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REVOLUTIONIZING ACUTE MYELOID LEUKAEMIA TREATMENT: EXPLORING AND UNRAVELING IPSC TECHNOLOGY FOR PERSONALIZED MEDICINE AS WELL AS THERAPIES

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Abstract

- The prognosis for acute myeloid leukemia (AML) is poor because of an advanced age, high rate of relapse, and resistance to common treatments. In recent years, IPSCs have proven to be effective and promising for the treatment of Acute Myeloid Leukemia. The development of cancer involves a complex interplay of genetic, epigenetic, and environmental factors. Such common treatments like chemotherapy and radiotherapy which often involve non-specific targeting have the potential to harm both malignant and healthy cells and tissues. These conventional therapies may also have a number of negative side effects, including weakened immune systems, nausea, and hair loss. In contrast, IPSC technology minimizes collateral damage to healthy cells and may lessen side effects by providing the possibility of more individualized and targeted treatment approaches. This review explores the application of induced pluripotent stem cell (IPSC) technology for personalized treatment of Acute Myeloid Leukemia (AML). It outlines the sequential steps involved in developing IPSCs and highlights the use of the Yamanaka factors in IPSC production. Additionally, it explores the utilization of gene editing and targeted therapies, exemplified through case studies, to achieve clinical translation and personalized medicine in AML treatment. Furthermore, the study reviews the potentials of IPSCs in various diseases using tissue engineering approaches. Overall, this project elucidates the novel and effective avenues of IPSC technology offered for managing and treating AML.

Keywords*: Acute Myeloid Leukemia (AML), Induced Pluripotent Stem Cells (IPSCs), personalized medicine, gene editing, targeted therapies, disease modeling, tissue engineering, genetic mutations, bone marrow suppression, cellular reprogramming, drug screening, clinical translation, regenerative medicine.*

INTRODUCTION

Leukemia, a form of blood cancer, is categorized based on the mutated precursor cell type (e.g., lymphoid or myeloid) and the pace of disease progression (e.g., acute or chronic). This classification encompasses acute lymphocytic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), and chronic myeloid leukemia (CML). Additionally, myeloproliferative neoplasm and systemic mastocytosis are rare blood disorders falling within this classification framework [1].

Acute myeloid leukemia (AML), the predominant form of acute leukemia observed in adults, exhibits significant biological diversity. Genetic modifications that promote cell proliferation or hinder cell differentiation contribute to the proliferation of immature blast cells, consequently impairing the normal function of the bone marrow. Several prevalent etiological variables linked to AML comprise; **Genetic alterations**: The onset of AML is highly correlated with specific genetic alterations. Genes like **FLT3, NPM1, CEBPA, and DNMT3A** are a few examples of mutated genes [2]. These mutations may cause aberrant myeloid cells to proliferate and expand out of control. Again; **environmental exposures**: Being exposed to radiation or specific chemicals can raise your risk of acquiring AML. For example, AML has been associated with exposure to benzene, specific chemotherapy medicines, or high radiation doses (from radiation therapy or nuclear accidents).

Mutations in specific genes contribute significantly to the development of acute myeloid leukemia (AML). Mutations can occur in a variety of genes that control cell proliferation, differentiation, and apoptosis.

Here are some major mutations related to AML:

FLT3: The **FLT3** gene encodes a receptor tyrosine kinase that controls cell growth and survival. FLT3 alterations, notably internal tandem duplications

(ITDs) and point mutations in the tyrosine kinase domain (TKD), are present in roughly 30% of AML patients [3]. These mutations activate FLT3 signaling pathways in a constitutive manner, encouraging uncontrolled cell proliferation and survival.

NPM1: The NPM1 gene encodes nucleophosmin, a protein that has a role in ribosome synthesis and the control of the tumor suppressor protein p53. NPM1 mutations are among the most common genetic changes in AML, occurring in approximately 35% of patients [4]. These mutations interfere with NPM1's normal function, resulting in dysregulation of cell proliferation and differentiation.

CEBPA: The CEBPA gene encodes a transcription factor that regulates myeloid cell development. CEBPA mutations are present in 10-15% of AML patients [5]. Thus, they frequently arise as biallelic variants (mutations in both copies of the gene). These mutations alter CEBPA's normal function, compromising myeloid cell differentiation and contributing to leukemia.

Acute Myeloid Leukemia (AML) can have significant effects on individuals both physically and emotionally which includes **Bone Marrow Suppression** being the most fatal key [6]. Normally, AML impairs normal hematopoiesis, the process by which blood cells are formed in the bone marrow. The fast multiplication of aberrant myeloid cells crowds out normal blood cell progenitors, causing bone marrow suppression. This results in a decline in the generation of healthy red blood cells, white blood cells, and platelets.

Anemia: A decrease in red blood cells can cause fatigue, weakness, shortness of breath, and pale complexion.

Neutropenia is a decrease in white blood cells (neutrophils), which raises the risk of infection. Because of their weakened immune system, people with AML can get severe infections from small ones.

Thrombocytopenia: A reduction in platelets can cause easy bruising, bleeding gums, nosebleeds, and prolonged bleeding from minor cuts or bruises.

Furthermore, people with AML may face *nutritional issues* as a result of reduced appetite, altered tastes, nausea, and trouble swallowing. For the body to recuperate throughout therapy and maintain its immune system, adequate nourishment is essential [7].

Moreover, *psychological impact* which relates to anxiety, despair, stress, and a sense of unpredictability about the future are all considered to be the physical signs of AML which greatly takes an emotional toll on the patients [7]. Like the majority of other malignancies, acute myeloid leukemia (AML) is often treated with chemotherapy, which includes consolidation therapy to further lower the risk of relapse, intense induction therapy to induce remission, and maybe maintenance therapy to extend remission. To lower the quantity of leukemia cells in the bone marrow and peripheral blood, induction therapy entails administering combination chemotherapy regimens, such as cytarabine and an anthracycline (daunorubicin or idarubicin), over a period of several days to weeks. To eliminate any leftover leukemia cells and stop the disease from recurring, consolidation therapy may entail more chemotherapy sessions or stem cell transplantation. **BUT**, Chemotherapy, which is necessary for the treatment of Acute Myeloid Leukemia (AML), severely affects the patients negatively in a number of ways as it can cause bone marrow suppression which results in anemia, infection susceptibility, and bleeding tendencies. Even gastrointestinal adverse effects including nausea, vomiting, and mucositis, all of which impact nutrition and hydration are all part and parcel of the negative impacts. AS SUCH, **Unraveling IPSC Technology for Personalized Medicine as well as Therapies on Acute Myeloid Leukemia** which has proven to be effective and with less side effects is the new answer to patients suffering from chronic Acute Myeloid Leukemia.

A. Induced Pluripotent Stem Cells

Induced pluripotent stem cells are a type of stem cell that is artificially derived from adult cells, usually skin or blood cells, through a process called reprogramming. Reprogramming involves the introduction of specific genes or factors that reset adult cells to a pluripotent state, similar to that of embryonic stem cells. With the help of Yamanaka factor genes, including **OCT4, SOX2, KLF4,** and **c-MYC**, thus possesses an extraordinary capability to induce the transformation of adult cells, such as those from skin or blood, into a pluripotent state akin to embryonic stem cells [8]. embryonic stem cells [8].

Hence, upon their insertion into somatic cells, these factors initiate a series of molecular processes that reset the cellular characteristics, restoring their ability to develop into diverse cell types within the body.

This breakthrough in cellular reprogramming has revolutionized regenerative medicine, disease modeling, and drug discovery, offering new avenues for personalized therapies and treatments for conditions like Acute Myeloid Leukemia (AML).

Embracing induced pluripotent stem cell (IPSC) therapy over chemotherapy for treating Acute Myeloid Leukemia (AML) offers compelling advantages. IPSC-based treatments can be personalized to each patient's genetic profile, potentially improving efficacy and reducing adverse effects compared to chemotherapy's non-specific targeting. By minimizing damage to healthy tissues, IPSC therapy may cause fewer side effects and improve quality of life. Additionally, IPSC technology enables disease modeling to reveal insights into AML biology and drug responses, unveiling new therapeutic targets. Moreover, the regenerative capacity of IPSCs may lead to curative cell-based therapies by replenishing healthy blood cells. Advances in IPSC technology also usher in an era of personalized medicine, allowing treatments tailored to individual disease biology and drug responses for better AML patient outcomes.

HARNESSING IPSCS TECHNOLOGY FOR PERSONALIZED TREATMENT OF AML

A. Introduction to iPSC Technology in the Context of AML:

1. Patient Sample Collection: Obtaining patient samples is the initial step in using iPSC technology in AML. These samples can be gathered from individuals diagnosed with AML and can include skin fibroblasts or peripheral blood cells. These samples can be collected through standard clinical procedures, such as skin biopsy or venipuncture.

2. Isolation and Culture of AML Cells: Isolate and cultivate AML cells from patient samples in vitro. AML cells, which are aberrant myeloid cells with abnormal functions originating from bone marrow, can be grown in suitable growth conditions to retain their viability and proliferative capabilities.

3. Reprogramming of AML Cells into iPSCs: Use reprogramming factors such as OCT4, SOX2, KLF4, and c-MYC in order to transform the isolated AML cells into pluripotent stem cells that are induced (iPSCs). This can be accomplished using a variety of ways, including retroviral or lentiviral transduction, episomal vectors, mRNA transfection, or protein transduction, which are similar to the methods used to reprogram somatic cells into iPSCs.

4. Characterization of AML-Derived iPSCs: Characterize the resulting AML-derived iPSC colonies to ensure they are pluripotent and suitable for downstream applications. This includes evaluating morphological characteristics, studying the expression of pluripotency markers, establishing karyotype stability, and doing functional experiments to reveal differentiation potential.

5. Differentiation of AML-Derived iPSCs into AML-Relevant Cell Types: Direct the development of AML-derived iPSCs into AML-relevant cell types, including hematopoietic stem cells, myeloid progenitor cells, and mature myeloid cells. This can be accomplished via controlled differentiation techniques that match the stages of normal hematopoiesis, allowing researchers to simulate AML formation and pathogenesis in vitro.

6. Drug Screening and Disease Modeling: Use AML-derived iPSC models to identify and evaluate new therapeutic medicines that target specific genetic alterations or molecular pathways involved in AML development. By assessing drug responses in AML-derived iPSC cells, researchers can develop personalized therapy plans for specific patients based on their genetic profiles.

Table I. An overview of the sequential steps involved in utilizing iPSC technology for studying and modeling AML. Each step contributes to the development and application of iPSC-based models for understanding AML pathogenesis and exploring potential therapeutic intervention.

Steps	Descriptions
Patient Sample Collection	Obtain samples from AML patients, such as skin fibroblasts or peripheral blood cells, through procedures like skin biopsy or venipuncture.
Isolation and Culture of AML cells	Isolate and culture AML cells from patient samples in vitro using appropriate growth media.
Reprogramming of AML cells into IPSCs	Reprogram isolated AML cells into IPSCs using reprogramming factors (OCT4, SOX2, KLF4, C-MYC) and various methods.
Characterization of AML - Derived IPSCs	Characterize resulting AML- derived IPSC colonies to confirm pluripotency and suitability for downstream applications.
Differentiation of AML-Derived IPSCs into cell types	Direct the differentiation of AML- derived IPSCs into AML- relevant cell types, such as hematopoietic stem cells and myeloid cells.
Drug Screening and Disease Modelling	Utilize AML- derived iPSCs models for drug screening and testing novel therapeutic agents targeting specific genetic mutations or molecular pathways implicated in AML

CURRENT WORKS REPORTED

A. A new iPSC-based model of AML Leukemia Stem Cells (LSCs)

As the first malignancy in which researchers could identify and isolate a stem cell population, AML Leukemia Stem Cells (LSCs) are the prototypical cancer stem cells. Like normal hematopoietic stem cells, AML LSCs possess self-renewal and multipotency, enabling them to initiate and maintain AML by producing identical daughter LSCs as well as differentiated progeny without tumor propagation abilities [9].

We recently unveiled a novel model of AML Leukemia Stem Cells (LSCs) (**Fig1**). By temporarily expressing the four Yamanaka factors, we derived iPSC lines from a female patient with AML. The patient's AML genetics included a deletion of chromosome 7q in the context of a complex translocation involving chromosomes 1, 7, and 14, as well as a subclonal KRAS G12D mutation. The process of reprogramming erases the epigenome globally but maintains the genome intact. We were able to derive multiple iPSC lines that contained the genetic lesions of this specific AML, including the translocation and chromosome 7q loss, and some of these also contained the KRAS G12D mutation. The AML epigenome was largely erased by the reprogramming process, and these AML-iPSCs

were indistinguishable from normal human pluripotent stem cells (hPSCs) in terms of their phenotype, transcriptome, chromatin, and teratoma formation ability [9].

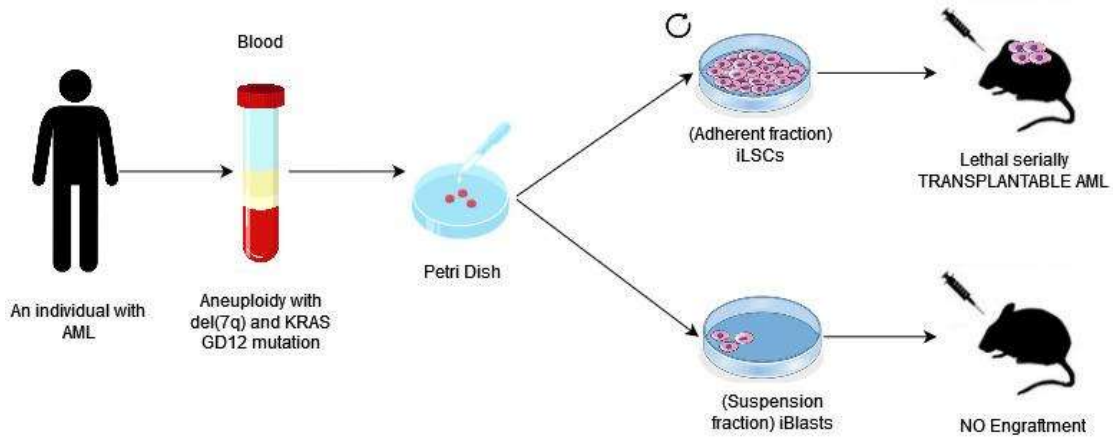

Fig 1. A novel model of AML Leukemia Stem Cells (LSCs).

As such, the importance of the study above lies in its contribution to advancing our understanding of AML in the following ways:

i. **Understanding AML Pathogenesis**: Thus, the study sheds light on the molecular underpinnings of AML's development and progression. By contrasting the transcriptome, epigenome, and chromatin architecture of AML-induced pluripotent stem cells versus normal pluripotent stem cells, researchers can pinpoint aberrant gene expression and epigenetic changes tied to AML, deepening our grasp of the disease's pathogenic mechanisms.

ii. **Drug Discovery and Personalized Medicine:** Using patient-derived induced pluripotent stem cell models of acute myeloid leukemia, researchers can perform high-throughput drug screening to find new therapeutic agents that target specific genetic mutations or disrupted pathways, enabling the creation of personalized treatment regimens tailored to each patient's genetic profile and propelling the field of precision medicine for this disease.

B. Gene Editing and Targeted Therapies:

Gene editing technologies like CRISPR/Cas9 have enabled precise manipulation of the genome in induced pluripotent stem cells derived from acute myeloid leukemia (AML-iPSCs). Researchers have used these techniques to introduce or correct AML-associated mutations, paving the way for developing targeted therapies that address specific molecular drivers of AML.

For instance, the gene editing technology CRISPR/Cas9 (**Fig2**.) can be used to target the FLT3 gene mutation in AML-iPSCs. This mutation is a common molecular driver of acute myeloid leukemia (AML) and is found in about one-third of AML patients, where it is associated with a poor prognosis [10][11].

Case example:

A patient with acute myeloid leukemia (AML) and a FLT3-internal tandem duplication (ITD) mutation had their peripheral blood cells reprogrammed into induced pluripotent stem cells (iPSCs). These iPSCs were then differentiated into myeloid progenitor cells to model the patient's diseased state. Using CRISPR/Cas9 technology, researchers introduced guide RNAs and Cas9 endonuclease to target and correct the FLT3-ITD mutation in the AML iPSC-derived myeloid progenitors. This gene editing approach aimed to restore normal FLT3 function. After editing, researchers evaluated cellular phenotypes like proliferation, differentiation, and apoptosis to determine the impact of FLT3 correction on AML cell behavior. They also performed functional assays and transcriptomic analysis to understand the molecular mechanisms of the FLT3 mutation's role in AML.

In a nutshell, by using gene editing to correct disease-causing FLT3 mutations in induced pluripotent stem cells from AML patients, researchers aim to develop new therapeutic strategies that restore normal cell function and improve treatment outcomes for this patient population.

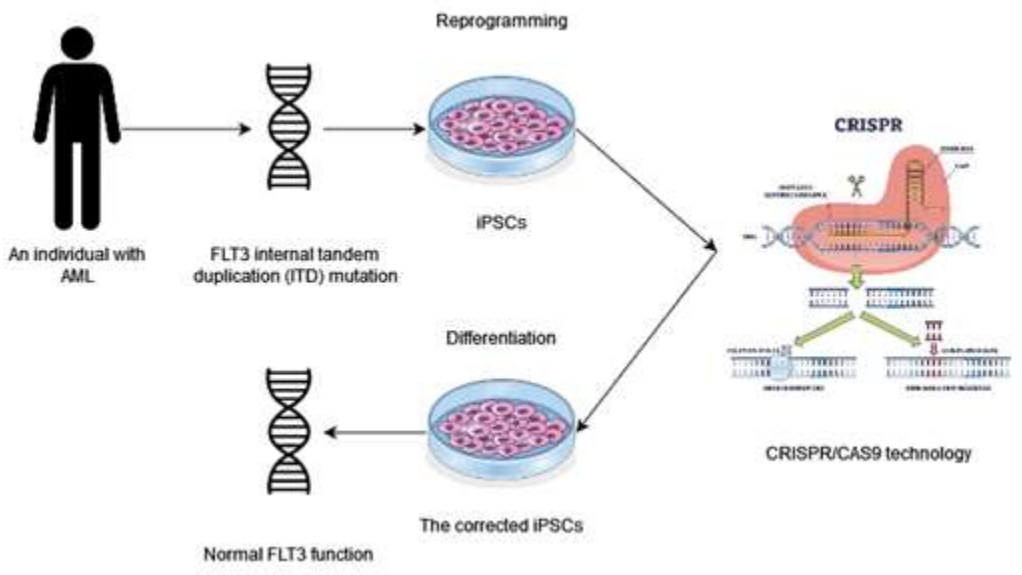

Fig 2. Genome editing using CRISPR/CAS9

C. Clinical Translation and Personalized Medicine:

There is ongoing effort to translate iPSC-based research findings into clinical applications for personalized medicine in AML. This includes the development of iPSC-based assays for predicting drug responses, patient stratification, and designing individualized treatment regimens based on patients' genetic profiles.

Case example: Mr. Andrews, a 55-year-old man, is diagnosed with acute myeloid leukemia (AML) and receives standard chemotherapy treatment. However, he responds poorly to the chemotherapy and experiences severe side effects like myelosuppression and infections. Given the heterogeneity of AML, Andrews' oncologist decides to explore personalized treatment options tailored to Andrews' genetic profile using induced pluripotent stem cell (iPSC) assays.

Mr. Andrews' peripheral blood cells are collected and reprogrammed into induced Pluripotent Stem Cells (iPSCs) to generate a personalized model of his acute myeloid leukemia (AML). The iPSCs derived from Mr. Andrews' cells are then differentiated into AML-specific cell types, such as myeloid progenitor cells, to perform a drug sensitivity assay. This assay tests the efficacy of different chemotherapy drugs and targeted therapies on Mr. Andrews' AML cells in vitro. Additionally, genetic profiling of Mr. Andrews' AML cells is conducted to identify specific genetic mutations and molecular abnormalities, such as FLT3 mutations or chromosomal abnormalities. Based on the genetic profile, Mr. Andrews' AML is classified into molecular subtypes associated with different prognoses and treatment responses. Using the results from the drug sensitivity assay and genetic profiling, Mr. Andrews' oncologist designs a tailored, individualized treatment regimen specific to his genetic profile. This personalized treatment may include targeted therapies for molecular drivers of Mr. Andrews' AML, like FLT3 inhibitors for FLT3 mutations, or combination chemotherapy based on the drug sensitivity testing. Mr. Andrews undergoes the personalized treatment regimen under close clinical monitoring to assess treatment response and manage potential side effects. Regular follow-up, including molecular monitoring for residual disease and evaluating treatment efficacy, allows optimization of Mr. Andrews' therapy based on ongoing results. Using cell-based assays that test how Mr. Andrews' cancer cells respond to different drugs and stratify patients, his oncologist can develop a personalized treatment plan matched to Mr. Andrews' unique genetic makeup. This tailored approach

seeks to boost treatment success, reduce side effects, and enhance Mr. Andrews' quality of life as he undergoes AML therapy. **Fig 3.** outlines the process starting from the collection of Mr. Andrews' peripheral blood cells, their reprogramming into induced pluripotent stem cells (iPSCs), differentiation into AML-specific cell types, genetic profiling, and drug sensitivity assay. It then illustrates the classification of AML based on genetic subtypes, the design of a personalized treatment regimen, and its implementation under clinical monitoring and follow-up. Finally, it highlights ongoing optimization of therapy based on results obtained through regular follow-up and molecular monitoring.

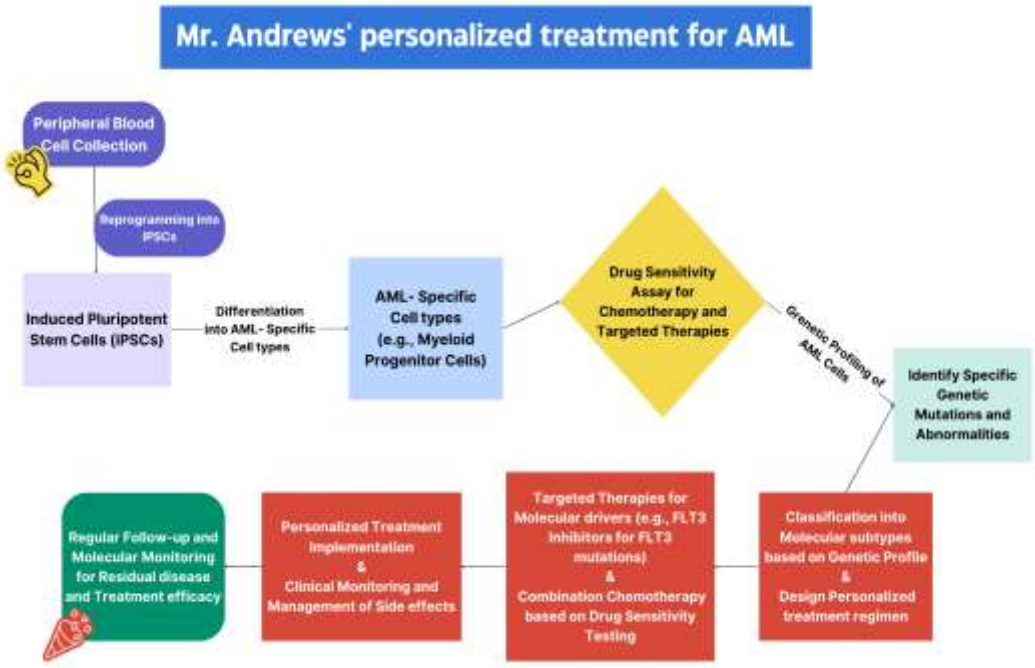

Fig 3. Mr. Andrews' personalized treatment for AML

IPSCS AND ITS POTENTIALS IN DIFFERENT DISEASES USING TISSUE ENGINEERING

Induced pluripotent stem cells were discovered by a great scientist called Shinya Yamanaka and his colleagues. Since their discovery, Induced Pluripotent Stem cells have become a great tool in tissue engineering as well as other fields at large. Induced Pluripotent stem cells offer a fresh avenue for tissue engineering and cell-based therapies which are free from the ethical considerations tied to embryo utilization hence giving them added advantages compared to other therapies and this is where they shine best at [12].

To begin with, **Induced Pluripotent Stem Cells (IPSCs) through tissue engineering technique holds great promise for addressing lost or damaged muscle tissue.** Induced Pluripotent Stem Cells (iPSCs) can be transformed into muscle satellite cells, which are vital for muscle repair. Researchers can then use these cells to generate artificial muscles in the lab. These lab-grown muscles have numerous potential applications: they could be transplanted into patients with muscular diseases or injuries to improve mobility, utilized to study diseases and discover new drugs, or even integrated into robots and prosthetic limbs to make their movements more natural [13].

Fig 4. Technical pathways of tissue-engineered iPSCs for artificial muscle applications.

Secondly, **the wound healing process through tissue engineering technique again shows promise for treating chronic wounds and diabetic foot ulcers.** Induced Pluripotent Stem Cells (iPSCs) offer unique advantages for tissue regeneration. As pluripotent cells capable of self-renewal and differentiation into various adult cell types, iPSCs are ideal candidates. Harvesting iPSCs from minimally invasive skin biopsies provides a relatively accessible cell source compared to bone marrow or adipose tissue. Moreover, iPSCs can be derived from any adult tissue, greatly expanding the potential donor pool. Transplanting autologous iPSCs also prevents immunogenicity issues and improves survival [14]. Once transplanted into wounds, iPSCs promote healing through direct and paracrine actions, recruiting cells, modulating immunity, remodeling extracellular matrices, and promoting angiogenesis via secreted factors. While adult mesenchymal stem cells (MSCs) have accelerated healing in diabetic populations with MSC deficiencies, embryonic stem cell-derived MSCs show superior potency, proliferation, and consistency. Therefore, these ESC-MSCs hold significant potential to improve wound healing outcomes clinically.

Thirdly, **IPSCs and tissue engineering techniques have proven to be therapeutic towards combating SARS COVID-19.** By reprogramming adult cells into a pluripotent state, iPSCs enable multifaceted contributions to combating SARS-CoV-2, the virus causing COVID-19. Notably, iPSC-derived lung cell cultures serve as invaluable models to study viral infection dynamics and resulting pathological changes. These cultures let researchers dissect the intricate interplay between virus and host cells, illuminating disease mechanisms and potential therapeutic targets.

Complementing iPSC approaches, tissue engineering has emerged as a powerful tool against COVID-19. By fabricating 3D tissue constructs mimicking native tissue architecture and function, researchers create highly relevant platforms to investigate SARS-CoV-2 infection and test interventions. In particular, engineered lung organoids and respiratory epithelial cultures offer a physiologically accurate environment to study viral entry, replication, and spread in the respiratory tract. Moreover, these engineered tissues facilitate screening antiviral and immunomodulatory compounds, expediting COVID-19 treatment development. The therapeutic potential of iPSCs and tissue engineering reaches beyond disease modeling to cell-based therapies and drug discovery. iPSCs can produce therapeutic molecules targeting SARS-CoV-2, like neutralizing antibodies or antiviral peptides.

Engineered iPSC products show promise as next-generation COVID-19 treatments, offering a renewable, scalable source of biologics to combat infection and mitigate severity. Furthermore, engineered constructs provide a versatile platform to test immunotherapies and vaccines, enabling rapid advancement from bench to bedside.

In summary, iPSCs and tissue engineering represent innovative approaches with significant therapeutic potential against COVID-19. By harnessing the versatility of iPSCs and precision of tissue engineering, researchers are gaining deeper insights into pathogenesis, developing new treatments, and ultimately curb SARS-CoV-2's devastating global impact.

Furthermore, **Skin cancer, encompassing both melanoma and non-melanoma skin cancers, has seen successful treatment outcomes through the utilization of iPSCs and skin tissue engineering approaches.** Skin cancer often necessitates surgical removal of the affected tissue, leaving behind skin defects in need of reconstruction. Induced pluripotent stem cell (iPSC)-based tissue engineering offers a promising solution by enabling the development of customized skin substitutes for post-cancer excision reconstruction. These engineered skin grafts have the potential to provide not just aesthetic but functional outcomes, as they can be tailored to match the patient's unique skin tone and texture. For example, iPSC-derived skin cells can be seeded onto biocompatible scaffolds and cultured to create skin equivalents that closely resemble native tissue. These engineered grafts can then be transplanted onto the site of excised skin cancer lesions to promote wound healing and restore skin integrity. Additionally, because iPSC-derived skin substitutes originate from the patient's own cells, they reduce the risk of rejection and enhance graft integration. In summary, iPSC-based tissue engineering represents a promising approach for improving surgical outcomes and patient satisfaction in skin cancer reconstruction.

CONCLUSION

All in all, the advent of induced pluripotent stem cell (iPSC) technology has catalyzed a paradigm shift in acute myeloid leukemia (AML) treatment, unlocking unprecedented opportunities for personalized medicine and therapeutic innovation. As we navigate AML's complex genetic heterogeneity and treatment challenges, iPSC-based approaches emerge as a beacon of hope, promising tailored solutions matched to patients' unique genetic profiles. By leveraging iPSCs, researchers have embarked on a journey towards precision oncology, pioneering personalized regimens that minimize collateral damage to healthy cells and mitigate traditional therapies' adverse effects. The integration of iPSC technology into AML research and clinical practice heralds a new era of transformative healthcare, where patient-specific models serve as invaluable tools for elucidating disease mechanisms and identifying novel therapeutic targets. Through iPSC-based disease modeling and drug screening, researchers gain deeper insights into AML pathogenesis, enabling the development of targeted therapies that address specific molecular drivers. Moreover, iPSC-derived models offer a platform for predicting drug responses, stratifying patients based on their genetic profiles, and designing tailored regimens that optimize efficacy while minimizing adverse effects. Recent strides in iPSC-based research underscore personalized medicine's promise in AML, where individualized approaches tailored to each patient's genetics hold the key to improved outcomes and enhanced quality of life. By leveraging iPSC technology, clinicians can tailor strategies to target specific mutations or dysregulated pathways, thereby maximizing benefits and minimizing relapse risk. Additionally, iPSC-based assays facilitate predicting drug responses and optimizing treatment selection, ensuring patients receive the most effective tailored therapies. As we enter the era of precision oncology, fueled by iPSC technology and personalized approaches, it is imperative to address impending challenges and limitations. Continued research is needed to further refine iPSC-based models, improve their predictive accuracy, and optimize their clinical utility. Moreover, interdisciplinary collaborations between researchers, clinicians, and industry partners are essential for translating iPSC-based discoveries into clinically actionable insights and new therapeutic interventions. In conclusion, integrating iPSC technology into AML research and clinical practice holds immense promise for revolutionizing patient care and transforming the treatment landscape. **LASTLY**, by embracing personalized medicine approaches and harnessing iPSCs' power, we can usher in a new era of precision oncology, where individualized strategies tailored to each patient's unique genetic profile pave the way towards improved outcomes, enhanced quality of life, and a brighter future for AML patients.

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