

Advantages of Induced Pluripotent Stem Cells in Regenerative Medicine: A Comparative Review with Embryonic and Adult Stem Cells

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Abstract—Although regenerative medicine holds significant potential in the treatment of organ failure and neurodegenerative diseases, traditional stem cell therapies face major limitations regarding ethical concerns, immune rejection, differentiation, and sourcing. These factors have prevented the widespread adoption of regenerative medicine. Since Takahashi and Yamanaka first generated induced Pluripotent Stem Cells (iPSCs) in 2006 and demonstrated that they possess the same proliferative capacity as normal stem cells, the technology for applying iPSCs in regenerative medicine has gradually matured. This has helped to fill, to some extent, the significant gap in regenerative medicine for organ failure and neurodegenerative diseases caused by the major limitations of traditional stem cell therapies. This paper investigates how iPSCs can, to some extent, mitigate or resolve the limitations of traditional stem cell therapies (Embryonic Stem Cells (ESCs) and Mesenchymal Stem Cells (MSCs)). Using a literature review methodology, this study examines past research to demonstrate that iPSCs have, to a certain degree, addressed the ethical limitations, immune rejection, and problems related to differentiation and sourcing associated with traditional stem cell therapies (embryonic or adult stem cells).

Keywords—induced Pluripotent Stem Cell (iPSC), regenerative medicine, Embryonic Stem Cell (ESC), Mesenchymal Stem Cell (MSC)

I. INTRODUCTION

As the global population ages at an accelerating rate, the incidence of intractable diseases such as organ failure, neurodegenerative diseases, myocardial infarction, diabetes, and extensive tissue damage continues to rise. Traditional drug therapies and surgical procedures often struggle to achieve functional restoration of damaged tissues and organs; consequently, regenerative medicine has emerged as a highly promising direction for modern medicine. Using stem cells as its core, regenerative medicine offers a novel therapeutic approach for patients with end-stage diseases by reconstructing, replacing, or regenerating damaged human tissues and organs, thereby holding immense clinical value and market potential.

However, prior to the advent of induced Pluripotent Stem Cell (iPSC) technology, clinical and research efforts primarily relied on two major categories of traditional stem cells: Embryonic Stem Cells (ESCs) and Mesenchymal Stem Cells (MSCs). Although relevant research has achieved some promising results, inherent ethical controversies, risks of immune rejection, limited differentiation capacity, and limited cell sources have consistently hindered technological translation and clinical adoption [1–4].

The development of iPSCs can be traced back to a 2006 article by Takahashi *et al.* [5], which demonstrated that adult cells could be “rejuvenated”—that is, reprogrammed into stem cells—using just four factors. A year later, Takahashi *et al.* published an article reporting the first successful reprogramming of human cells, officially ushering in a new era of human regenerative medicine [6].

This paper employs a literature review approach to systematically outline the advantages of iPSCs over ESCs and MSCs in terms of ethical considerations, immunogenicity, differentiation potential, and cell source availability, while also analyzing their existing risks. It aims to clearly present the developmental trajectory and current research status of this technology to beginners in the field of regenerative medicine, serving as a practical reference for future research and applications.

II. OVERCOMING ETHICAL DILEMMAS

In the research process of traditional ESCs, scientists inevitably need to destroy human blastocysts. This has generated significant legal conflicts, leading some countries to classify such practices as criminal acts and to ban related research projects, while many other countries impose funding restrictions and strict regulations, resulting in slow progress [1, 6].

However, induced Pluripotent Stem Cells (iPSCs) do not present such issues. For instance, Takahashi *et al.* [6] clearly demonstrated that pluripotency can be achieved by reprogramming adult skin cells, eliminating the need to extract the inner cell mass from 5–7-day-old blastocysts, as is required for traditional ESCs. The article notes that iPSCs effectively circumvent the perennial debate over whether a fertilized egg constitutes

a human being, as iPSCs do not require the use of any cells from a blastocyst; all raw materials can be derived from adult skin cells. Another scholar expressed the same view, noting that the emergence of iPSCs has resolved the long-standing deadlock over whether “embryos possess personhood”, marking a major leap forward in the social acceptance of regenerative medicine [1]. Policy shifts also attest to the ethical advantages of iPSCs. Many countries and regions that previously strictly prohibited embryonic stem cell research, including some with deep Catholic traditions, have gradually relaxed restrictions on iPSC research and even introduced special policies to provide financial support and research incentives, driving the rapid development of related technologies [7]. The removal of ethical barriers has not only created a more conducive environment for basic research but has also cleared major obstacles for subsequent clinical trials, industrial application, and clinical adoption, thereby establishing the social foundation for the widespread public promotion of stem cell therapy.

III. ELIMINATION OF IMMUNOGENICITY

Traditional stem cell therapy (ESC) has a major drawback: the embryonic stem cells and their derived tissues produced by this therapy are highly immunogenic, causing the patient’s immune system to mistakenly identify them as foreign invaders and attack them. This necessitates that patients who undergo traditional stem cell therapy (ESC) take immunosuppressants for life (except in the theoretical case of using embryonic stem cells derived from the patient themselves via somatic cell nuclear transfer, which is rarely feasible in practice). One scholar highlighted this point in this paper, noting that ESCs and their derived tissues possess strong immunogenicity. The recipient’s immune system recognizes them as “foreign bodies” and triggers a rejection response, forcing patients to face the risks of nephrotoxicity and infection associated with long-term immunosuppressant use—a factor that undoubtedly limits the efficacy of traditional therapies [8].

iPSC technology has fundamentally transformed this situation. iPSCs can be derived directly from the patient’s own somatic cells; the functional cells obtained after reprogramming and directed differentiation are fully genetically matched to the recipient, eliminating immunological mismatches at the source and significantly reducing the risk of immune rejection. Lucas *et al.* [9] resolved the early controversy regarding the claim that “even autologous iPSCs can cause rejection”. Through rigorous experiments, they demonstrated that iPSC-derived tissues exhibit extremely low immunogenicity during autologous transplantation, consistent with the behavior of ESCs from an identical genetic background (e.g., via somatic cell nuclear transfer). Clinical surgical cases have further validated the immunological safety advantages of iPSCs. The world’s first clinical trial using autologous iPSC-derived retinal pigment epithelial cells to treat macular degeneration showed that patients experienced no immune rejection within one-year post-surgery without

taking any immunosuppressants [10]. This demonstrates in practice that iPSCs significantly reduce the risk of immune rejection for patients.

Furthermore, the combination of gene editing technology with iPSCs has further expanded the scope of immune compatibility. Research has utilized CRISPR-Cas9 technology to knock out genes associated with HLA-I class molecules in iPSCs, creating “universal iPSCs” that can evade host immune surveillance, thereby achieving low or even zero rejection rates during allogeneic transplantation [11]. The establishment of a universal iPSC bank holds promise for standardized, large-scale cell production, shifting stem cell therapy from individualized customization to bulk supply and further reducing the clinical risks associated with immune rejection.

IV. FLEXIBILITY IN DIFFERENTIATION AND SOURCE

Traditional stem cell therapies typically rely on very limited sources, often requiring human biological materials such as umbilical cord blood (embryonic stem cells) or bone marrow as raw materials for extraction. This is very challenging for critically ill patients and can easily lead to worsening of their condition. Furthermore, as a person ages, the aging of their own stem cells renders them unusable, as one scholar noted in a paper [12]. This significantly reduces the feasibility of traditional therapies. More critically, traditional MSCs face severe limitations in differentiation; they primarily differentiate into bone, fat, and cartilage, making it difficult to differentiate them into muscle or nerve cells, which limits their therapeutic applications. A scholar pointed out in a paper that adult stem cells (such as MSCs) are multipotent rather than pluripotent. They can primarily differentiate only into bone, fat, and cartilage, and it is difficult for them to differentiate across lineages into neurons or cardiomyocytes, which greatly limits their application in neurodegenerative diseases [13].

iPSCs demonstrate significant advantages in terms of source and differentiation potential. First, iPSCs can be easily derived from cells taken from any part of an adult’s body; a researcher demonstrated in a published paper that renal tubular epithelial cells can be isolated from urine and reprogrammed into iPSCs [14]. This is undoubtedly more patient-friendly for children and critically ill patients. iPSCs also possess exceptional differentiation capabilities, enabling them to achieve the same level of differentiation as ESCs. A researcher demonstrated through transcriptomic comparisons that iPSCs and ESCs are highly consistent in terms of differentiation potential. This is evidenced by their ability to differentiate into all cell types of the three germ layers—endoderm, mesoderm, and ectoderm—including neural, cardiac, and hepatic cells [15].

Furthermore, because induced Pluripotent Stem Cells (iPSCs) possess the unlimited proliferative capacity similar to cancer cells—unlike traditional stem cells that age with each division—iPSCs can be produced rapidly and in large quantities. In their paper, Wang *et al.* [16] noted that because iPSCs possess unlimited proliferative

capacity, they can be cultured on a large scale in bioreactors, thereby addressing the shortcomings of traditional stem cells (such as primary cells), which tend to age and lose viability during passage. Through these characteristics, iPSCs overcome the disadvantages of traditional stem cells, including their narrow differentiation range, limited availability, and difficulties in isolation and expansion.

V. RISKS AND CHALLENGES

Although iPSCs have addressed many of the limitations of traditional stem cell therapies, they have introduced new issues regarding tumorigenicity, genetic stability, cost, and differentiation efficiency.

The risk of tumorigenesis is the most significant safety concern in the clinical application of iPSCs. Given their potent proliferative capacity, residual iPSCs may continue to proliferate in vivo and form teratomas or teratocarcinomas if reprogramming is incomplete or undifferentiated cells are not thoroughly eliminated prior to transplantation. Studies have shown that even if the transplanted cells contain as little as one in ten thousand undifferentiated iPSCs, tumor formation may still be induced [17]. Early iPSC preparation often relied on retroviral or lentiviral vectors; viral sequences can easily integrate into the host genome, disrupting tumor suppressor genes or activating oncogenes, thereby further increasing the risk of carcinogenesis [18].

The reprogramming process itself involves drastic changes in cell morphology, making it highly prone to genetic mutations. It has been reported that during in vitro culture and passaging of iPSCs, chromosomal abnormalities and point mutations are likely to occur due to expansion pressure, which may lead to loss of cell function or malignant transformation [19].

Furthermore, cost remains a significant barrier to the widespread adoption of iPSCs. Although iPSC therapies demonstrate excellent therapeutic outcomes, these personalized treatments inevitably entail extremely high costs. Research indicates that the current cost of autologous iPSC therapy often runs into the hundreds of thousands of dollars, making it difficult to popularize among the general population [20].

VI. CONCLUSION

Through a literature review, this paper examines the core advantages of iPSC technology compared to traditional ESCs and MSCs, confirming that iPSCs have overcome the inherent limitations of traditional stem cell therapies in multiple dimensions. From an ethical perspective, iPSCs do not require the destruction of human embryos, thereby completely avoiding ethical controversies surrounding embryos and garnering broader policy support and social acceptance; on the immunological front, autologous iPSCs significantly reduce the risk of immune rejection; when combined with gene editing technology, they can further be engineered into universal cells, enabling allogeneic transplantation with low rejection rates; regarding source and

differentiation, iPSCs are obtained non-invasively and conveniently from a wide range of sources, possess totipotent differentiation potential and the ability for unlimited proliferation, and can meet the therapeutic needs of diseases affecting multiple systems. Overall, iPSCs provide a safer, more flexible, and clinically viable cell source for regenerative medicine, effectively addressing the shortcomings of traditional stem cell therapies and accelerating the transition of regenerative medicine from basic research to clinical application.

This study has several limitations. For example, it selected only a subset of key papers and did not cover certain specific areas, so the findings may not be fully comprehensive. Improvements could be made by expanding the scope of paper selection and increasing the research coverage.

Future iPSC research can be advanced in the following directions: First, optimize reprogramming techniques to develop integration-free, high-efficiency, and low-cost preparation methods, thereby reducing the risk of tumorigenesis and the probability of genetic mutations; second, establish standardized clinical-grade iPSC platforms and universal cell banks to enable large-scale production and significantly reduce treatment costs; third, integrate organoids, 3D bioprinting, and gene editing technologies to construct highly realistic tissue and organ models, thereby improving the accuracy of disease modeling and drug screening; forth, conducting more large-scale, long-term follow-up clinical trials to validate the long-term safety and efficacy of iPSC therapies; fifth, refining ethical guidelines and quality control systems to facilitate the translation of technical standards and the widespread adoption of these therapies. As the technology continues to mature, iPSCs hold the promise of truly realizing accessible regenerative medicine treatments, bringing new hope to patients with intractable diseases worldwide.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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