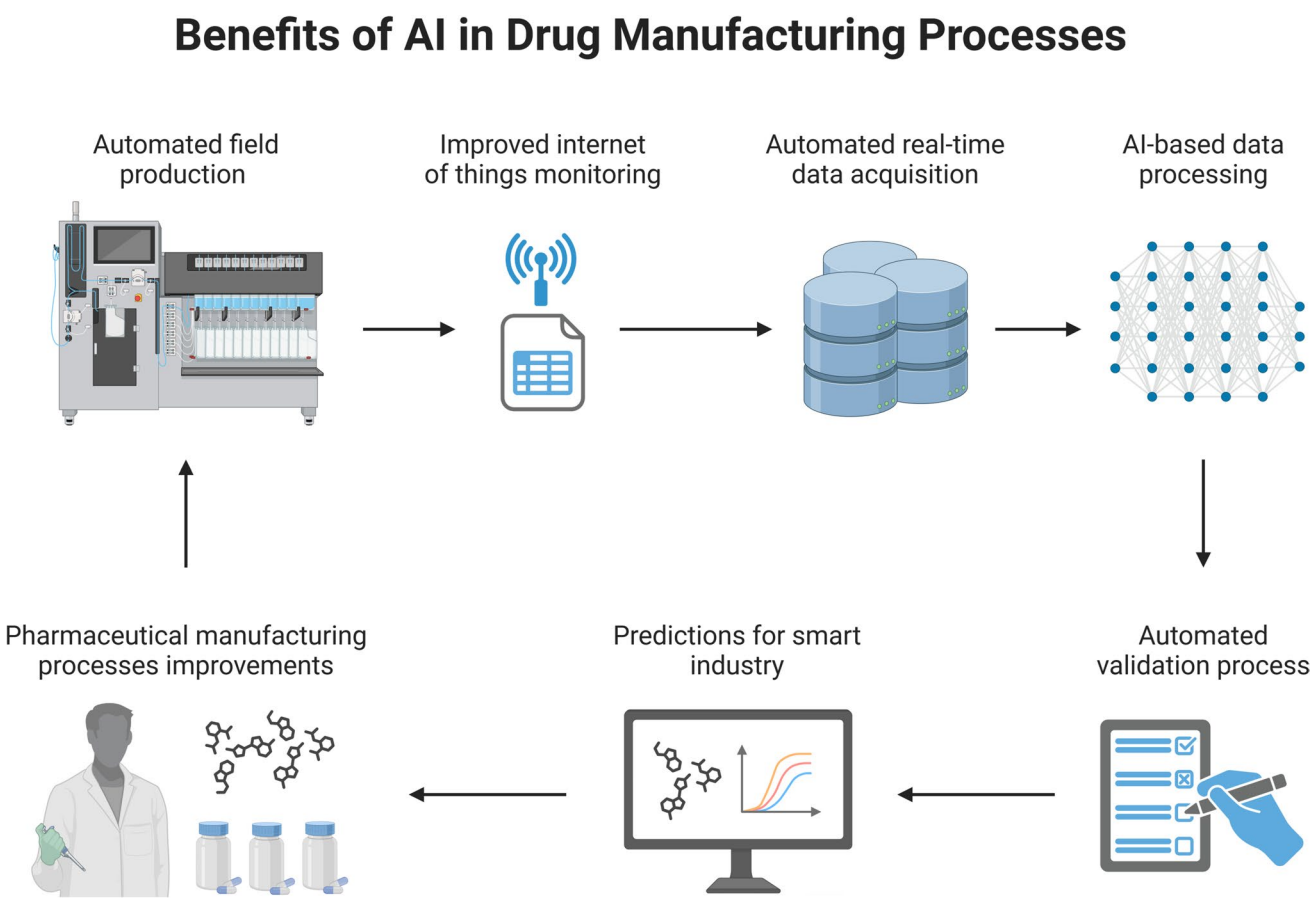

Fig. 4 Benefits of AI in drug manufacturing processes. Utilizing the process of optimization at every manufacturing level, AI is transforming the pharmaceutical industry. AI's extensive dataset analysis identifies optimal settings to ensure consistency, increase yields, and minimize waste. It is especially crucial in predictive maintenance, as it monitors real-time equipment performance to prevent breakdowns and reduce downtime. AI enhances quality control by ensuring regulatory compliance and facilitating the early detection of defects. AI forecasts demand in supply chain management, optimizing inventory, and reducing disruptions. AI also helps generate personalized medicines by modifying treatments to meet specific patient needs, thereby accelerating the global delivery of life-saving drugs and improving efficiency, cost-effectiveness, and quality (Chaudhary et al. 2023)

a comprehensive dataset for DCM modeling. These multimodal datasets are analyzed using ML approaches to help identify disease-specific biomarkers and phenotypes. This approach clarifies potential medicinal targets and enhances our understanding of the molecular basis of DCM. The method used for AI and data fusion could enhance precision treatment for cardiovascular diseases (Wali et al. 2024) and disease modeling.

Investigating how medications affect cells derived from iPSCs accelerates drug development. Using multi-omics data, ML techniques that forecast pharmacological efficacy and toxicity help to identify possible therapeutic candidates. High-throughput screening methods driven by AI have helped find creative treatments for complex diseases, such as Alzheimer's and Parkinson's. One might focus on how AI can optimize the medication development process by utilizing AI-enhanced iPSCs in drug screening and employing iPSC-derived models to predict therapeutic efficacy and safety profiles. Extensive omics data produced by iPSC-based systems are examined using AI approaches like ML and DL, therefore enabling the identification of possible therapeutic targets, biomarkers, and medication candidates. Research shows AI could develop new treatments, increase the consistency of in vitro models for tailored medicine, and raise the accuracy and efficacy of drug screening (Yildirim et al. 2024).

Using AI and genetic technologies to examine large databases, identify disease-specific biomarkers, and forecast therapy reactions speeds the development of specialized drugs. These innovative technologies could lead to reduced reliance on conventional animal models, enhanced drug research efficacy, and greater precision in treatments, thereby increasing the accuracy of therapeutic interventions.

AI's transformative potential in stem cell research and medical development is demonstrated by its integration into biomedical science, thereby accelerating procedures such as

differentiation, reprogramming, and quality assurance. This examines how AI enhances personalized medicine, identifies new therapeutic targets, and predicts treatment efficacy, thereby accelerating the development of drugs. It was clear how AI-driven data analysis in genomics and multi-omics could provide fresh insights into disease etiology and treatment choices. The paper highlights how AI may drive stem cell technologies, advance precision medicine, and hasten drug discovery projects (Kim and Hong 2024).

Using human iPSC-derived neurons in conjunction with sophisticated deep morphological learning approaches, a new microphysiological system for predicting neurotoxicity has been constructed. Many neurotoxic compounds are evaluated utilizing many induced pluripotent stem cells combined into neural models. Extensive morphological studies examine minute changes in cellular structure that may indicate toxicity in neural form. By providing more accurate and efficient forecasts of neurotoxic effects, this method enhances the safety assessment of new drugs and chemicals during preclinical phases, thereby enabling high-throughput screening (Han et al. 2024).

AI models diseases using produced pluripotent stem cells; therefore, guiding treatment is unique to every individual patient. Particularly related to neurological and cardiovascular diseases, the study demonstrates how AI can rapidly evaluate complex data from iPSC-based studies, thereby accelerating the identification of therapeutic targets and the prediction of treatment outcomes. While highlighting challenges such as data uniformity, model generalizability, and ethical concerns in the development of AI-driven medicine (Kusumoto et al. 2022), the findings also reveal possibilities.

An analysis was conducted on the possibility of combining AI and ML with iPSC-based technologies to improve individualized treatments and regeneration medicine. It highlights how AI and ML can simplify iPSC derivation, differentiation, and quality control procedures, as well as identify new therapeutic targets and drug candidates. It also emphasizes the constraints of using modern technologies, which include the need for correct datasets, validation of computational models, and ethical issue resolution using modern technologies. Induced pluripotent stem cells, combined with AI and ML, could help address current challenges in cellular therapies and advance precision medicine (Coronnello and Francipane 2022).

The merging of nonlinear analysis and human iPSC-based platforms for pharmaceutical cardiotoxicity with ML approaches was investigated. This clarifies the complexity of patterns in iPSC-derived cardiomyocytes through nonlinear dynamics, thereby improving the sensitivity and specificity of cardiotoxic impact detection. Through these tests, ML analyzes high-dimensional data to improve adverse drug reaction prediction. The study highlights the need for this approach in enhancing the accuracy of preclinical drug safety assessments, thereby enabling more effective drug development strategies and reducing clinical trial failures (Kowalczewski et al. 2022).

The work utilized high-content screening data from cardiomyocytes generated from iPSCs to demonstrate how DL can predict cardiotoxicity patterns. The approach utilizes advanced neural network models to identify subtle changes in phenotypes and cellular responses associated with drug-induced cardiotoxicity. The results demonstrate the effectiveness of DL in handling complex, high-dimensional datasets and enhancing the expected accuracy of preclinical drug safety assessments. This approach provides a scalable means to integrate AI with iPSC technologies, enhancing the early identification of cardiotoxic risk and enabling the development of safer drugs (Grafton et al. 2021).

Human-induced pluripotent stem cells (hiPSCs) led to a DL approach for assessing drug-induced structural toxicity in hepatocytes and cardiomyocytes. Models for detecting and quantifying minute structural and cellular changes associated with drug toxicity were developed using high-content imaging data. Indicating its potential for high-throughput drug screening, the method demonstrates notable sensitivity and accuracy compared to existing treatments. The combination of modern AI methods with hiPSC-derived cellular models gives a strong basis for assessing pharmaceutical safety. This helps to quickly identify molecules that can cause adverse effects throughout the entire pharmaceutical development process (Maddah et al. 2020).

Using ML methods, calcium transients in cardiomyocytes produced from human induced pluripotent stem cells were investigated to forecast pharmacological inotropic effects. Using calcium signaling data, precise construction of models for evaluating drug-induced changes in cardiac contractility was undertaken. The ML method proved better sensitivity and specificity than conventional techniques, thereby underlining its importance in evaluating inotropic effects. This mix of AI with iPSC-derived cardiomyocytes offers a feasible paradigm for improving the accuracy of preclinical cardiotoxicity evaluations and simplifying drug discovery methods (H. Yang et al. 2023).

The cooperative evaluation of pharmaceuticals using AI and organ-on-a-chip technology highlights their ability to change preclinical research. By mimicking the functions of human tissues and organs, organ-on-a-chip technologies offer a therapeutically relevant platform for drug testing. Using reliable evaluations of pharmaceutical efficacy and toxicity, AI improves the accuracy and efficiency of data processing. The study emphasizes how new technology might improve personalized medicine, reduce reliance on animal models, and advance medication development (Deng et al. 2023).

The developmental toxicity of drugs and environmental toxins was assessed using stem cell–based high-throughput

screening and ML approaches. This work aims to construct more exact, human-relevant models for evaluating negative consequences during development using stem cells, mainly induced pluripotent stem cells (iPSCs). ML helps analyze large amounts of screening data, enhancing the accurate identification of harmful chemicals. This approach provides a reasonable substitute for conventional animal testing since it improves the efficacy of developmental toxicity research and helps to enable safer medicine development methods (Zhang 2021).

Using human iPSC-derived cardiomyocytes and silico models helped to enhance cardiovascular toxicity screening. As these cells faithfully reproduce human heart tissue, the researchers combine computational models with the biological relevance of iPSC-derived cardiomyocytes to forecast possible drug-induced cardiovascular damage. To improve the accuracy and sensitivity of cardiotoxicity evaluation, the work uses both computational and experimental approaches. Early-stage drug safety research (Sinitsyna et al. 2025) has a more effective and predictive platform when preclinical drug assessment's accuracy is improved and reliance on animal models is minimized.

ML approaches and organ-on-chip systems were investigated as novel technologies to replicate human heart damage and pathology. This work shows the use of ML techniques in combination with organs-on-chips that replicate fundamental cardiac tissue dynamics, therefore enabling a more exact prediction and assessment of drug-induced cardiac effects. The integration of sophisticated technology emphasizes that improving cardiotoxicity predictions can help to enhance drug development and lower the need for animal testing, thus boosting preclinical safety assessments and developing personalized medicine in cardiac care (Taniguchi 2023).

Silico analysis and phenotypic drug screening of induced pluripotent stem cells allowed suitable candidates for the therapy of pulmonary arterial hypertension (PAH) to be identified. Drug-induced phenotypic changes were exposed by high-throughput screening of human iPSC-derived endothelial cells. They ran data-based computational models. Based on its mode of action, Tyrphostin-AG1296 is a possible PAH treatment drug. This work highlights the potential of combining silico approaches with iPSC-based drug screening to identify new treatments and enhance personalized therapy for complex cardiovascular diseases (Gu et al. 2021).

AI evaluations of pharmaceutical safety and toxicity can improve the drug development process by providing more accurate predictions of medication-induced adverse effects through the analysis of large and sophisticated datasets from preclinical research. DL and ML, among other AI techniques, aim to enhance the accuracy and efficacy of safety assessments, reduce reliance on conventional animal models, and facilitate the early identification of potential side effects during the drug development process. The study highlights the transformative power of AI in accelerating safer and more effective pharmaceutical development (Joshi-Barr and Wampole 2024).

Human organoids, three-dimensional cellular models that duplicate human organs, clearly have uses in predictive toxicology research and drug development. They provide a more biologically suitable and exact framework for studying drug toxicity and efficacy. The authors investigate how organoids can be used to evaluate adverse drug reactions, improve forecasts of human-specific responses, and aid in the development of safer and more efficient treatments. This approach could help overcome the restrictions of traditional in vitro models and animal testing, supporting pharmaceutical research and individualized treatment (Matsui and Shinozawa, 2021).

Using iPSC-derived cardiomyocytes, multidimensional model platforms assessing cardiotoxicity in cancer treatment underscore the need to reproduce human cardiac responses to chemotherapeutic drugs, which may have cardiotoxic side effects. The researchers aim to integrate multidimensional models encompassing various aspects of drug-induced toxicity, including cellular, molecular, and functional changes. This enhances the prediction and understanding of cardiotoxic hazards associated with cancer treatments. This approach provides a more accurate and human-relevant method for assessing preclinical safety and supporting the development of improved cancer treatments (Thomas et al. 2021).

Using high-throughput imaging of HepaRG cells and ML-based phenotypic characterization, the study of direct hepatocyte damage in humans, the HepaRG human liver cell line, and high-throughput screening tracked cellular changes brought forth by medications. Later analyses of the phenotypic data for tendencies suggestive of hepatotoxicity examined ML approaches. The integrated approach enhances drug development by utilizing early risk identification, a more dependable and human-relevant alternative to conventional hepatotoxicity testing techniques, and providing an accurate prediction of drug-induced liver toxicity (Hussain et al. 2020).

Micro-engineered systems composed of iPSC-derived cardiac and hepatic cells will be used to evaluate pharmaceutical side effects. These micro-fabricated platforms can provide a more realistic depiction of drug interactions with these organs in vivo by simulating human cardiac and hepatic tissue. The authors emphasize the potential of these technologies for high-throughput screening to assess drug-induced toxicities, thereby enabling more precise and efficient identification of side effects. Using iPSC technology combined with microengineering, the safety and efficacy assessment of new drug candidates is improved,

providing a suitable alternative to traditional animal models (Dame and Ribeiro 2021).

Using patient-derived iPSCs, sometimes called "clinical trial in a dish," concerns about drug-induced cardiotoxicity were found using patient-specific models created using iPSC cultivation from individuals with various genetic backgrounds, investigating pharmacological responses and toxicity at the cellular level. The work shows that, considering individual responses, iPSC-derived cardiomyocytes can consistently predict the pharmacologic effects of drugs. This approach offers a more customized and relevant way to evaluate medications, maybe reducing cardiotoxicity in clinical trials and improving evaluations of pharmacological safety (Lam and Wu, 2021).

Research on developments in AI-driven cardiotoxicity detection and assessment could be used with other experimental models, including cardiomyocytes generated from iPSCs, to precisely and effectively find drug-induced cardiotoxic effects. By examining complex datasets produced from high-throughput testing, AI approaches such as DL and ML might help forecast cardiotoxicity outcomes. This highlights how AI technology could improve the safety assessments of medications, reduce dependency on animal testing, and help enhance the process of developing drugs (Ahmed et al. 2024).

Automated medication categorization is made possible by examining heart tissue produced from human pluripotent stem cells by ML, enabling automated drug classification. The effect of medications on the contractile performance of heart tissue was assessed using ML approaches. The study shows that using ML to automate the identification of medication-induced effects on cardiac performance may improve drug screening procedures' efficacy and accuracy. This approach provides a suitable framework for the first evaluation of cardiotoxic impacts in drug development, enabling medication safety research (Lee et al. 2017).

General chemical toxicity gene network predictions based on gene expression data from iPSC-derived models helped to identify possibly harmful compounds. They used transfer learning using already available embryonic stem cell data to improve the expected accuracy of their toxicity assessments. This work shows that merging iPSCs with modern ML algorithms can produce a completer and more predictive tool for evaluating chemical safety, supporting improved and human-relevant toxicity assessments in drug development (Yamane et al. 2022).

By automating data analysis, trend identification, disease modeling, and toxicity evaluation enhancement, AI could help research organoid systems. This integration improves the predicted accuracy and efficiency of replies tailored for human use regarding drugs and treatments. The results show that AI-informed organoid research can hasten biological discoveries, lower dependency on animal models, and enhance precision medical tools (H. Wang et al. 2024).

Using PSCs—especially iPSCs—a range of approaches were investigated to replicate developmental processes and assess the adverse effects of drugs and contaminants in early life. More accurately, human-relevant models created from PSCs help to highlight possible developmental issues missed by more traditional testing techniques. The study underlines that PSC-based tests could improve safety assessments in medicine development and help reduce the need for animal testing (Piersma et al. 2022).

Using ML approaches might improve 3D cell culture models, which more faithfully depict the complexity of human tissues than conventional 2D models, boosting drug testing. By using three-dimensional models and ML, researchers may automate data processing, detect trends, and offer more precise assessments of pharmaceutical efficacy and toxicity. This approach provides a more dependable and effective high-throughput screening platform, thereby helping to accelerate the development of safer and more potent drugs (de Silva et al. 2024).

Modern computer techniques in AI could assess several treatment strategies and grasp the complex molecular dynamics of Huntington's disease. Using induced pluripotent stem cell (iPSC)–derived models of Huntington's disease (HD), we can offer a thorough phenotypic characterization, thereby strengthening our understanding of disease etiology and increasing the efficacy of treatment screening. This approach can forward HD research, point up fresh therapeutic targets, and produce more potent HD treatments (Finkbeiner, 2024).

A microfluidic device modeling the complex environment of peripheral neurons was examined closely to evaluate neurotoxic effects at low chemical concentrations. Using microfluidic technology and DL algorithms, scientists can determine cellular reactivity to various substances, therefore enabling early prediction of neurotoxic hazards. This technology improves the safety evaluation of chemicals and medications by means of a high-throughput, more sensitive instrument for toxicological evaluations and drug screening (Han, Xue, et al, 2022).

The ML platform uses iPSC to replicate SARS-CoV-2 infection, enabling drug identification and reusing during viral pandemics. Induced pluripotent stem cells (iPSCs) are used by researchers to reproduce human infections by combining stem cell technology with ML techniques to evaluate potential therapeutic agents and investigate viral connections. This approach speeds up the identification of current medications that might fight pandemics like COVID-19, therefore enabling more exact and relevant studies on human viral infections. Using a quicker approach to pharmaceutical development, the platform improves pandemic readiness (Esmail and Danter 2019).

A novel scoring system assesses neurotoxicity based on cellular response to drug exposure. Early identification of possible neurotoxic effects in drug development has a more physiologically meaningful basis from using crucial brain cells. AI can lower costs and improve accuracy by means of large-scale data analysis, molecular interaction prediction, and improvement of clinical trial design, which helps to accelerate drug development. Citing sixty (Narayanan et al. 2022), the paper emphasizes how AI is transforming pharmaceutical research and optimizing the development of drugs.

Analyzed in significant numbers of biological data, AI-driven approaches found possible ALS therapeutic targets using degenerative neurological disease. Using AI methods, including DL and ML, the study aims to hasten the creation of new drugs and treatments meant to stop or slow the progression of ALS. The research shows how AI can speed the creation of focused therapies for ALS and improve our knowledge of ALS at the molecular level (Myszczynska 2021).

Because of their better fit to human liver function than conventional cell culture models, liver organoids can be used to assess drug-induced toxicity. Drug metabolism depends on cytochrome P450 enzymes and organoids, providing a more reasonable model for understanding the hepatic pharmacological processing of drugs. The paper emphasizes how these models might reduce reliance on animal research, enhance human pharmacology and toxicity forecasts, and increase safety testing using their potential (Kim and Park 2025).

Using ML and DL, AI technology may examine large datasets to forecast a chemical's toxicity before clinical trial review. Including AI in toxicological studies helps to lower side effects, maximize drug compositions, and find possible early dangers. The study underlines the increasing relevance of AI in improving the accuracy and efficacy of toxicological forecasts, reducing the need for animal testing, and accelerating the development of drugs (Yingngam 2025).

AI can help analyze complex phenotypic data obtained from high-throughput drug screening, enabling more exact identification of possible therapeutic agents. It can also spot patterns in phenotypic responses using traditional machine-learning techniques that would be difficult to find. The paper emphasizes how AI might hasten the discovery of novel drugs by speeding up the drug research process, improving the accuracy of medication efficacy assessments, and pointing out creative treatment targets (Malandraki-Miller 2021).

A sophisticated imaging technique that captures several cellular characteristics using advanced AI methods was applied to show how integrating AI with cell painting could find drugs that influence macrophage polarization, a vital component of inflammation and immune response. When synthesizing medications for inflammatory diseases, this approach helps spot new therapeutic molecules and clarify immune modulation routes (Brüggenthies et al. 2024).

Stem cell treatment helps to maximize data across several biological spheres, including molecular interactions and tissue reactions. Using large-scale datasets to train ML models to improve therapeutic efficacy, guide the development of regenerative medicines, and forecast the outcomes of stem cell-based therapies will highlight the paper's claim that integrating stem cell biology with computational methods will hasten the evolution of modern regenerative medicine technologies (Pandita et al. 2024).

The limitations and opportunities were analyzed in the creation of numerous testing models, including in vitro, computational, and organ-on-chip technologies. Unlike traditional animal models, they emphasize that these NAMs can produce more precise and human-relevant data, clarifying the molecular and cellular aspects of drug response information. The report reflects the challenges in verifying and standardizing these techniques for general application. Using creative models to improve projections, reduce reliance on animal testing, and ensure the manufacturing of safer drugs will help advance the push for drug development (Pang et al. 2024).

ML and DL, among other AI technologies, help forecast drug efficacy, find new therapeutic targets, and hasten the development of Alzheimer's disease treatments. Using conventional methods, AI searches vast amounts of biological data, including clinical, proteomic, and genomic information, and identifies conflicting trends. The paper argues that improving the speed and accuracy of medication candidate selection using AI could significantly alter the direction of Alzheimer's disease treatment and address the unmet medical demand for efficient therapies (Cheng and Cummings 2022).

By offering a more accurate representation of human physiology than conventional cell cultures, organoids—three-dimensional in vitro models that faithfully replicate human organ design and function—are revolutionizing biomedical research. They enable better disease modeling, individualized drug testing, and the identification of new therapeutic targets. The integration of organoids into regenerative medicine for possible organ regeneration therapies and tissue-engineering techniques is discussed in this work (Yao et al. 2024).

By advocating the use of human cells, organoids, and AI/ML approaches in pharmaceutical research, the FDA Modernizing Act 2.0 seeks to reverse traditional animal models. Preclinical drug testing's accuracy, applicability, and efficiency could all improve with this fresh method. Human cell-derived models like organoids offer data more relevant to human physiology, even while AI and ML tools help analyze complex biological data to predict pharmacological reactions. The study emphasizes how these new approaches

could maximize regulatory processes, reduce dependency on animal testing, and hasten the creation of safer and more successful treatments (Zushin et al. 2023).

IPSC work combines multi-omics with AI

Integrating AI with multi-omics technologies, including transcriptomics, epigenomics, and proteomics, has produced a hitherto unheard-of understanding of the biology of iPSCs. Integrative approaches search complex data for biomarkers linked to regulatory networks, pluripotency, and differentiation. Natural language processing (NLP) has lately advanced to speed hypothesis development and enable the curation of knowledge from scientific literature. Using metabolomics data combined with genomic information, scientists were able to pinpoint critical metabolic pathways that may be linked to diseases. This thorough investigation shows the relationships between changes in gene expression and metabolic activities, therefore clarifying the pathophysiology of schizophrenia (Spathopoulou et al. 2024). The study emphasizes specific networks that might lead to new therapeutic approaches for schizophrenia and the viability of stem cell-derived models for clarifying complex mental diseases.

Combining several omics data layers—genomics, transcriptomics, proteomics, and epigenomics—helps to find critical molecular regulators and signaling pathways guiding the course of Alzheimer's disease. This approach defines future therapy goals and offers a fresh perspective on the complex biology of Alzheimer's disease. By identifying essential nodes in the molecular circuitry of the disease, network-based study seems to hasten the progress of new treatments (Wang et al. 2021).

Stem cell therapy, AI, and multi-omics techniques were combined to investigate creative paths to enhance Duchenne muscular dystrophy (DMD) treatments. The result emphasizes the possibility of stem cells—especially iPSCs—as a model for disease and a basis for subsequent treatments. The study stresses how AI can examine enormous volumes of omics data—including transcriptomics, proteomics, and genomes—to find important biomarkers, forecast disease paths, and improve individualized treatment plans. Using creative technologies, we can improve our knowledge of the molecular causes of DMD and open the path for precision medicine, enabling highly targeted and successful treatments (Vera et al. 2022).

Investigating several multi-omics data integration approaches and their possible applications for knowledge of mental diseases. This work highlights modern methods for combining proteomic, epigenomic, transcriptomic, and genomic data, demonstrating their ability to fully show the complicated biological processes behind mental diseases. The benefits of multi-omics integration were analyzed to clarify disease processes, spot new biomarkers, and refine diagnosis and treatment plans. They underline the need to create reliable computer models to control the large and varied datasets produced, therefore enabling more individualized and exact medical interventions for mental disorders (Satyanarayanan et al. 2023).

We investigated extensively produced neurons using human iPSCs, combining numerous omics data—including transcriptomics, proteomics, metabolomics, and genomics—using several omics tools. This paper provides a comprehensive molecular profile of iPSCs and their differentiation into brain cells. This multi-omics method enhances our understanding of the molecular foundations and cellular mechanisms underlying brain development and the onset of neural disorders. The investigation highlights key markers and regulatory systems, offering new opportunities for personalized therapy approaches. It clarifies the possible character of iPSC models for neurodegenerative disorders (Lee et al. 2024).

A comprehensive multi-omics approach will investigate how microenvironmental dynamics influence stem cell fate decisions. This work combines genomic, transcriptomic, proteomic, and metabolomic data to show how environmental cues, cellular interactions, and extrinsic factors—including the stem cell niche—impact stem cell activity and differentiation. Using molecular-level studies of these intricate interactions, researchers identify essential regulating networks that control stem cell fate decisions. The results have a significant impact on the development of stem cell-based treatments, as they clarify strategies for controlling stem cell differentiation and enhancing regenerative medicine applications through environmental changes (Shanthanam et al. 2024).

We investigated the use of multi-omics analysis to understand human diseases and the potential of a multi-omics strategy in identifying new biomarkers, thereby clarifying disease pathways and promoting precision medicine. Combining several omics layers—such as genomics, transcriptomics, proteomics, and metabolomics—helps one grasp the molecular mechanisms behind different diseases. This work shows that combining data from several omics platforms allows a thorough investigation of the complexities of human diseases, including cancer, neurodegenerative disorders, and metabolic conditions, opening the path for more individualized and successful therapeutic approaches (Chen et al. 2023).

Induced pluripotent stem cells (iPSCs) might be coupled with several omics technologies in neurodegenerative diseases. Recent developments in integrating induced pluripotent stem cells (iPSCs) with genomic, transcriptomic, proteomic, and metabolomic data have been examined to enhance understanding of the molecular mechanisms underlying neurodegeneration. This work

utilizes iPSC-derived disease models to demonstrate how multi-omics approaches can provide novel insights into the pathophysiology of various disorders, including Parkinson's disease. These combined approaches highlight their potential applications in identifying new biomarkers, elucidating disease-specific molecular signals, and developing personalized therapy plans, thereby enhancing individualized medicine in neurodegenerative disease studies (Streubel-Gallasch and Seibler 2025).

Single-cell omics technology has shown critical new directions in cardiovascular research. The work clarifies the approaches for examining single-cell genomes, transcriptomics, proteomics, and epigenomics to evaluate the high-resolution heterogeneity of cardiovascular cells generated from iPSC. Through these creative approaches, the authors underline that single-cell research can clarify intricate cellular dynamics—such as differentiation, function, and treatment responsiveness—that help to grasp cardiovascular disease. This work shows how single-cell omics and iPSC models may be combined to improve knowledge of cardiovascular disorders, pinpoint new therapeutic targets, and streamline cardiovascular treatment plans (Kim et al. 2025).

Using iPSC-derived motor neurons from C9ORF72-associated amyotrophic lateral sclerosis (ALS), we investigated multi-omics holistically. The work combines genomics, transcriptomics, proteomics, and metabolomics to elucidate the molecular changes associated with C9ORF72-related ALS using iPSCs derived from ALS patients, thereby replicating ALS within a cell-specific context and identifying critical metabolic pathways related to motor neuron degeneration. Apart from stressing possible biomarkers and therapeutic targets for the following clinical interventions for this crippling neurodegenerative disease, the results offer a vital fresh insight into the pathogenic causes of ALS (Phatnani et al. 2021).

Using AI and multi-omics data to show the negative consequences of post-transcriptional control. The study demonstrates how combining modern AI approaches with omics data—specifically transcriptomics, proteomics, and genomics—can enhance understanding of the molecular mechanisms of toxicity and their impact on gene regulation. The author highlights how AI can analyze large-scale omics data, identify hidden trends, and predict the future effects of harmful compounds on cellular function. Emphasizing post-transcriptional control and illustrating how deviations in RNA processing, stability, and translation can have negative consequences, this work enhances our understanding of molecular toxicity. It makes advanced therapy methods more readily available (Asensio 2022).

AI frameworks and computational platforms driving iPSC advancements

The combination of advanced artificial intelligence (AI) frameworks with induced pluripotent stem cell (iPSC) techniques has altered several aspects of reprogramming, differentiation, and disease modeling. AI models, intense learning (DL), and reinforcement learning (RL), provide scalable, real-time solutions for addressing the complexities of high-dimensional iPSC data, predicting biological effects, and enhancing experimental design. This is different from traditional bioinformatics tools.

AI models and algorithms in iPSC research

Convolutional neural networks (CNNs) are widely used to analyze imaging data from iPSC colonies, enabling the examination of colony morphology, genetic stability, and pluripotency without the need for physical handling. Models based on CNNs, such as those developed by (Chu et al. 2023). We can categorize stem cell phases and predict the effectiveness of reprogramming by utilizing features extracted from time-lapse microscopy and bright-field images.

Deep reinforcement learning (DRL) frameworks enhance differentiation protocols by identifying the optimal environmental variables, such as growth factors and time intervals, for lineage-specific differentiation (Etezadi et al. 2024b). A DRL-guided method was used to create protocols for cardiac differentiation. These protocols had better repeatability and maturation rates than standard methods.

Utilizing AutoML platforms, such as TPOT (Tree-based Pipeline Optimization Tool) and AutoKeras, to automate the process of combining multi-omics data and forecasting the fate of iPSCs. These systems can mimic interactions between transcriptome and epigenomic networks, making it easier to identify regulatory networks that control the efficiency of reprogramming and the degree of cell commitment to a specific type (Capponi and Wang 2024; Lee et al. 2024).

AI-enabled platforms for drug screening and disease modeling

DeepNEU and other AI-enhanced high-content screening methods combine omics data with in silico gene regulation network modeling to mimic how cells behave in a disease-specific manner. Researchers utilized these models to explore potential treatments for rare diseases, such as juvenile Pompe disease and dilated cardiomyopathy (Esmail and Danter 2019; Wali et al. 2024).

Deep learning–based deep phenotyping platforms are beneficial in assessing the risk of cardiotoxicity using cardiomyocytes derived from induced pluripotent stem cells (iPSCs) (Grafton et al. 2021). Employed deep learning to identify subtle structural abnormalities in cardiomyocytes exposed to drugs. This was far better than manual grading in terms of both sensitivity and speed.

Microphysiological systems powered by AI, which utilize iPSC-derived neurons and CNNs, can now screen chemicals in real-time to predict neurotoxicity (Han et al. 2024). This technology enables the evaluation of drug safety in its early stages by precisely predicting neurotoxicity at the cellular level at a low cost (Fig. 5).

Emerging frontiers: AI and organoid intelligence

"Organoid intelligence" is a complex blend of artificial intelligence and three-dimensional, induced pluripotent stem cell-derived organoid models. These systems utilize various types of AI models, including image-based CNNs, omics-based transformers, and temporal neural networks, to examine how organoids grow, behave, and respond to treatment (Ballav et al. 2024; Shi et al. 2024b). AI-driven organoid platforms offer us an unprecedented glimpse into how the brain develops, how diseases function, and how to tailor treatments to each individual in a way that works best for them.

Challenges and future direction

AI combined with multi-omics technologies—including transcriptomics, epigenomics, and proteomics—has provided a previously unattainable understanding of iPSC biology. Integrative models analyze challenging data to identify biomarkers associated with pluripotency, differentiation, and

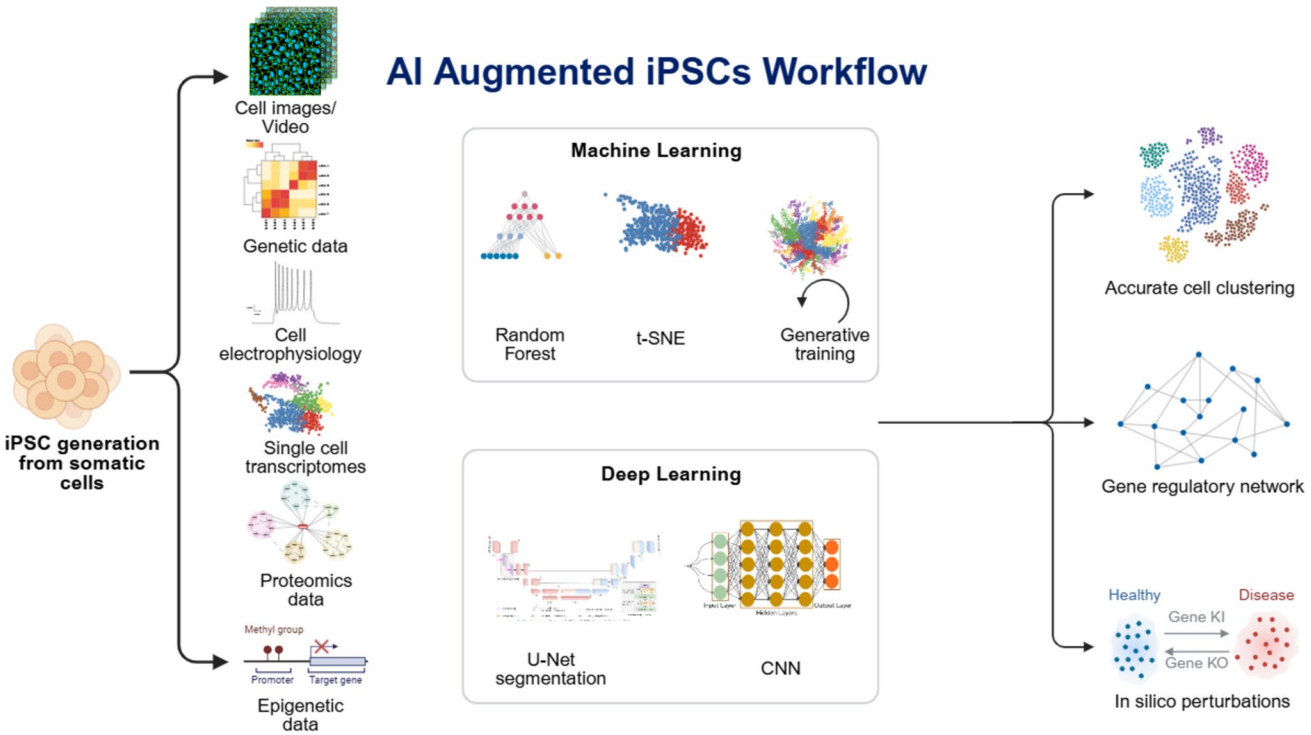

Fig. 5 AI-augmented iPSC workflow integrating multi-omics and machine learning pipelines. This diagram shows how artificial intelligence (AI) can be used with induced pluripotent stem cell (iPSC) technology. The first step in the procedure involves reprogramming somatic cells to generate iPSCs. After that, these iPSCs are studied using a variety of data types, such as high-content images and video, single-cell transcriptomics, epigenomic profiles, proteomic studies, electrical recordings, and genomic sequencing. AI methods utilize advanced algorithms, including machine learning (ML) and deep learning (DL), to work with the high-dimensional datasets generated by this process. Some of the ML methods used are random forest classifiers, *t*-distributed stochastic neighbor embedding (t-SNE) for reducing the number of dimensions and grouping data, and generative training models. DL protocols utilize convolutional neural networks (CNNs) to identify phenotypes in images and U-Net architectures to segment images into distinct parts. The AI-driven study yields several understandable results, including the accurate categorization of cell types, the reconstruction of gene regulatory networks (GRNs), and in silico perturbation modeling, such as gene knockout (KO) and knock-in (KI) simulations. These findings facilitate the distinction between healthy and disease-specific iPSC phenotypes, thereby enhancing differentiation processes, disease models, and individualized treatment plans

regulatory networks. Natural language processing (NLP) has lately improved knowledge organization from scientific publications and boosted hypothesis generation. Using metabolomics data and genomic information, they identified critical metabolic pathways that may be linked to the disease. This thorough research clarifies the pathophysiology of schizophrenia by explaining the interactions between changes in gene expression and metabolic activities (O'Shea et al. 2020). The study emphasizes the possibility of stem cell-derived models for comprehending complicated mental diseases and makes recommendations for the treatment of schizophrenia using targeted networks.

Combining several omics data layers—genomics, transcriptomics, proteomics, and epigenomics—helps identify key molecular regulators and signaling pathways connected during Alzheimer's disease. This method offers a fresh perspective on the disease's complex biology and identifies potential treatment targets. The network-based approach accelerates the identification of key nodes in the disease's molecular circuitry, facilitating the development of new treatments (Volpato and Webber 2020).

Integrating AI, stem cell therapy, and multi-omics approaches to improve treatments for Duchenne muscular dystrophy (DMD) explored the possibility of creativity. The finding highlights the potential of stem cells—mainly induced pluripotent stem cells (iPSCs)—as a model for disease and a basis for subsequent treatment trials. The study highlights how AI can analyze extensive omics data, including transcriptomics, proteomics, and genomics, to identify key biomarkers, predict disease progression, and inform individualized treatment plans. Promising prospects for more focused and effective treatments arise from improving our knowledge of the molecular basis of DMD and enabling precision medicine by integrating these new technologies (Volpato and Webber 2020).

Examining several multi-omics data integration methods and their possible use in understanding mental diseases. The work investigates creative approaches for combining proteomic, epigenomic, transcriptomic, and genomic data to clarify how these approaches might improve knowledge of the complex biological processes linked with mental diseases. The advantages of multi-omics integration were analyzed to describe disease processes, identify new biomarkers, and improve diagnosis and treatment strategies. They emphasize the need to develop accurate computer models to manage the large and diverse datasets generated, thereby enabling more targeted and precise pharmaceutical therapies for mental disorders (Cai et al. 2021).

We have extensively investigated multiparametric neurons generated from human induced pluripotent stem cells (iPSCs). The analysis and other omics data concentrated on the interactions among transcriptomics, proteomics, metabolomics, and genomes. The work provides a comprehensive molecular profile of iPSCs and their differentiation into brain cells. This multi-omics approach enhances our understanding of the molecular pathways and cellular dynamics that drive brain differentiation and the progression of neural diseases. The paper identifies essential markers and regulatory systems, offering fresh possibilities for tailored therapy choices. It clarifies possible features of iPSCs as a paradigm for neurodegenerative diseases (Hasib 2022).

A thorough multi-omics approach will examine how microenvironmental dynamics affect decisions about stem cell fate. This work combines genomic, transcriptomic, proteomic, and metabolomic data to show how extrinsic factors—including the stem cell niche, cellular connections, and environmental signals—impact stem cell activity and differentiation. Using their analysis of complex chemical interactions, researchers find fundamental regulating systems influencing stem cell fate decisions. The results are essential for developing stem cell–based treatments since they clarify the control of stem cell differentiation and enhance applications of regenerative medicine using microenvironment manipulation (Walker et al. 2022).

We investigated how multi-omics analysis might be used to understand human diseases and the possibilities of a multi-omics strategy to find new biomarkers, explain disease pathways, and advance precision medicine. Combining several omics layers—such as genomics, transcriptomics, proteomics, and metabolomics—helps one grasp the molecular mechanisms behind different diseases. This work shows that using data integration from several omics platforms, one can obtain significant insights into the complexity of human diseases, including cancer, neurological diseases, and metabolic disorders, opening the path for more individualized and successful treatment regimens (Halama et al. 2022).

In neurodegenerative diseases, iPSCs could be coupled with many omics methods. To better understand the molecular pathways causing neurodegeneration, recent developments in integrating iPSCs with genomic, transcriptomic, proteomic, and metabolomic data were examined. This work uses iPSC-based disease models to demonstrate how multi-omics techniques can provide critical fresh viewpoints on the pathophysiology of diseases, including Parkinson's. These integrated approaches also underscore their probable uses in identifying new biomarkers, revealing disease-specific molecular signals, and devising therapeutic approaches, thereby improving individualized medicine in neurodegenerative disease research (Song et al. 2024).

Conclusion

AI and iPSC-based technology have opened new doors for understanding and changing cell biology. AI can accelerate the transition of iPSC technology from research to clinical

use by addressing key challenges and employing multidisciplinary approaches. Investigating induced pluripotent stem cells (iPSCs) and applications in pharmacology. High-quality datasets, experimental validation, and continuous AI algorithm advancements will cause significant changes in discovery, regenerative medicine, and disease modeling. New developments in technology using iPSCs and AI have great potential to transform stem cell research and related therapeutic applications. AI-driven approaches encompass improvements in cultural settings, the acceleration of disease-specific model discovery, and the enhancement of iPSC differentiation accuracy. Moreover, the analysis of large-scale omics data, the identification of latent biological trends, and the use of customized medicine methods depend on AI. Notwithstanding these developments, problems, including data quality, model interpretability, and regulatory concerns, still exist in combining AI with iPSC technology. On the other hand, if AI continues to develop, it could spur further advancements in stem cell therapies, disease modeling, and drug discovery, thereby generating new prospects for precision medicine and regenerative medicine.

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