The ACTO Times

Asian Cellular Therapy Organization

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SPOTLIGHT Regional CGT Updates

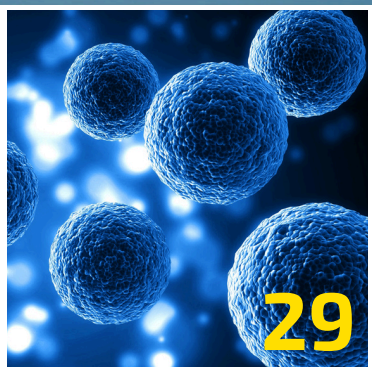
2026 ACTO Annual Meeting

Academic Highlight: iPSCs 20th Year, CGT Community & Industry

2026 SPRING EDITION

The ACTO Times
Asian Cellular Therapy Organization
2026 SPRING EDITION

CONTENTS



EDITORIAL

03 GREETING FROM ACTO CHAIRPERSON
04 GREETING FROM THE EDITOR-IN-CHIEF
05 ACTO COMMITTEE
07 EDITORIAL BOARD MEMBERS
08 EDITORIAL OFFICE
09 CALL FOR DONATION & ADVERTISEMENT
10 ABOUT ACTO
13 **ACTO-ASPI Co-organization:** Advancing cell-based and emerging CGT ecosystem in Indonesia: the strategic role of the Indonesian Stem Cell Association (ASPI)

SPOTLIGHT: REGIONAL CGT UPDATES

21 The university perspective in cell & gene therapy in Indonesia: landscape, challenges, progress, and a strategic vision for breakthrough
25 Current picture in cell and stem cell therapy research in Vietnam
29 Cell and gene therapy in Vietnam: between scientific momentum and regulatory maturation
32 Japan's dual-track regulatory framework for iPSCs therapies: lessons, limitations, and global implications

ACTO 2026 ANNUAL MEETING

35 ACTO 2026 annual meeting in highlight
36 Discover Indonesia Through ACTO Annual Meeting 2026 in Jakarta

ACADEMIC HIGHLIGHT: IPSCS 20TH YEAR

37 The 20-year journey of induced pluripotent stem cells (iPSCs) in regenerative medicine
39 Oxidative stress-driven metabolic reprogramming failure in MERRF patient's iPSC-derived neurons: from neurodevelopmental deficits to novel therapies
44 iPSC-derived cardiac cell sheets for heart regeneration: Progress toward clinical translation
48 Therapeutic potentials of induced pluripotent and mesenchymal stem cell-derived exosomes

CGT COMMUNITY

51 Taiwan Association for Cellular Therapy (TACT)
54 From Formosa to the world: leading the new era of regenerative medicine and cellular therapy in Taiwan (Formosa Association 0f Regenerative Medicine/FARM)

SPECIAL TOPIC (CGT INDUSTRY)

56 Overcoming Manufacturing Bottlenecks in Cell and Gene Therapy: The Emergence of the Intelligent Development and Manufacturing Organization (IDMO) Model in Asia
59 NEWS

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Greetings
The ACTO Chairperson

Dear ACTO members and supporters

We are happy to distribute the second edition of ACTO Times 2026. Thank you for your support for Journal as well as whole ACTO activities.

ACTO annual meetings were held already 16 times in many cities and the 17th Annual Meeting will be held in Jakarta on August 26~28, 2026 organized by Indonesia organizing team under the guidance of Meeting President, Dr. Amin Soebandrio.

We would like to encourage you not only to join but also to submit abstract, then you will have chance to win best abstract award. Again, this year, best abstract will be selected by the abstract review team members and award will be handed at the meeting sponsored by ACTO HQ office.

Another important news is 18th Annual meeting, 2027 meeting will be held in Niigata City, Japan organized by Prof. Shuji Terai, Niigata University, August 21~23,2027.
Today, still there are several issues related to the use of exosome. So far, I learned from clinical study conducted at Duke university and IGR, France, Dendritic cell (DC) derived exosome can transfer the information to all immune related cells if exosome carrying proper information. Even DC derived exosome, if it is not carrying proper information, DC derived exosome case, antigen, is not effective.

Another point we should emphasize is regulatory step for such new material/therapy. Any material administered in human must have safety data and efficacy suggesting data. And protocol must be reviewed by proper ethics committee and submitted local regulatory agency. Our two studies were reviewed by US FDA and approved for clinical study. We proposed the idea how to measure safety and efficacy of exosome derived from DC.
Today we are concerned that there are so many clinical use of exosome without proper regulatory agency involvement. Situation is similar to when we published appeal for cell therapy 2010. (Cell therapy medical tourism: Time for action: Cytotherapy, 2010; 12: 965–968)
I do believe our member will follow proper regulatory process for the new study. ACTO regulatory committee members will be ready to support your new idea.
Best regards

Best regards,

Chairperson, Asian Cellular Therapy Organization (ACTO)
Akihiro Shimosaka, Ph.D.

Editor's Column

The ACTO Times Editor-in Chief

Dear readers and friends of The ACTO Times,

It is my great pleasure to welcome you to the 2026 Spring Edition of The ACTO Times. As the season of renewal and growth begins, this issue offers a timely opportunity to reflect on major advances in cellular therapy and regenerative medicine, while also looking ahead to the scientific collaborations and translational achievements that continue to shape our field.

In this edition, we are especially pleased to focus on two major themes of exceptional importance. First, we highlight the 2026 ACTO International Annual Meeting in Jakarta, Indonesia, an important gathering that will bring together scientists, clinicians, innovators, and policymakers from across the region and beyond. This meeting represents not only a key academic event for ACTO, but also a valuable platform for strengthening international exchange. In this context, we are pleased to introduce key cell and gene therapy societies in Indonesia and Taiwan, including APSI, TACT, FARM, and TSSCR. Through these connections, we hope to foster new partnerships and advance the shared mission of translational and clinical innovation in cell and gene therapy globally.

Second, this year marks the twentieth anniversary of induced pluripotent stem cell (iPSC) research. In recognition of this important milestone, this issue presents a broad and forward-looking examination of global advances in iPSC science. We feature perspectives on regulatory frameworks for iPSC research and applications across multiple countries, as well as the growing importance of translational readiness in this rapidly evolving field. We also examine recent progress in iPSC-related product approvals. Most notably, Japan has recently granted conditional approval to two new allogeneic iPSC-based products, Amchepry (raguneprocel) and ReHeart, a landmark achievement that underscores the maturity and promise of regenerative medicine. These advances offer not only hope for patients, but also important reference points for countries seeking to develop their own regulatory and clinical strategies.

Beyond cell product development, this Spring Edition also turns attention to mitochondrial medicine, an increasingly important area in understanding how to maintain stem cell function and vitality for translational medicine. As our understanding of mitochondrial function, dysfunction, and therapeutic targeting continues to expand, this field is opening important new directions for the study and treatment of a broad range of diseases.

As Editor-in-Chief, I am deeply grateful to our authors, reviewers, editorial colleagues, and readers for your continued support and contribution. Your dedication sustains the mission of The ACTO Times and strengthens the collective spirit of our academic and professional community.

I hope this Spring Edition will inform, inspire, and encourage further dialogue and collaboration in the months ahead. We look forward to meeting many of you at ACTO Jakarta 2026 and to continuing this important journey together.

Sincerely,

Yen Hua Huang, PhD
Editor-in-Chief, The ACTO Times
ACTO, Asian Cellular Therapy Organization
Distinguished Professor
College of Medicine, Taipei Medical University

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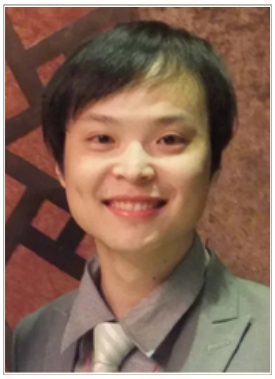

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Nova, MD, Ph.D.
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Nova is a faculty member in the Pediatric Surgery Division, Department of Surgery, Universitas Gadjah Mada (UGM), Indonesia. His research interests include stem cell biology, organoid technology, and translational applications of regenerative medicine in pediatric surgery.

Karen Kitchley, M.Sc
Madurai

Karen is a PhD student at the Taipei Medical University. Her research focuses on exosomal therapy on hepatocellular carcinoma and exploring their mechanism of action.

Yu-Xiu Lin, M.Sc
Taipei

Tony is a PhD student at the Graduate Institute of Pharmacology, National Taiwan University College of Medicine. His research focuses on MSC culture and therapy, specifically exploring their role in regenerative medicine.

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UNVEILING THE TIMELESS TAPESTRY

THE CHRONICLE OF ACTO THROUGH TIME

ACTO
Asian Cellular Therapy Organization

ACTO, the Asian Cellular Therapy Organization, serves as a dedicated platform for fostering the growth and progress of cellular therapy in the Asian context. It aims to respond more dynamically to the specific challenges and opportunities found in the diverse healthcare and research landscape across Asia.

ACTO is dedicated to driving advancements in cell and gene therapy (CGT), including research, clinical applications, industry collaborations, and global regulation. It seeks to facilitate collaborative environment where professionals, researchers, industry leaders, and regulatory agencies can come together to share knowledge, experiences, and innovations in CGT.

By doing so, ACTO envisions creating a comprehensive ecosystem that accelerates the translation of CGT research into practical applications, benefiting patients and contributing to the broader field of regenerative medicine. Through its activities, publications, and events, ACTO aims to play a crucial role in shaping the future of cellular therapy in Asia and contributing to the global discourse on regenerative medicine.

Since its establishment stemming from the ISCT Asian Regional Meeting, ACTO has evolved into a dynamic organization with a broad presence covering 15 regional territories, including Bangladesh, China, India, Indonesia, Iran, Japan, Jordan, Israel, Korea, Malaysia, Taiwan, Thailand, Singapore, Vietnam, and Pakistan. The expansion of ACTO into these territories not only amplifies the impact of CGT initiatives but also facilitates the exchange of knowledge and expertise across borders.

This collaborative approach aligns with ACTO's overarching mission to create a vibrant and interconnected network dedicated to advancing CGT within the diverse landscape of Asia.

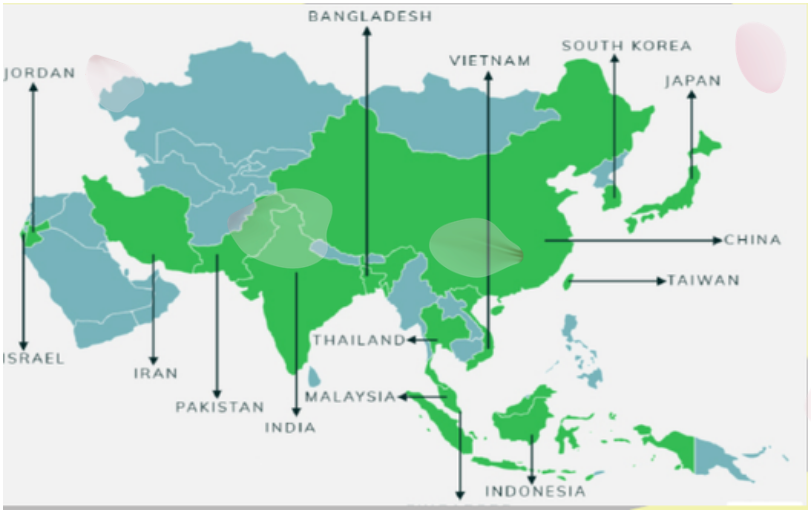
The inclusion of these 15 regional territories served by ACTO highlights the varied landscapes, healthcare systems, and research environments across Asia. It demonstrates ACTO's recognition of the importance of tailoring CGT initiatives to the unique needs, challenges, and opportunities specific to each region.

Looking ahead, the ACTO organization remains committed to its regional focus, striving to further expand its presence and influence to better serve the diverse needs of the Asian CGT community.

PRELUDE

NAVIGATING THE UNIQUE DYNAMICS OF CGT IN ASIA

In the vibrant landscape of CGT. "The ACTO Times" unfolds as a chronicle attuned to the distinctive characteristics that define the Asian population. This prelude invites readers into a realm where the convergence of a large and diverse populace, intricate gene backgrounds, evolving regulations, and culture-related intricacies shape the narrative of CGT in Asia.



Large Population Dynamics

Asia, with its colossal and diverse population, charts a path for CGT that is both unprecedented and dynamic. "The ACTO Times" embarks on a journey to unravel how the sheer scale of population diversity influences research, clinical applications, and the industrial landscape of CGT.

Gene Background Diversity

Within the mosaic of Asian societies lie rich variations in gene backgrounds. This prelude delves into the intricacies of genetic diversity, exploring how the tapestry of genes across Asian populations influences the trajectory of CGT, from personalized medicine to targeted therapies.

Culture-Related Pre-Clinical Research

Cultural contexts weave through the fabric of pre-clinical research. This publication uncovers the cultural nuances influencing the design and execution of pre-clinical studies, shedding light on how diverse cultural perspectives impact the trajectory of CGT research in Asia.

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Manufacturing and Industry Evolution

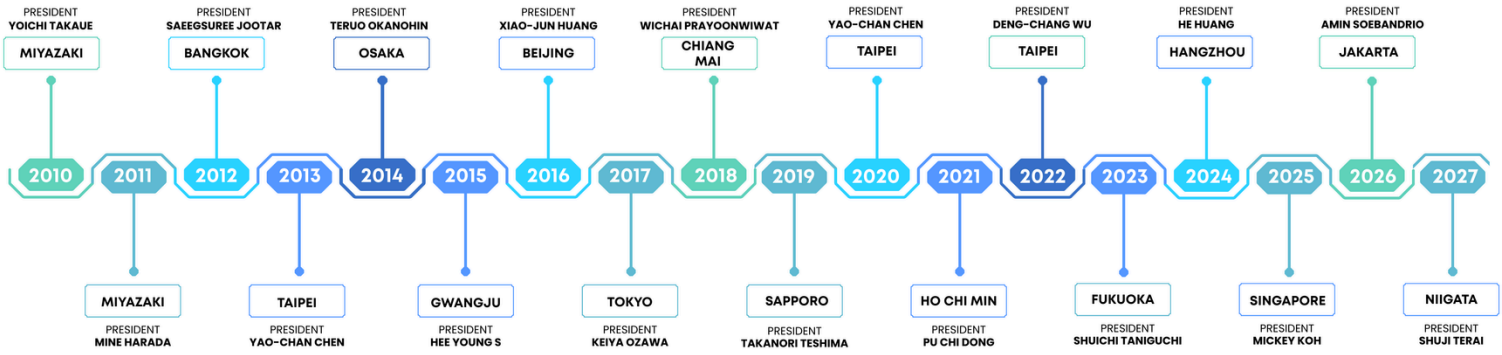
The industrial heartbeat of cellular therapy in Asia is a testament to innovation and growth. "The ACTO Times" investigates how manufacturing practices, deeply entwined with cultural norms, contribute to the dynamic evolution of the CGT industry in this expansive region.

Regulatory Frontiers

The diverse regulatory frameworks and rich cultural tapestry across Asian regions stand as influential forces shaping the intricate process of CGT in the region. In navigating this dynamic landscape, each nation brings its own set of regulations, reflecting unique perspectives on ethical considerations, patient safety, and research practices.

OUR JOURNEY THROUGH TIME

IMAGE FROM CANVA.COM



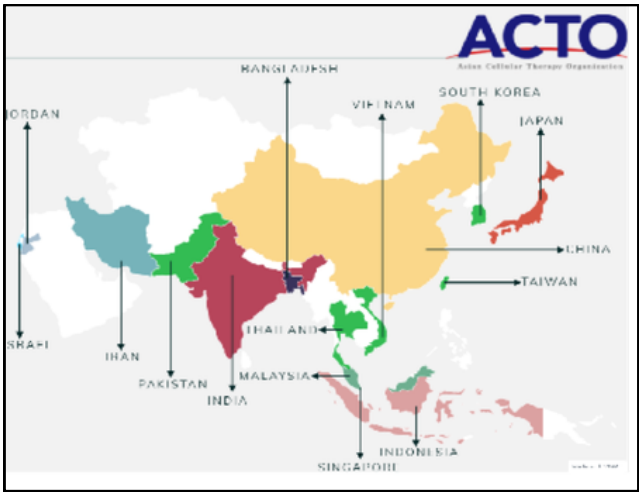
Over the years, the ACTO meetings became a cornerstone for professionals in the field, providing a platform for networking, sharing knowledge, and forging international partnerships. As the organization evolved, reflecting the dynamic landscape of CGT in the Asia-Pacific region.

The ACTO meeting was started from the first International Society of Cellular Therapy (ISCT) Asian-Pacific Regional Meeting 2010 in Japan. The primary objective of this gathering is to facilitate the exchange of knowledge and expertise among researchers, clinicians, business professionals, and regulators in the realm of CGT.

The focus is on advancements in equipment and treatments, encompassing areas such as expansion or modification for transplantation, immunotherapy, regenerative medicine, and gene therapy.

In many Asian regions, there has been limited exploration of expertise in innovative cellular therapy and the development of equipment for clinical purposes. Additionally, there is a notable absence of well-established regulatory guidelines for approval processes, which are crucial for fostering new ideas in clinical applications.

These challenges pose significant hurdles to the progress of our research initiatives. The intention is that this meeting will serve to improve communication among Asian professionals and foster collaborations with their Western counterparts, thereby contributing to overcoming these obstacles.



As of the present moment, the Asian Cellular Therapy Organization (ACTO) has seen the enthusiastic engagement of 15 regional territories in its annual meetings. This collective involvement underscores the organization's commitment to fostering collaboration and knowledge exchange among diverse regions within the realm of CGT. Joining ACTO provides an opportunity for regions to contribute their unique insights, experiences, and expertise to the ongoing discourse in CGT. As we embrace a spirit of inclusiveness, our shared journey towards scientific and medical advancements becomes even more robust and impactful.

ACTO - ASPI Co-organization

Amin Soebandrio[1], Rahyussalim[2], Cynthia Retna Sartika[1,2]
Rusdy Ghazali Malueka[1,2],Isabella Kurnia Liem[2], Angliana Chouw[2]
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IMAGE FROM CANVA.COM

Advancing cell-based and emerging CGT ecosystem in Indonesia: the strategic role of the Indonesian Stem Cell Association (ASPI)

Abstract

Cell and gene therapy (CGT) has emerged as an important field of modern medicine, integrating regenerative medicine, stem cell science, and advanced biologics to address diseases with limited therapeutic options. In Indonesia, the CGT ecosystem remains primarily driven by stem cell–basedregenerative medicine, particularly mesenchymal stem cell (MSC)-based therapies andsecretome-related products. Over the past decade, Indonesia has demonstrated progressive development in translational research, clinical implementation, and regulatory strengthening through collaboration among government institutions, academia, healthcare providers, and industry stakeholders. This article reviews the current development of Indonesia's cell-based and emerging CGT ecosystem, including regulatory evolution, research progress, clinical applications, translational development, and implementation challenges. Indonesia's regulatory framework has gradually evolved toward a more structured system aligned with advanced therapy medicinal product (ATMP) principles through complementary oversight by the Ministry of Health and the Indonesian Food and Drug Authority (BPOM).

Current development remains dominated by regenerative medicine and MSC-based translational programs, while gene therapy and immune-cell engineering activities are still at an early stage. Major challenges persist in GMP-compliant infrastructure, manufacturing readiness, funding, long-term evidence generation, and public awareness. In this evolving landscape, the Indonesian Stem Cell Association (ASPI) plays an important role in supporting scientific exchange, education, standardization, and regional collaboration.

Keywords: cell therapy, stem cell, regenerative medicine, Indonesia, ASPI

Indonesia Stem Cell Association (ASPI)

Indonesia Stem Cell Association (ASPI) is a professional organization focused on the advancement of stem cell research, regenerative medicine, and emerging cell and gene therapy development in Indonesia.

Prof. dr. Amin Soebandrio WK, Ph.D. SpMK(K)

Advisory board of ASPI

Introduction

Cell and gene therapy (CGT) has rapidly emerged as an important field of modern medicine, combining genetic engineering with stem cell-based approaches to treat diseases that remain difficult to manage using conventional therapies. Stem cells have become a major foundation of CGT development, supporting regenerative medicine and gene-modified therapeutic platforms. Over the past decade, CGT has expanded significantly, with multiple advanced therapy medicinal products (ATMPs), including CAR-T and gene-modified therapies, receiving regulatory approval in major markets worldwide [1,2]. In parallel, the global CGT pipeline continues to grow through advances in stem cell technologies, viral vectors, and translational biomanufacturing [3].

Across the Asia-Pacific region, CGT development has accelerated through supportive regulatory frameworks, translational infrastructure, and expanding clinical research activities [17]. Within this landscape, Indonesia is emerging through stem cell-based regenerative medicine programs, particularly mesenchymal stem cell (MSC)-based therapies and translational applications. The Indonesian Stem Cell Association (ASPI) plays an important role in this ecosystem by connecting researchers, clinicians, regulators, academic institutions, and industry stakeholders to support regenerative medicine and emerging CGT development in Indonesia [14–18].
This article highlights the current development of Indonesia's cell-based and emerging CGT ecosystem, focusing on regulatory evolution, translational progress, implementation challenges, and the strategic role of ASPI in supporting national and regional advancement.

Overview of ASPI (Indonesian Stem Cell Association)

The Indonesian Stem Cell Association (Asosiasi Sel Punca Indonesia, ASPI) is a professional non-profit organization established to support the advancement of stem cell science, regenerative medicine, and cellular therapy in Indonesia. The organization emerged from collaborations among clinicians, researchers, academic institutions, government representatives, and industry stakeholders involved in regenerative medicine and translational biomedical research.

Vision and Mission

ASPI aims to become a leading national and regional platform for stem-cell education, scientific collaboration, and regenerative medicine development, positioning Indonesia as an active contributor within regional cellular therapy networks [14,15].

The organization promotes high-quality and ethical stem cell research and supports evidence-based clinical applications in regenerative medicine. In addition, ASPI facilitates scientific exchange, training activities, workshops, and collaborative engagement among Indonesian and international stakeholders, including scientists, clinicians, regulators, healthcare institutions, and industry representatives [14,15].

Over time, ASPI has evolved into an important national platform connecting clinicians, researchers, academic institutions, regulators, and industry stakeholders involved in stem cell and cellular therapy development. The organization actively organizes scientific meetings, educational seminars, workshops, and collaborative programs related to stem cell research, regenerative medicine, and translational cellular therapy [15].

ASPI also contributes to efforts toward harmonization between national practices and evolving international standards in cellular therapy and regenerative medicine. The organization supports ethical and evidence-based implementation of stem cell therapies while promoting capacity building, scientific collaboration, and public education in emerging CGT-related fields [13,15].

Regulatory landscape in Indonesia

Indonesia has progressively developed a more structured regulatory framework for stem cell-based therapies and advanced therapy medicinal products (ATMPs), transitioning from a predominantly service-based approach in the early 2000s toward a more comprehensive framework aligned with ATMP-related regulatory principles [5–9]. This regulatory evolution reflects both the growing clinical adoption of regenerative medicine and the increasing need to address safety, efficacy, quality control, and commercialization concerns associated with emerging cellular therapies.

The Indonesian regulatory system operates under a dual-track structure in which the Ministry of Health (MoH) and the Badan Pengawas Obat dan Makanan (BPOM) hold complementary roles. The Ministry of Health regulates healthcare services and the clinical implementation of stem cell therapies within licensed healthcare facilities, whereas BPOM regulates therapeutic products, including biologics and advanced therapy products, covering manufacturing, product evaluation, clinical trials, and post-marketing oversight [5,7,9].

The legal foundation for this framework is anchored in national health legislation, including Health Law No. 17/2023, which replaced the earlier Health Law No. 36/2009 [6].

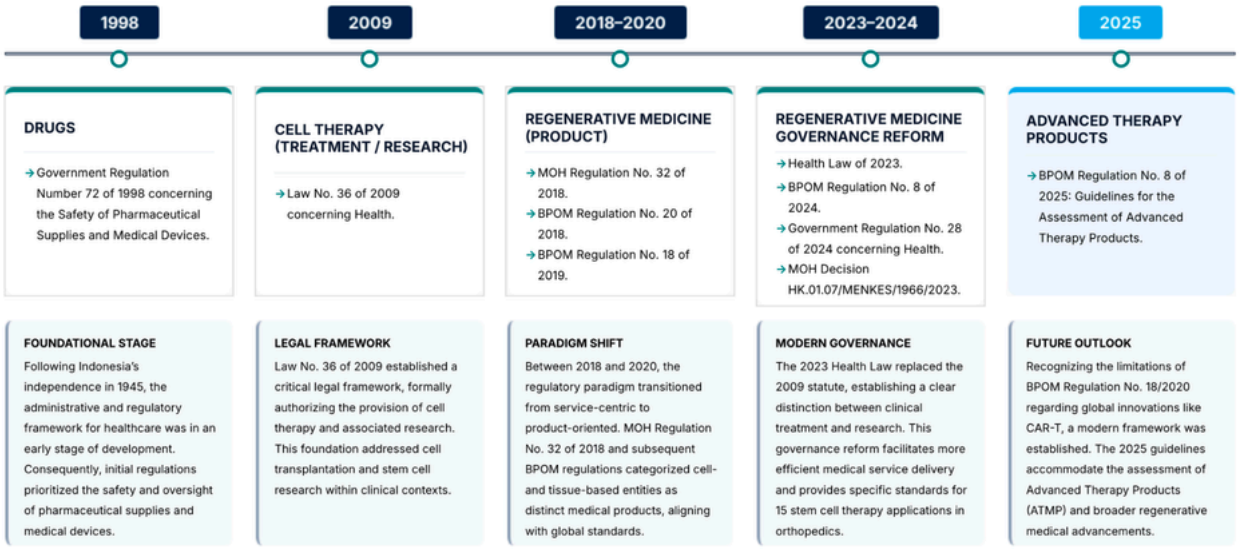

Figure 1. Evolution of Indonesia's regulatory framework for stem cell therapy and advanced therapy medicinal products (ATMPs) from 1998 to 2025, illustrating the transition from limited oversight toward increasingly comprehensive regulation of regenerative medicine and advanced cellular therapies.

Additional implementation guidance was introduced through the Ministry of Health Regulation No. 32/2018 concerning stem cell services, which established standards for the provision of stem cell-based medical services within healthcare facilities [7]. BPOM subsequently strengthened the product-based regulatory pathway through BPOM Regulation No. 18/2020 concerning the evaluation of human cell-based medicinal products [5].

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Between 2018 and 2025, Indonesia experienced substantial regulatory refinement in regenerative medicine and advanced therapies. BPOM Regulation No. 8/2025 further expanded the regulatory framework toward broader ATMP concepts and clarified evaluation pathways for advanced therapy products [9]. Government Regulation No. 28/2024 also strengthened implementation standards under the Health Law framework and clarified distinctions between healthcare services, clinical research, and therapeutic product oversight [8,22].

Under the current regulatory approach, minimally manipulated and homologous-use cell therapies may still be implemented as healthcare services within licensed hospitals under Ministry of Health supervision, provided they are not commercialized as pharmaceutical products [7,20]. This distinction is particularly relevant for stem cells, secretome-based products, exosomes, and extracellular vesicles, which may fall under either service-based or product-based regulation depending on their degree of manipulation, intended use, and commercialization pathway [9,21].

Ethical and compliance considerations remain integral components of Indonesia's regenerative medicine governance framework. Clinical research involving stem cell or ATMP-based interventions must undergo institutional ethics review and comply with Good Clinical Practice principles [13]. BPOM regulations also emphasize risk-benefit assessment, protocol evaluation, patient safety monitoring, and informed consent procedures prior to human clinical application [5,9].

Manufacturing and processing activities for commercialized cell-based products are required to comply with GMP/CPOB standards and quality-control requirements [5,9]. Meanwhile, hospital-based cell-processing facilities that do not possess full GMP certification remain limited to internal and non-commercial clinical applications. Indonesian regulatory authorities also impose restrictions on the promotion and advertisement of stem cell therapies, particularly regarding unsupported therapeutic claims and misleading patient communication [21].

Despite these advancements, several regulatory challenges remain. The distinction between service-based implementation and product-based therapeutic classification continues to evolve, particularly for autologous and minimally manipulated therapies [19,20]. In addition, implementation of GMP standards, harmonization between institutions, long-term pharmacovigilance systems, and consistent enforcement against unapproved stem cell practices remain important areas for further development.

Overall, Indonesia's regulatory landscape for stem cell therapies and ATMPs is undergoing a significant transition toward greater standardization, stricter oversight, and closer alignment with international regulatory practices [5–9]. Recent policy developments indicate a clear national direction toward strengthening evidence-based evaluation and patient safety while maintaining controlled clinical access to regenerative medicine applications.

Current development of cell-based therapy & emerging CGT in Indonesia

Indonesia's cell and gene therapy (CGT) ecosystem is still emerging, with stem cell-based approaches serving as the primary driver of innovation and clinical translation. The research and academic dimension is increasingly coordinated by the National Research and Innovation Institute (BRIN), particularly through its Health Research Organisation. Meanwhile, clinical translation, safety oversight, and implementation are shaped by the Indonesian Ministry of Health and the Indonesian Food and Drug Agency (BPOM). This institutional alignment is critical, as CGT development depends not only on scientific capability but also on governance, regulation, and the ability to translate laboratory advances into clinical practice.

Research & Academic Development

Research activity in Indonesia is currently dominated by stem cell-based regenerative medicine, particularly mesenchymal stem cell (MSC) research. Universities, hospitals, research institutes, and translational laboratories have increasingly collaborated in programs involving MSCs derived from umbilical cord tissue, adipose tissue, bone marrow, and other biological sources. Current research activities largely focus on regenerative medicine applications, immunomodulation, tissue repair, inflammatory disorders, and degenerative diseases.

The National Research and Innovation Agency (BRIN), particularly through its Health Research Organization, plays an important role in coordinating national biomedical research priorities and supporting translational research initiatives related to regenerative medicine and emerging cellular therapies [12]. BRIN's expanding involvement in genomics, biobanking, biomedical data management, and translational infrastructure development may further support future CGT-related innovation in Indonesia [12].

In recent years, growing interest has also been observed in secretome-, exosome-, and extracellular vesicle-based approaches. These strategies are considered attractive due to their potentially lower manufacturing complexity, broader scalability, and reduced logistical challenges compared with live-cell therapies [21]. Several academic institutions, healthcare centers, and biotechnology-related initiatives have begun exploring translational applications involving conditioned medium, secretome products, and extracellular vesicle technologies.

Compared with stem cell-based regenerative medicine, gene therapy development in Indonesia remains at an earlier stage. Current activities are still limited primarily to exploratory translational research and early-stage investigation involving molecular therapies, immune-cell engineering, and immunomodulatory platforms. As a result, Indonesia's current CGT ecosystem remains predominantly cell therapy-driven rather than gene therapy-driven.

Clinical Applications

In Indonesia, clinical applications of CGT remain largely centered on cell-based therapies, particularly within orthopedic, neurological, aesthetic, and broader regenerative medicine indications. Current clinical practice is dominated by mesenchymal stem cell (MSC)-based approaches, alongside dendritic cell-related therapies and emerging secretome or conditioned-medium applications.

Therapeutic targets commonly include osteoarthritis, musculoskeletal disorders, spinal injuries, stroke, cerebral palsy, and degenerative conditions. These therapeutic areas reflect both clinical demand and the relative maturity of MSC-based regenerative platforms within Indonesia's existing healthcare infrastructure.

Despite ongoing clinical implementation, the field remains in a transitional phase between research-based therapy and regulated clinical practice. While several stem cell-based interventions are already offered in healthcare settings, many applications continue to rely on early-stage clinical evidence and translational research support. Data from ClinicalTrials.gov and the Indonesia Clinical Research Registry (INA-CRR) indicate that CGT-related activities in Indonesia are still predominantly concentrated in early clinical development phases, with many studies categorized as phase I or phase II clinical investigations rather than large-scale confirmatory trials [3,4].

Standardization of manufacturing protocols, long-term safety monitoring, efficacy validation, and multicenter clinical evaluation remain ongoing challenges. These factors highlight the importance of continued clinical validation to ensure that regenerative medicine and emerging CGT applications in Indonesia remain scientifically grounded, ethically implemented, and sustainably integrated into healthcare systems.

Recent regulatory developments from the Ministry of Health have contributed to improved clinical guidance and standardization for stem cell-based medical services. KMK No. HK.01.07/MENKES/1359/2024 introduced guidance for orthopedic and traumatology applications, while KMK No. HK.01.07/MENKES/1200/2025 provided implementation guidance for plastic reconstructive and aesthetic indications [10,11].

Together with BPOM oversight and evolving ATMP-related regulations, these policies represent important steps toward strengthening evidence-based clinical implementation and reducing variability in regenerative medicine practices across Indonesia.

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CGT products and translational pipeline in Indonesia

Indonesia's current CGT landscape is characterized primarily by hospital-based implementation, translational products, and early commercialization initiatives rather than fully mature mass-market advanced therapy products. Current development remains strongly focused on mesenchymal stem cell (MSC)-based platforms, including umbilical cord-derived MSCs, conditioned medium, secretome products, and extracellular vesicle-related approaches [5,7,9].

Several healthcare institutions, biotechnology companies, and university-industry collaborations are actively involved in these developments. Regenerative medicine centers, translational laboratories, and industry-linked biologics programs have gradually expanded their activities in cell processing, translational bioprocessing, and regenerative medicine services. These developments indicate gradual movement toward a more product-oriented regenerative medicine ecosystem in Indonesia.

Indonesia's translational pipeline also includes exploratory work involving immune-cell therapies such as natural killer (NK) cells and other immunomodulatory approaches.

However, most products and technologies remain in early translational or investigational stages and have not yet progressed into large-scale commercial deployment or late-phase clinical development. The expansion of GMP-compliant manufacturing facilities and translational bioprocessing infrastructure is expected to play an important role in supporting future CGT development within Indonesia [5,9].

Challenges in CGT development in Indonesia

Regulatory gaps

Although Indonesia's regulatory framework for regenerative medicine and advanced therapies has improved substantially, several areas remain challenging, particularly the distinction between service-based implementation and product-based therapeutic classification. Ministry of Health Regulation No. 32/2018 established the healthcare-service pathway for stem cell implementation within licensed facilities, while BPOM Regulation No. 18/2020 and BPOM Regulation No. 8/2025 strengthened product-based oversight for human cell-based medicinal products and advanced therapy medicinal products (ATMPs) [5,7,9]. Nevertheless, harmonization between healthcare-service regulation and ATMP-style product evaluation continues to evolve, especially for minimally manipulated and autologous therapies [19,20].

Indonesian regulators have introduced progressive measures to address these gaps through clearer regulatory pathways, strengthened ethical oversight, implementation guidance for stem cell-based clinical services, and broader ATMP-oriented frameworks [5,7–9]. However, long-term follow-up requirements, pharmacovigilance systems, and post-marketing evaluation mechanisms for advanced therapies remain under further development. Recent efforts by the Ministry of Health and BPOM to strengthen monitoring systems, manufacturing standards, clinical governance, and evidence-based implementation represent important steps toward improving regulatory consistency and patient safety in regenerative medicine applications [5,8,9,13].

Infrastructure and Manufacturing Limitations

CGT manufacturing requires GMP-compliant facilities, advanced quality-control systems, and specialized technical expertise, which remain limited in Indonesia. Current challenges include the lengthy development and validation process for GMP facilities, restricted local availability of critical reagents and consumables, and limited capacity for advanced cell processing and vector-related manufacturing [5,9]. Dependence on imported materials and overseas manufacturing support may further increase production costs and reduce long-term scalability.

Nevertheless, important progress has been made to address these limitations. Government institutions, academic centers, hospitals, and industry stakeholders have increasingly invested in GMP-compliant infrastructure, translational bioprocessing facilities, and collaborative manufacturing platforms [9,12]. Public-private collaboration models and shared translational infrastructure initiatives are also beginning to emerge to strengthen domestic manufacturing readiness, reduce long-term dependence on foreign production systems, and support more sustainable CGT development within Indonesia.

Funding and Translational Ecosystem

Most CGT activities in Indonesia remain concentrated within academic research and early translational development phases. Long development timelines, high manufacturing costs, and uncertain reimbursement pathways continue to limit investment attractiveness, particularly for advanced therapies requiring complex manufacturing processes and extensive clinical validation.

Nevertheless, support for translational development has gradually increased through public-sector funding, academic-industry collaboration, and government-supported research initiatives involving BRIN, universities, hospitals, healthcare institutions, and biotechnology-related industry partners [12]. Emerging partnerships between academia, biotechnology companies, and clinical centers have started to strengthen translational capacity and improve pathways toward clinical implementation.

In recent years, government-supported grant mechanisms have increasingly encouraged the participation of both private and state-linked industries in downstream product development and translational commercialization. These initiatives aim to ensure that research outputs can be further developed into healthcare products and services with broader societal impact. Although funding remains fragmented and relatively limited for large-scale late-phase clinical development, these developments represent important progress toward building a more sustainable national CGT ecosystem [12].

Public awareness issues

Public understanding of stem cell and CGT technologies remains variable and may not always align with current scientific evidence and clinical limitations. Regenerative medicine is occasionally associated with unrealistic expectations or unsupported therapeutic claims, increasing the risk of misinformation and unregulated clinical practices [13,21].

The International Society for Stem Cell Research (ISSCR) guidelines emphasize the importance of evidence-based communication, ethical clinical translation, and responsible public engagement in regenerative medicine [13]. In Indonesia, concerns regarding misleading promotional claims and unverified regenerative medicine services have also been discussed in regulatory and practice-oriented summaries [21].

Limited public understanding regarding potential risks, long-term safety considerations, and the developmental timelines required for advanced therapies may contribute to vulnerability toward unverified commercial offerings. In response, regulators, professional organizations, academic institutions, and stakeholders including ASPI have increasingly supported public education initiatives through scientific seminars, educational materials, and collaborative communication programs aimed at improving public literacy and clarifying which therapies are evidence-based, investigational, and appropriately regulated [13–15,21].

Strengthening evidence-based communication and public awareness will remain essential to support responsible clinical implementation and sustainable development of regenerative medicine and CGT in Indonesia [13].

Emerging opportunities to address CGT challenges in Indonesia

Indonesia possesses several strategic advantages for future CGT development, including a large patient population, growing biomedical research capacity, and an expanding biotechnology sector. Emerging initiatives in biobanking, bioinformatics, GMP-compliant manufacturing, and translational bioprocessing infrastructure may strengthen domestic readiness for advanced therapies while reducing dependence on overseas manufacturing systems [9,12].

Recent regulatory developments by BPOM and the Ministry of Health have also improved alignment between research, manufacturing, and clinical implementation through stronger frameworks for stem cell–based products and advanced therapy medicinal products (ATMPs) [5,7,9]. Collaboration among regulators, BRIN, academic institutions, healthcare providers, professional organizations, and industry stakeholders is gradually supporting a more coordinated national CGT ecosystem [5–12].

Regional and international collaboration, particularly through organizations such as the Asian Cellular Therapy Organization (ACTO), also provides opportunities for scientific exchange, regulatory harmonization, and capacity building across the Asia-Pacific region [16–18].

ASPI's strategic role moving forward

ASPI is expected to continue playing a strategic role in advancing regenerative medicine and CGT in Indonesia through scientific exchange, education, and regional collaboration within the Asian Cellular Therapy Organization (ACTO) network [16–18]. Recent progress in regulation, institutional coordination, GMP-compliant infrastructure, and translational bioprocessing has strengthened Indonesia's emerging CGT ecosystem through collaboration among the Ministry of Health, BPOM, BRIN, academic institutions, healthcare providers, and industry stakeholders [5–12].

In this context, the 17th ACTO Annual Meeting in conjunction with ASPI, to be held in Jakarta on 26–28 August 2026, represents an important platform to promote scientific exchange, regional collaboration, and regulatory harmonization for safe and evidence-based CGT development across Asia [13,16–18]. Continued investment in human resources, public education, digital health systems, and multi-stakeholder collaboration will remain essential to support sustainable CGT growth in Indonesia.

Conclusion

Indonesia has significant potential for the development of cell and gene therapy (CGT) through its large patient population, growing biomedical ecosystem, expanding research capacity, and increasing collaboration among regulators, academic institutions, healthcare providers, and industry stakeholders. Ongoing improvements in regulatory frameworks, GMP-compliant infrastructure, translational research, and public–private collaboration reflect Indonesia's commitment to advancing safe and evidence-based regenerative medicine. In this context, the 17th ACTO Annual Meeting in conjunction with ASPI, which will be held in Jakarta on 26–28 August 2026, represents an important opportunity to strengthen scientific exchange, regional collaboration, and regulatory harmonization across Asia. Such collaboration is expected to support the responsible development of CGT while strengthening each country's capacity to develop and provide advanced therapies within their own healthcare systems.

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Conflict of interest

The authors declare that they have no conflicts of interest related to this article. The authors also declare that they have no financial, institutional, or commercial affiliations that could be perceived as influencing the objectivity, interpretation, discussion, or conclusions presented in this manuscript.

References

1. U.S. Food and Drug Administration. Approved cellular and gene therapy products [Internet].
2. Silver Spring (MD): FDA; 2025 [cited 2026 May 11]. Available from: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cell ular-and-gene-therapy-products
3. U.S. Food and Drug Administration. Cellular & gene therapy products [Internet]. Silver Spring (MD): FDA; 2025 [cited 2026 May 11]. Available from: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products
4. National Institutes of Health. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2025 [cited 2026 May 11]. Available from: https://clinicaltrials.gov
5. Indonesia Clinical Research Registry. INA-CRR Registry [Internet]. Jakarta: INA-CRR; 2025 [cited 2026 May 11]. Available from: https://ina-registry.org
6. Badan Pengawas Obat dan Makanan Republik Indonesia. Peraturan Badan Pengawas Obat dan Makanan Nomor 18 Tahun 2020 tentang Pedoman Penilaian Obat Berbasis Sel Manusia [Internet]. Jakarta: BPOM RI; 2020 [cited 2026 May 11]. Available from: https://jdih.pom.go.id/download/file/1222/Perka_BPOM_2020.pdf
7. Republik Indonesia. Undang-Undang Republik Indonesia Nomor 17 Tahun 2023 tentang Kesehatan [Internet]. Jakarta: Pemerintah Republik Indonesia; 2023 [cited 2026 May 11]. Available from: https://peraturan.bpk.go.id
8. Kementerian Kesehatan Republik Indonesia. Peraturan Menteri Kesehatan Republik
9. Indonesia Nomor 32 Tahun 2018 tentang Penyelenggaraan Pelayanan Sel Punca [Internet]. Jakarta: Kementerian Kesehatan RI; 2018 [cited 2026 May 11]. Available from: https://peraturan.bpk.go.id
10. Republik Indonesia. Peraturan Pemerintah Nomor 28 Tahun 2024 tentang Peraturan Pelaksanaan Undang-Undang Kesehatan [Internet]. Jakarta: Pemerintah Republik Indonesia; 2024 [cited 2026 May 11]. Available from: https://peraturan.bpk.go.id
11. Badan Pengawas Obat dan Makanan Republik Indonesia. Peraturan Badan Pengawas Obat dan Makanan Nomor 8 Tahun 2025 tentang Pedoman Penilaian Produk Terapi Advanced [Internet]. Jakarta: BPOM RI; 2025 [cited 2026 May 11]. Available from: https://www.pom.go.id/berita/bpom-perkuat-regulasi-produk-terapi-advanced-jamin-keama nan-dan-mutu-terapi-regeneratif
12. Kementerian Kesehatan Republik Indonesia. Keputusan Menteri Kesehatan Republik Indonesia Nomor HK.01.07/MENKES/1359/2024 tentang Pedoman Pelayanan Orthopaedi dan Traumatologi Berbasis Sel Punca [Internet]. Jakarta: Kementerian Kesehatan RI; 2024 [cited 2026 May 11].
13. Kementerian Kesehatan Republik Indonesia. Keputusan Menteri Kesehatan Republik
14. Indonesia Nomor HK.01.07/MENKES/1200/2025 tentang Pelayanan Bedah Plastik Rekonstruksi dan Estetik Berbasis Sel Punca [Internet]. Jakarta: Kementerian Kesehatan RI; 2025 [cited 2026 May 11].
15. Badan Riset dan Inovasi Nasional. BRIN research programs [Internet]. Jakarta: BRIN; 2025 [cited 2026 May 11]. Available from: https://www.brin.go.id
16. International Society for Stem Cell Research. ISSCR guidelines for stem cell research and clinical translation [Internet]. Skokie (IL): ISSCR; 2021 [cited 2026 May 11]. Available from: https://www.isscr.org/policy/guidelines-for-stem-cell-research-and-clinical-translation
17. Asosiasi Sel Punca Indonesia. About us [Internet]. Jakarta: ASPI; 2025 [cited 2026 May 11]. Available from:https://aspindonesia.co.id/about-us
18. Asosiasi Sel Punca Indonesia. Official homepage [Internet]. Jakarta: ASPI; 2025 [cited 2026 May 11]. Available from: https://aspindonesia.co.id
19. Asosiasi Sel Punca Indonesia. 17th Annual Meeting ACTO-ASPI 2026 [Internet]. Jakarta: ASPI; 2026 [cited 2026 May 11]. Available from: https://aspindonesia.co.id/event/17th-annual-meeting-acto-advancing-research-clinical-tran slation-of-cell-based-therapies-academia
20. Asian Cellular Therapy Organization. ACTO official website [Internet]. 2025 [cited 2026 May 11]. Available from:https://acto-hq.org
21. ACTO TIMES. ACTO-ASPI cooperation news [Internet]. 2025 [cited 2026 May 11]. Available from:https://theactotimes.com/news/
22. Dewi NNM, et al. Legal and ethical perspectives on stem cell services regulation in Indonesia.
23. Eduvest J Universal Stud. 2022;2(8):1487–1498. Available from:https://eduvest.greenvest.co.id/index.php/edv/article/view/508
24. Return: Study of Management, Economic and Bussines. Legal review of stem cell services implementation in Indonesia [Internet]. 2023 [cited 2026 May 11]. Available from: https://return.publikasikupublisher.com/index.php/return/article/download/298/516
25. Regenic. Apakah terapi secretome legal di Indonesia? Cek regulasi terbaru [Internet]. Jakarta: Regenic; 2025 [cited 2026 May 11]. Available from: https://www.regenic.co.id/id/artikel/umum/apakah-terapi-secretome-legal-di-indonesia-cekregulasi-terbaru
26. Akset Law. A closer look at the standards of medical services under GR 28/2024 [Internet]. Jakarta: Akset Law; 2024 [cited 2026 May 11]. Available from:https://aksetlaw.com/news-event/newsflash/a-closer-look-at-the-standards-of-medical-servi ces-under-gr-28-2024/

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IMAGE FROM UGM.AC.ID

The university perspective in cell & gene therapy in Indonesia: landscape, challenges, progress, and a strategic vision for breakthrough

Introduction: A Nation at the Inflection Point

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As the ACTO Annual Meeting 2026 convenes in Jakarta, a fitting recognition of Indonesia's growing prominence in the Asian cellular therapy landscape, the country finds itself at a defining inflection point. With a population exceeding 280 million, an escalating burden of non-communicable and degenerative diseases, and a life sciences ecosystem in active formation, Indonesia is no longer merely a peripheral observer of the global cell and gene therapy (CGT) revolution. Universities, long regarded as the intellectual backbone of the nation, are now emerging as active architects of this transformation.

From the university perspective, the CGT landscape in Indonesia presents both exceptional promise and sobering complexity. This article examines the current state of academic engagement in CGT, highlights concrete research contributions emerging from leading institutions, recognizes the pioneering role of Universitas Indonesia and Universitas Airlangga, identifies the progress being made by Universitas Gadjah Mada (UGM) and Dr. Sardjito Hospital as its principal academic hospital, and proposes a strategic framework for breakthrough — one that places universities not at the margins, but at the center of Indonesia's future advanced-therapy ecosystem.

The Academic landscape: from pioneering nodes to a national network

Indonesian universities have been laying the groundwork for CGT and regenerative medicine for more than a decade, although progress has been uneven because of resource constraints, regulatory transition, and the high capital intensity of good manufacturing practice (GMP)-grade cell production. The most important development is that the national landscape is no longer defined by isolated laboratories. It is gradually taking the shape of an academic-clinical network, with several universities acting as pioneering nodes and others beginning to build specialized capacity. Universitas Indonesia (UI), through the Faculty of Medicine UI and Dr. Cipto Mangunkusumo Hospital (FKUI-RSCM), deserves clear recognition as one of Indonesia's earliest academic pioneers. FKUI-RSCM began stem-cell research in 2008 and subsequently developed a service-based translational research platform by involving more than 30 subspecialist clinicians across indications such as non-union fractures, long-bone defects, spinal cord injury, osteoarthritis, diabetic foot, stroke, osteoporosis, heart disease, skin rejuvenation, and alopecia.

Universitas Airlangga (UNAIR) is another major pioneer, particularly through its dedicated Stem Cell Research and Development Center, which explicitly aims to become a nationally and internationally standardized center for stem-cell and regenerative-medicine research, testing, laboratory training, and public-facing research support. In 2024 UNAIR publicly highlighted the expansion of stem-cell applications from degenerative disease toward autoimmune disease and cancer, including immunomodulation, dendritic-cell vaccines, T-cell modification concepts, and hematopoietic recovery after cancer treatment.

Taken together, UI and UNAIR helped establish the intellectual, clinical, and institutional foundation for Indonesian stem-cell development. Their experiences show that academic leadership matters in at least three ways: building multidisciplinary clinical platforms, producing translational evidence, and legitimizing a field that is vulnerable to both premature commercialization and public misunderstanding.

Universitas Gadjah Mada, Dr. Sardjito Hospital, and UGM academic hospital: consolidating an academic-hospital platform

At UGM, academic CGT engagement is anchored through a formal institutional structure spanning the Faculty of Medicine, Public Health and Nursing (FK-KMK UGM), Dr. Sardjito Hospital as the main teaching hospital, and UGM Academic Hospital. Dr. Sardjito Hospital has been designated by the Indonesian Ministry of Health as one of Indonesia's hospital centers for the development of stem-cell medical services, research, and education. Although stem-cell services had not yet been operational there before 2015, the subsequent creation of the Dr. Sardjito Stem Cell Team and the FK-KMK UGM core stem-cell team marked a deliberate institutional transition from aspiration to organized capacity-building.

This development began with structured benchmarking and partnership-building. In December 2015, the FK-KMK UGM team conducted a comparative study to the Tissue Engineering and Cell Therapy (TECT) Laboratory at the National University Hospital, Singapore, and to the Stem Cell and Cancer Institute in Jakarta. The process led to cooperation among FK UGM, Dr. Sardjito Hospital, UGM Academic Hospital, and PT Bifarma Adiluhung, a Kalbe Farma subsidiary active in stem-cell development. The UGM platform therefore emerged not merely as a laboratory initiative, but as a university-hospital-industry collaboration model.

This foundation has since translated into verifiable research output. The Stem Cell Team of FK-KMK UGM and Dr. Sardjito Hospital, in collaboration with Dr. Moewardi Hospital Solo and Hasan Sadikin Hospital Bandung, conducted a double-blind, multicenter, randomized, placebo-controlled clinical trial of normoxic allogeneic umbilical-cord mesenchymal stem cells as adjunctive therapy for severe COVID-19. Published in Scientific Reports in 2023, the study reported encouraging clinical results, including improved patient recovery, and represents an important example of a rigorous, GCP-compliant stem-cell clinical trial conducted within an Indonesian academic-hospital network.

The FK-KMK UGM and Dr. Sardjito Hospital translational programs are being developed as formal clinical trials and research-based clinical services, with knee osteoarthritis and post-traumatic spinal cord injury among the earliest indications developed. These programs include stem-cell approaches using autologous bone-marrow-derived cells and allogeneic umbilical-cord/Wharton's jelly-derived mesenchymal stem cells, supported by structured clinical and imaging follow-up.

The broader FK-KMK UGM–Dr. Sardjito Hospital roadmap extends to additional indications, including ischemic stroke, Parkinson disease, cerebral palsy, intractable epilepsy, chronic kidney disease, diabetic nephropathy, diabetes mellitus, autoimmune diseases, pulmonary disease, dermatologic applications, chronic ulcers, and retinitis pigmentosa. These programs are at different stages, ranging from ongoing or planned clinical trials and structured service-based research to protocol development, partnership negotiation, and regulatory-permit preparation. The hospital currently has complete application capability for intravenous, intramuscular, intra-articular, intrathecal, intracranial, intra-arterial, local, and regional delivery, while cell processing is performed through formal cooperation with licensed processing facilities, including Regenic and Prostem/Prodia Stem Cell as GMP -certified partners.

More recently, UGM signed a new memorandum of understanding in January 2025 with PT Stem Cell and Cancer Research Indonesia (SCCR) and Yayasan Agung Putra Ibrahim (YAPI) for cooperation encompassing medical services, clinical trials, and stem cell research and technology development, with full institutional support from UGM for accelerating stem cell and cancer research.

In the clinical translation area, researchers at FKKMK UGM have also contributed to the scientific discourse on emerging modalities beyond conventional stem cell therapy. Prof. Y. Widodo Wirohadidjojo from the Department of Dermatology and Venereology noted that the academic community is moving progressively from secretome-based approaches toward exosome-based therapies, reflecting alignment with the frontiers of international regenerative medicine science.

The regulatory and ecosystem progress

The broader enabling environment for university-led CGT is also evolving favorably. The Indonesian government established the Indonesia Clinical Research Centre (INA-CRC) in mid-2024 to streamline clinical trial processes and attract international sponsors. In late 2025, INA-CRC jointly hosted a national workshop with the WHO Indonesia Country Office and the WHO Western Pacific Regional Office (WPRO), piloting the WHO Clinical Trial Unit-Maturity Framework — aligning with the Global Action Plan for Clinical Trial Ecosystem Strengthening.

On the regulatory side, BPOM Regulation No. 24 of 2024 establishes stringent requirements for pre-clinical and clinical data submissions, including facility standards, quality control measures, and licensing for cell and gene therapy products, creating formal approval pathways for advanced therapy medicinal products. Meanwhile, BPOM has reported that the global market for cell and gene therapies has climbed from USD 9 billion to USD 22.6 billion in just two years, and the domestic Indonesian stem cell therapy market is projected to reach substantial scale — underscoring the strategic economic imperative alongside the therapeutic one.

Nationally, BRIN and ASPI co-hosted an international seminar in August 2025 on stem cell innovation featuring BPOM regulatory insights, a scientific competition, and concrete steps toward building a national regenerative medicine roadmap — demonstrating that the institutional will to cohere this ecosystem is real and growing.

Persistent challenges: an honest assessment

Despite this progress, universities continue to face structural, financial, and systemic barriers that require frank acknowledgment. The infrastructure gap remains substantial. Most Indonesian university laboratories operate well below GMP standards, which are increasingly required not just for product commercialization but for compliant clinical trial execution.

BPOM has issued guidelines requiring GMP certification for cytokines, growth factors, and transfection reagents used in ex vivo manufacturing, pushing developers to transition from research-grade to GMP-grade inputs — a transition that demands capital investment few university budgets can accommodate independently.

Import dependency compounds the challenge. An estimated 95% of raw materials for stem cell production in Indonesia come from imports, creating a structural vulnerability and a challenge for national self-sufficiency in advanced therapies. Universities are ideally positioned to contribute upstream solutions through biomaterial research and process development, but only with targeted funding mandates.

The clinical trial pipeline, while improving, remains thin. Most active CGT trials in Indonesia are still in early-phase (Phase I/II) stages, focusing on stem cell-based therapies and regenerative medicine, typically conducted in collaboration between hospitals, universities, and biotech firms under Ministry of Health and BRIN oversight. Transitioning from these exploratory studies to well-powered, pivotal trials requires not just scientific readiness, but also coordinated capacity in biostatistics, data management, regulatory affairs, and clinical operations — competencies that must be systematically built within academic medical centers.

There is also the persistent challenge of unproven therapies. Across the region, unvalidated stem cell offerings at unregulated clinics continue to erode public trust in legitimate science. Universities must assume their role not merely as knowledge producers, but as public educators and institutional guardians of ethical standards in CGT.

A strategic framework for breakthrough

The path forward for Indonesian universities in CGT is clear in direction, even if demanding in execution. Several strategic priorities stand out.

Establishing CGT Centers of Excellence.
Not every institution needs to cover the entire CGT value chain. A nationally coordinated strategy — led by the Ministry of Education and Research in partnership with Ministry of Health and BRIN — should designate a small number of universities as national CGT Centers of Excellence with dedicated GMP-capable manufacturing units, translational research programs, and clinical trial infrastructure. UGM and UNAIR, given their existing commitments, are natural anchors for such a network in Java; other institutions in Sumatra, Sulawesi, and Eastern Indonesia should be strategically developed to ensure equitable geographic coverage.

Co-designing regulatory pathways.

Universities must engage BPOM as a co-design partner rather than a compliance endpoint. Academic institutions carry the scientific credibility and impartiality to help shape adaptive regulatory frameworks — particularly for investigator-initiated trials, academic-sponsored studies, and hospital-based CGT services operating under the Ministerial permit system.

Building a deliberate talent pipeline.

Indonesia continues to lose trained CGT scientists to overseas institutions, not solely due to compensation differentials, but also due to the absence of structured domestic career pathways in this specialty. Universities should design dedicated doctoral and postdoctoral programs in CGT — co-supervised with international partners, ideally through ACTO and regional networks — with clear re-entry pathways and retention incentives anchored to national research programs.

Leveraging Indonesia's unique research advantages.

Indonesia's remarkable genetic diversity, its unique tropical disease burden, and its large patient population represent genuine research assets that are underutilized in the global CGT literature. Academic researchers should be strategically encouraged to design studies that address conditions disproportionately affecting Indonesian and Southeast Asian populations — conditions for which existing global CGT pipelines offer little coverage, and for which Indonesia could become a scientific leader.

Strengthening the university-hospital-industry triangle.

The collaboration model between UGM, hospitals (Dr. Sardjito and UGM Academic hospital), and industry partners demonstrates what is achievable when this triangle functions. Formalizing, expanding, and incentivizing such models — with clear intellectual property frameworks, revenue-sharing mechanisms, and joint academic output expectations — should become a national policy priority.

Closing perspective: the role universities cannot afford to cede

Universities occupy a distinctive position in the CGT ecosystem — one that neither government agencies nor private industry can fully replicate. They are the sites of disinterested inquiry, long-horizon thinking, and the training of the next generation of scientists, clinicians, and regulators.

They are also, at their best, the institutional conscience of a field where commercial pressures and patient desperation can easily converge in ways that are neither scientifically nor ethically sound. As Jakarta hosts the ACTO Annual Meeting 2026, this moment offers Indonesian academic institutions a rare and consequential opportunity: to articulate a university-led vision for CGT development that is rigorous, equitable, globally connected, and distinctly Indonesian. UI and UNAIR helped build the early intellectual and clinical foundations; UGM and Dr. Sardjito Hospital now illustrate how an academic medical center can consolidate service readiness, multicenter research experience, clinical protocols, digital governance, and a growing trial pipeline in osteoarthritis, spinal cord injury, COVID-19, and other target indications.

The national roadmap being crafted through BRIN-ASPI and the emerging regulatory maturity under BPOM should now be matched by greater academic coordination, transparent data reporting, and a shared commitment to ethical translation.

Science is advancing. The regulation is maturing. The global community is watching. What remains is the strategic will — and that, more than any single breakthrough, is what universities are uniquely positioned to provide.

References:

1. Indonesia CGT 2026 Update — The ACTO Times https://theactotimes.com/2026/03/20/indonesia-cell-gene-therapy-cgt-2026-update/
2. BPOM CGT Regulation Perspective — The ACTO Times https://theactotimes.com/2026/03/20/regulation-of-cell-and-gene-therapy-cgt-in-indonesia-perspective-of-bpom/
3. UC-MSC Clinical Trial in Severe COVID-19 (UGM/RSUP Dr. Sardjito et al.) — Scientific Reports, Nature, August 2023 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10397314/
4. Stem Cell Team FKKMK UGM — Official Website https://stemcell.fkkmk.ugm.ac.id/tentang-kami/
5. UGM – MoU with SCCR & YAPI, January 2025 https://ugm.ac.id/en/news/ugm-collaborates-on-stem-cell-technology-with-yapi-and-pt-stem-cell-indonesia/
6. BRIN-ASPI International Seminar on Stem Cell Innovation, August 2025 https://aspindonesia.co.id/brin-aspi-international-seminar-2025-future-directions-and-opportunities-in-stem-cell-innovation-for-clinical-application-and-the-health-industry-lights-the-path-for-indonesia/
7. Universitas Airlangga Stem Cell Research and Development Center https://unair.ac.id/en/stem-cell-research-center/
8. BPOM Legal Framework for Cell-Based Medicine (ICLG) https://iclg.com/briefing/14597-bpom-introduces-legal-framework-for-human-cell-based-medicine
9. UGM — Affordable Stem Cell Therapy Needs Stronger Support (December 2025) https://ugm.ac.id/en/news/affordable-stem-cell-therapy-services-need-stronger-support-experts-say/
10. Standard Regulation for Stem Cell Products in Indonesia — ResearchGate / Cytotherapyhttps://www.researchgate.net/publication/351499168_Standard_regulation_for_stem_cell_products_in_indonesia

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IMAGE FROM CANVA.COM

Current picture in cell and stem cell therapy research in Vietnam

Introduction

In recent years, cell and gene therapy (CGT) has experienced remarkable growth in Vietnam, mirroring global innovation while leveraging local scientific expertise. CGT in Vietnam has transitioned from early experimental efforts to a more structured and translational phase, marked by increasing clinical application, technological refinement, and national-level strategic direction. Since the mid-1990s, Vietnam has achieved significant milestones, such as its first hematopoietic stem cell transplantation (HSCT) for children with Wiskott-Aldrich syndrome (WAS) [1], especially those derived from adipose tissue, has expanded rapidly, with clinical trials demonstrating their safety and efficacy in treating aging-related low-grade inflammation, cartilage injury, and psoriasis-like inflammation [2-4]. Next-generation approaches under investigation encompass MSC-derived exosomes for treating photoaging and promoting wound repair [5, 6], as well as protocols to enrich Muse cells from umbilical cord–derived mesenchymal stem cells (MSCs) [7]. Notably, the country's transition from pioneering research to the development of national strategies and standardized clinical applications. Collectively, these advances underscore Vietnam's growing leadership in regenerative medicine and the integration of CGT into mainstream healthcare.

Preclinical and clinical trials of CGT in Viet Nam

Over the past decade, CGT in Vietnam has made remarkable progress, transitioning from pioneering research to clinical implementation and national strategic planning. Currently, Viet Nam has developed a nationwide network of hospitals performing hematopoietic stem cell transplantation and MSC–based therapies, with dozens of clinical trials conducted across multiple disease indications [8-12].

Based on published data, Vietnamese centers have collectively performed at least several hundred HSCT procedures, including over 500 cases nationwide by 2017–2018 and 547 procedures at the National Institute of Hematology and Blood Transfusion alone by 2022 [9, 13]. In this context, Vietnam has also reported its first successful HSCT for children with WAS [1].

MSC-based therapy, especially using adipose-derived mesenchymal stem cells (AD-MSCs), has become a cornerstone of translational research and clinical application in Vietnam. In Vietnam, the application of autologous AD-MSCs is gaining traction, with early clinical observations indicating acceptable safety profiles and practical feasibility, particularly in conditions linked to age-related inflammation. Complementing these findings, experimental studies suggest beneficial effects in cartilage regeneration and immune-driven dermatologic disorders. Notably, a phase I, open-label, single-arm clinical investigation carried out in Ho Chi Minh City explored the biological impact and safety of infusing autologous AD-MSCs in individuals experiencing chronic low-grade inflammation and metabolic complications associated with aging. In this study (NCT05827757), twelve patients received two intravenous infusions of 100 million autologous AD-MSCs each, with the trial strictly adhering to Vietnamese Good Clinical Practice guidelines and Ministry of Health approval [2]. No adverse events were reported throughout the follow-up period, indicating a favorable safety profile.

By day 180, a pronounced shift in the biological profile was observed: levels of key pro-inflammatory mediators—including tumor necrosis factor alpha, interleukin (IL)-6, IL-1β, IL-1α, and IL-8—were substantially reduced, while ratios reflecting anti-inflammatory activity (such as IL-4/IL-10 and IL-2/IL-10) showed a corresponding increase [2]. Taken together, these immunologic shifts indicate that systemic infusion of AD-MSCs represents a safe strategy with meaningful immunomodulatory potential for controlling age-related inflammation [2, 14].

Vietnamese pediatric centers have recently initiated curative HSCT programs for children with rare immunodeficiencies such as WAS. A retrospective series at Vietnam National Children's Hospital reported 15 allogeneic HSCT procedures in 13 children with WAS between 2020 and 2024. A minority of procedures employed reduced-intensity conditioning (26.7%), whereas the majority were preceded by myeloablative regimens (73.3%) [1]. The origin of donors varied considerably, comprising mismatched related individuals (40%), unrelated cord blood units (33.3%), matched sibling donors (20%), and a smaller fraction from phenotypically identical family members (6.7%) [1]. Median times to engraftment were 14 days for neutrophils and 48 days for platelets. By day +100, about 77% of patients had established full donor chimerism, and overall survival reached 92.3% [1]. The main cause of mortality was chronic graft-versus-host disease (GVHD). Additionally, a separate published case documented a successful haploidentical HSCT with post-transplant cyclophosphamide for WAS, resulting in full immune reconstitution and no GVHD at 32 months follow-up [15]. These outcomes demonstrate that complex allogeneic HSCT, including haploidentical transplantation, is now a feasible and effective treatment option for non-malignant diseases in Vietnam [1, 9, 15].

Whether persistent neurological deficits after ischemic stroke could be mitigated was examined in a phase II randomized controlled trial, which evaluated the effects of delivering allogeneic umbilical cord–derived mesenchymal stem cells (UC-MSCs) either through intrathecal administration into the cerebrospinal fluid or via systemic intravenous infusion. Thirty-two individuals aged 40–75 years with established post-stroke sequelae were allocated to receive UC-MSCs: 16 were treated with two intrathecal administrations plus a standardized rehabilitation program, and 16 with two intravenous infusions plus the same rehabilitation regimen, while a further 16 matched participants underwent rehabilitation alone without UC-MSC therapy [16].
UC-MSC treatment was administered at a dose of 1.5 × 10^6 cells/kg at two time points (study entry and month 3).

Follow-up continued for 12 months, during which neurological and functional outcomes were serially assessed using standard stroke severity (NIHSS), functional independence (FIM), spasticity (MAS), motor function (FMS), and quality-of-life (SF-36) scales [16]. No serious treatment-related complications were detected, and participants receiving cells intravenously experienced fewer adverse events than those treated intrathecally [16]. By the 6-month visit, the intravenous cohort had already achieved statistically meaningful improvements on the SF-36, FIM, and NIHSS scales, and by 12 months, both stem-cell-treated groups had significant clinical and quality-of-life improvements compared with baseline, with larger benefits in the intravenous arm, particularly for SF-36 [16]. When compared with rehabilitation alone, enhancements in neurological function and quality of life were observed alongside a favorable safety profile for both delivery routes of UC-MSCs. Among these approaches, systemic intravenous administration demonstrated the most advantageous combination of therapeutic effect and tolerability [16].

Parallel to clinical advances, preclinical and mechanistic studies are addressing key challenges in efficacy and safety. Interestingly, an in vitro work systematically dissects how MSCs trigger coagulation, supporting its role as a mechanistic investigation of thrombosis risk [17]. Quantitative profiling of tissue factor (TF) and a panel of pro- and anticoagulant regulators was performed in mesenchymal stromal cells maintained under xeno- and serum-free conditions and derived from dental pulp, adipose tissue, umbilical cord, and bone marrow, revealing pronounced dependence of TF, collagen type 1 alpha 1 chain (COL1A1), phosphatidylserine, tissue factor pathway inhibitor (TFPI), and prostaglandin I2 receptor (PTGIR) expression [17]. Using plasma-based clotting assays, Hoang and colleagues found that MSCs from multiple tissue sources could directly trigger fibrin clot generation in normal donor plasma; this procoagulant effect was only partly attenuated by blockade with an anti–tissue factor monoclonal antibody, and, importantly, even human umbilical vein endothelial cells lacking detectable TF expression were still capable of displaying measurable coagulation activity in vitro [17]. Together, these experiments clarify the cellular and molecular mechanisms underlying MSC-associated coagulation, and explain why TF expression alone is an incomplete predictor of thrombotic risk.

Other disease models such as psoriasis-like inflammation [3] provide insights into dose-response relationships and immunomodulatory mechanisms, helping to refine therapeutic protocols before large-scale clinical trials.

Another key achievement is the diversification of therapeutic strategies beyond conventional cell transplantation. Vietnam has increasingly explored cell-free approaches, particularly exosome-based therapies. Derived from AD-MSCs, exosomal preparations have been applied as a cell-free therapy that not only hasten closure and regeneration of cutaneous wounds but also counteract UV-induced skin aging changes in both animal models and early-stage trials [5, 6]. These findings support the growing interest in cell-free approaches, especially exosome-based therapies, which offer regenerative and anti-aging effects while potentially presenting fewer safety concerns compared to whole-cell transplantation. Building on this direction, research teams in Viet Nam have generated extracellular vesicles from human fibroblasts engineered to express ETV2. These vesicles drive robust endothelial proliferation in vitro and markedly augment neovessel formation in a mouse hindlimb ischemia model, pointing to a powerful cell-free modality for therapeutic vascular regeneration [18]. In addition, efforts to optimize stem cell sources and quality represent another important area of progress. Techniques such as hypoxia-induced enhancement and selective enrichment of specialized subpopulations (e.g., Muse cells) have been explored [7]. Moreover, hypoxic culture combined with ETV2 overexpression markedly increases the efficiency of directly reprogramming fibroblasts into functional endothelial progenitor cells, offering an improved source for ischemic therapies [19]. Alongside advances in characterization methodologies [20], these studies contribute to improving reproducibility, potency, and standardization, critical factors for regulatory approval and clinical scalability. Collectively, these achievements reflect Vietnam's ability to keep pace with global trends, positioning the country at the forefront of cutting-edge developments in CGT.

Additionally, combinatorial strategies integrating supportive biologics have also been investigated. Within regenerative orthopedics, evidence points to a cooperative therapeutic effect when adipose-derived stem cell transplantation is paired with activated platelet-rich plasma. This combination appears to enhance stem cell engraftment and cartilage repair, suggesting a synergistic approach to regenerative therapy [4]. Although such strategies remain relatively limited in recent Vietnamese publications, they highlight an emerging interest in improving therapeutic outcomes through multi-component systems. Several constraints persist notwithstanding these advances: the majority of clinical investigations remain limited to early-stage or small cohorts, and robust confirmation of efficacy is hindered by the scarcity of large-scale randomized controlled trials.
Standardization of protocols, long-term safety monitoring, and harmonization with international regulatory frameworks are ongoing challenges.

Within the country, the development of cutting-edge interventions, such as gene-engineered cellular treatments exemplified by CAR-T, remains at an early, formative stage, indicating that these approaches have yet to achieve widespread clinical maturity.

Summary

In summary, Vietnam has made substantial progress in recent years by establishing clinical feasibility, advancing mechanistic insights, and adopting next-generation therapeutic approaches in cell and stem cell therapy. While the field is still developing, the current trajectory suggests strong potential for Vietnam to become a significant regional contributor to regenerative medicine, provided that future efforts focus on scaling clinical evidence, standardization, and regulatory maturity. One of the most notable achievements is the expansion of clinical applications, particularly MSCs and hematopoietic stem cells. Early-phase clinical work [2], demonstrates that locally developed therapies can meet initial safety and feasibility benchmarks in human subjects. In parallel, the successful implementation of HSCT for rare diseases [1], reflects increasing clinical sophistication and the ability to manage complex, high-risk procedures within the national healthcare system. These milestones indicate that Vietnam is no longer limited to preclinical investigation but is actively delivering advanced therapies in clinical settings.

References

1. Nguyen-Ngoc-Quynh L., et al., First report of hematopoietic stem cell transplantation for children diagnosed with Wiskott-Aldrich syndrome in Vietnam. J Blood Med, 2025. 16: p. 373–383.
2. Nguyen N.T., et al., Safety and efficacy of autologous adipose tissue-derived stem cell transplantation in aging-related low-grade inflammation patients: a single-group, open-label, phase I clinical trial. Trials, 2024. 25(1): p. 309.
3. T.T.P., et al., Efficacy and dose response of adipose-derived stem cells in ameliorating psoriasis-like inflammation in a mouse model. MINERVA, 2024. 36(3): p. 144–60.
4. Van Pham P., et al., Activated platelet-rich plasma improves adipose-derived stem cell transplantation efficiency in injured articular cartilage. Stem Cell Res Ther, 2013. 4(4): p. 91.
5. Quynh D.T., et al., Wound healing capacity of using mesenchymal stem cell-derived exosomes originated from human adipose tissue and cold atmospheric plasma. Clin Ter, 2024. 175(2): p. 135–143.
6. Huynh C.B., et al., Effects of exosomes from hypoxia-Induced adipose-derived stem cells on ameliorating photoaging.Clin Cosmet Investig Dermatol, 2025. 18: p. 1683–1702.
7. Le T., et al., Efficient enrichment of Muse cells from human umbilical Cord mesenchymal stem cells using collagenase and hypoxic stress. Biomed Res Ther, 2025. 12: p. 7265–7276.
8. Van Pham P., The evolution and future of cell therapy in Viet Nam: A 30-year journey from pioneering steps to national strategy (1995-2025). Prog Stem Cell, 2025. 12(2): p. 421–421.

9. Van Pham P., et al., An evolution of stem cell research and therapy in Viet Nam. Prog Stem Cell, 2018. 5(1): p. 235–250.
10. Van Pham P., Current status of stem cell transplantation in Vietnam. Biomed. Res. Ther., 2016. 3(4): p. 15.
11. Liem N.T., et al., Phase I clinical trial using autologous ex vivo expanded NK cells and cytotoxic T lymphocytes for cancer treatment in Vietnam. Int J Mol Sci, 2019. 20(13): p. 3166.
12. Tran T., ID3026 Current use and clinical studies of stem cells therapy for osteoarthritis in Viet Nam. Biomed. Res. Ther.,
13.
14. Khanh B.Q., et al., Forging international collaboration and alliances to establish the largest transplant center in the north of Vietnam. Semin Hematol, 2023. 60(4): p. 243–250.
15. Hoang D.M., et al., Stem cell-based therapy for human diseases. Signal Transduct Target Ther, 2022. 7(1): p. 272.
16. Nguyen Ngoc Quynh L., et al., Haploidentical stem cell transplantation with posttransplant cyclophosphamide in children with Wiskott-Aldrich syndrome: a case report. Front Immunol, 2025. 16: p. 1495666.
17. Nguyen L.T., et al., Intrathecal versus intravenous umbilical cord mesenchymal stem cells for ischemic stroke sequelae. Stem Cells Transl Med, 2025. 14(12): p. szaf063.
18. Hoang V.T., et al., Impact of tissue factor expression and administration routes on thrombosis development induced by mesenchymal stem/stromal cell infusions: re-evaluating the dogma. Stem Cell Res Ther, 2024. 15(1): p. 56.
19. Van Pham P., et al., Extracellular vesicles of ETV2 transfected fibroblasts stimulate endothelial cells and improve neovascularization in a murine model of hindlimb ischemia. Cytotechnology, 2017. 69(5): p. 801–814.
20. Van Pham P., et al., Significant improvement of direct reprogramming efficacy of fibroblasts into progenitor endothelial cells by ETV2 and hypoxia. Stem Cell Res Ther, 2016. 7(1): p. 104.
21. Phat Duc H., et al., Next-generation approaches for mesenchymal stem cell characterization and therapeutic application. J Adv Biotechnol Exp Ther, 2025. 8(3): p. 433–453.
22. 2017. 4: p. 36.

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Cell and gene therapy in Vietnam: between scientific momentum and regulatory maturation

Introduction

Cell and gene therapy (CGT) is reshaping modern medicine by enabling interventions at the level of cellular function and genetic programming. From hematologic malignancies to rare inherited disorders, these therapies have shifted from experimental promise to clinical reality in many parts of the world.

In Vietnam, CGT is emerging within a distinctive context: a system with growing scientific capability, early clinical successes, and an evolving regulatory framework that is still catching up with technological advances. Understanding this landscape requires examining not only clinical progress, but also the legal instruments that govern how such therapies are developed, tested, and applied.

Scientific Foundations and the Scope of Application

The biological basis of CGT lies in the unique properties of stem cells, particularly their ability to self-renew and differentiate into specialized cell types. These characteristics enable applications in regenerative medicine and targeted therapies, but they also introduce significant biological risks if not properly controlled.

In Vietnam, the most mature application remains hematopoietic stem cell transplantation, widely used in the treatment of hematologic diseases at institutions such as Vietnam National Children's Hospital and National Institute of Hematology and Blood Transfusion (NIHBT). This procedure reflects a high degree of clinical standardization and regulatory acceptance.

Beyond this domain, stem cell–based interventions have been explored in neurology, orthopedics, cardiology, and aesthetic medicine. However, most of these applications remain experimental, lacking sufficient clinical evidence for routine use.

The 2020 National Guideline: Defining Cell Therapy as a High-Risk Biomedical Intervention

A defining feature of Vietnam's regulatory approach is the issuance of the national guideline on research and application of cell-based products by the Ministry of Health in 2020. This document provides the first systematic framework for understanding and managing cell therapy within the country.

The guideline explicitly defines cell therapy as the use of living cells administered into the human body for therapeutic purposes. More importantly, it establishes that such interventions must be treated as high-risk biomedical technologies, requiring rigorous control across all stages of development and application. Rather than being categorized as routine medical techniques, cell-based therapies are framed as interventions that demand structured evaluation of safety and efficacy.

A key principle embedded in the guideline is the classification of cell products according to their level of manipulation and associated risk.

This approach aligns with international regulatory thinking and underscores that minimally manipulated cells and highly engineered products should not be treated equivalently. The document also emphasizes that all cell-based products must be manufactured under conditions consistent with Good Manufacturing Practice (GMP), ensuring traceability, sterility, and quality control.

Equally important is the requirement that clinical use must be preceded by appropriate research and evaluation. The guideline reinforces that any application of cell therapy must be grounded in scientifically validated protocols and subject to ethical oversight. In effect, it institutionalizes a "research-first" model, in which clinical deployment is contingent upon prior evidence rather than market demand.

This framework has significant implications. It formally distinguishes legitimate clinical innovation from unregulated practice, and it provides a legal and technical basis for restricting the use of cell therapies outside controlled settings.

Clinical Research Governance: The Expanding Role of Circular 50/2025

The introduction of Circula 50/2025 from Vietnam Ministry of Health marks a significant step in strengthening the legal infrastructure for clinical research in Vietnam. While originally designed for drug trials, its scope and principles are highly relevant to CGT, particularly for advanced therapies that function as biological products.

This regulation reinforces key requirements for clinical trials, including ethical approval, protocol standardization, safety monitoring, and data integrity. It also aligns Vietnam more closely with international clinical research standards, thereby facilitating more rigorous evaluation of emerging therapies such as CAR-T and gene-based interventions.

When viewed alongside the 2020 national guideline, Circular 50 contributes to a more coherent regulatory pathway: from laboratory research to clinical testing, and eventually to controlled therapeutic application. Together, these frameworks strengthen the legitimacy of CGT research while setting clear boundaries against premature or unauthorized clinical use.

Research Capacity and the Limits of Translation

Vietnam has demonstrated notable capacity in CGT-related research. According to Vinmec, several areas of stem cell research, particularly mesenchymal stem cells and regenerative medicine, were initiated relatively early and have progressed alongside global developments.

Despite this progress, a significant gap persists between research output and clinical implementation. This reflects structural challenges, including limited GMP-compliant manufacturing infrastructure and the absence of fully developed regulatory pathways for advanced therapies.

As a result, CGT in Vietnam remains largely research-driven, with only a limited number of applications transitioning into standardized clinical practice.

CAR-T Therapy and the Emergence of Domestic Innovation

The introduction of CAR-T therapy represents a defining moment in Vietnam's CGT landscape. This advanced immunotherapy, which involves engineering a patient's T cells to target cancer, has already transformed oncology globally.

In Vietnam, early clinical applications have been pioneered by Vinmec Healthcare System. Reported cases, including successful treatment in pediatric leukemia, demonstrate that highly complex therapies can be implemented domestically when supported by appropriate infrastructure and expertise.

These achievements highlight the emergence of a localized translational ecosystem, where research, manufacturing, and clinical care are integrated. At the same time, they underscore the uneven distribution of such capabilities across the national healthcare system.

Regulatory Structure: Between Control and Incompleteness

Vietnam's regulatory framework for CGT combines general healthcare law, technical classifications, and specialized guidance. The Law on Medical Examination and Treatment (2023) and Circular 23/2019/TT-BYT provide a legal basis for certain cell-based procedures.

However, it is the combination of the 2020 national guideline and Circular 50/2025 that most clearly defines the current regulatory approach. Together, they establish a continuum from research to clinical application, grounded in risk assessment, quality control, and ethical oversight.

Nevertheless, a comprehensive legal framework specifically tailored to CGT—particularly gene therapy and engineered cell therapies has yet to be fully developed.

The Persistent Challenge of Misuse

Despite a structured regulatory philosophy, enforcement challenges remain. Reports from mainstream media indicate the proliferation of clinics offering so-called stem cell therapies without scientific validation or regulatory approval.

Such practices directly contradict established principles, including GMP requirements and mandatory clinical evaluation. They also expose patients to serious risks, ranging from immune reactions to infections and tumor formation.

This disconnect between regulatory intent and real-world practice remains one of the most pressing issues in Vietnam's CGT landscape.

Conclusion

Cell and gene therapy in Vietnam is at a critical stage of development. The country has established a strong scientific foundation and demonstrated early success in advanced therapies such as CAR-T. At the same time, its regulatory framework—anchored by the 2020 national guideline and reinforced by Circular 50/2025—reflects a cautious, research-centered approach.

Yet, the system remains incomplete. Bridging the gap between research and clinical practice, strengthening enforcement, and developing a dedicated legal framework for advanced therapies will be essential steps moving forward.

Vietnam's experience illustrates a broader global challenge: how to translate cutting-edge biomedical innovation into safe, effective, and accessible healthcare—without losing control of its risks.

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IMAGE FROM CANVA.COM

Japan's dual-track regulatory framework for iPSCs therapies: lessons, limitations, and global implications

The Rise of iPS Cells: From Concept to Clinical Hope

Regenerative medicine is a multidisciplinary field addressing diseases characterized by irreversible tissue loss—conditions that historically relied on organ transplantation. However, transplantation is often stymied by chronic donor shortages, ethical dilemmas, and the risk of immune rejection. Regenerative medicine offers a transformative hierarchy of solutions, ranging from gene therapy and stem cell transplantation to tissue engineering [1].

Early stem cell therapies faced significant hurdles: autologous or allogeneic stem cells often exhibited inconsistent quality and limited expansion capacity [2]. A paradigm shift occurred in 2007 when Shinya Yamanaka's team successfully reprogrammed human somatic cells into induced pluripotent stem cells (iPSCs) [3]. This breakthrough allowed patient-specific cells to serve as a sustainable, standardized source for cell therapy. Despite this promise, iPSCs carry inherent risks, including high production costs, potential tumorigenicity (teratoma formation), and challenges in achieving high differentiation purity [4].

These factors have created bottlenecks in standardizing iPSC therapies for clinical application, even as the unmet medical needs for neurodegenerative diseases, heart failure, and muscular atrophy accelerate the push for regulatory approval.

The Japanese Milestone and the Shift to "Active Repair"

In December 2025, Japan marked a historic milestone by approving two iPSC-derived products: a cardiomyocyte sheet therapy and a neuronal transplantation therapy. This ended the long wait for commercialized iPSC products since the technology's inception. For diseases involving irreversible cell loss—such as Parkinson's disease (PD), multiple sclerosis, and heart failure—traditional pharmacology can only delay degeneration. iPSCs offer a shift from conservative management to active repair.

In PD, for instance, the death of dopaminergic neurons in the substantia nigra leads to motor dysfunction. By transplanting iPSC-derived dopaminergic precursor neurons into the striatum, clinicians can restore localized dopamine secretion. This approach surpasses traditional drugs by mimicking physiological rhythms and providing long-term effects without daily medication [5]. Furthermore, compared to using embryonic tissues, iPSCs mitigate ethical controversies, reduce immune rejection, and provide a stable cell source.

Regulatory Challenges

The path to commercialization is fraught with regulatory obstacles. Primary concerns include:

- Tumorigenic Risk: Residual undifferentiated stem cells can form tumors; the use of viral vectors in gene editing may further increase oncogenic risks.
- Standardization Difficulties: Unlike chemical compounds, iPSC batches are highly sensitive to culture environments, leading to disparate international standards for safety and purity.

- Small Sample Sizes: Prohibitive costs limit clinical trial scales, often resulting in Type II errors or overly wide confidence intervals, making it difficult to statistically confirm stable efficacy [6, 7].

Globally, regulatory stances vary: the EU maintains a stringent pre-approval system; the US offers flexibility through a "pre-notification" system (though this remains subject to evolving federal rulings); and Japan adopts a pragmatic "dual-track" approach [8].

Japan's Regulatory Framework: ASRM vs. PMD Act

Since 2014, Japan has managed iPSC therapies under two frameworks:

- The Act on the Safety of Regenerative Medicine (ASRM): Focuses on medical institutions. It treats iPSC therapy as a medical procedure (intervention), allowing for rapid, small-scale clinical research and self-funded treatments after reporting to the Ministry of Health, Labour and Welfare (MHLW).
- The Pharmaceuticals and Medical Devices Act (PMD Act): Focuses on biopharmaceutical enterprises. It treats iPSCs as "products" requiring rigorous clinical trials for commercialization [9]. The PMD Act allows for the conditional, time-limited approval of iPSC-derived products. If a product is proven safe and shows probable efficacy, it can enter the market for seven years with medical insurance support.

This "probationary" period allows companies to treat patients and collect real-world data, which is required to secure permanent approval later.

While the dual-track system's flexible management has successfully boosted the number of clinical research applications, significant hurdles remain. There is a persistent "standardization chasm" between research projects governed by the ASRM and those under the PMD Act. Because these frameworks operate on different criteria, data and protocols are often not interchangeable, creating inefficiencies in the field [9].

The PMD Act's conditional, time-limited approval pathway features a relatively low threshold for entry. This "lenient" approach may lead companies to overestimate the commercial potential of iPS-cell products. If these products fail to meet long-term expectations after hitting the market, it could result in substantial financial losses for investors and developers alike [10].

The Role of Regulatory Guidelines and Technical Guidance

Beyond "hard" legislation, regulatory agencies issue detailed guidelines and technical guidance that play a crucial role in iPSC clinical development. These cover aspects such as trial design, data privacy, and manufacturing processes.

1. Risk Mitigation: Unlike conventional drugs, regenerative products carry unique risks like tumorigenicity due to insufficient cell purity. In response, Japanese regulators have issued specific guidance on genomic stability and cell purity assays to strictly monitor oncogenicity.
2. Accelerating Approval: While these guidelines are not always legally mandatory, enterprises strictly adhere to them to expedite the review process.
3. Bridging the Gap: These guidelines intervene early in clinical research (under ASRM), ensuring that early-stage trial designs align with the rigorous quality standards required for eventual commercialization (under the PMD Act). By clarifying the "key data" required for final review, these rules prevent companies from misjudging a product's clinical potential, thereby reducing unnecessary investment risks [8, 9].

Toward a Global Consensus

The future of iPSC therapy transcends national borders. The experience gained by pioneers like Japan in managing iPSC clinical research and trials can significantly accelerate the progress of developing nations in this field. By operating under a unified set of standards and frameworks, these emerging countries can contribute a massive influx of clinical data.

This data, in turn, helps address the issue of small sample sizes often found in pioneer nations' studies. Particularly developing countries like China—are seeing an explosion in clinical trials, backed by massive patient cohorts and state funding [11]. This creates a powerful positive feedback loop that drives the entire field of regenerative medicine forward.

Currently, global regulations resemble "isolated islands." Establishing international standards—such as unified purity assays and tumorigenicity benchmarks—is essential to achieve data interchangeability. By harmonizing regulatory consensus, we can avoid redundant trials and significantly shorten the time-to-market. When data is shared and validated under a global framework, iPSC therapy will evolve from an expensive "bespoke science" into a standardized global industry, providing accessible, life-changing solutions for millions of patients suffering from organ failure and neurodegeneration.

References

1. Sampogna, G., S.Y. Guraya, and A. Forgione, Regenerative medicine: Historical roots and potential strategies in modern medicine. J Microsc Ultrastruct, 2015. 3(3): p. 101-107.
2. Yamanaka, S., Pluripotent Stem Cell-Based Cell Therapy-Promise and Challenges. Cell Stem Cell, 2020. 27(4): p. 523-531.
3. Takahashi, K., et al., Induction of pluripotent stem cells from adult human fibroblasts by defined factors. Cell, 2007. 131(5): p. 861-72.
4. Dhaiban, S., et al., Clinical translation of human iPSC technologies: advances, safety concerns, and future directions. Front Cell Dev Biol, 2025. 13: p. 1627149.
5. Sawamoto, N., et al., Phase I/II trial of iPS-cell-derived dopaminergic cells for Parkinson's disease. Nature, 2025. 641(8064): p. 971-977.
6. Hamad, A.A. and S.K. Ahmed, Understanding the Lower and Upper Limits of Sample Sizes in Clinical Research.Cureus, 2025. 17(1): p. e76724.
7. Neofytou, E., et al., Hurdles to clinical translation of human induced pluripotent stem cells. J Clin Invest, 2015. 125(7): p. 2551-7.
8. Song, S.J., et al., Comparative analysis of regulations and studies on stem cell therapies: focusing on induced pluripotent stem cell (iPSC)-based treatments. Stem Cell Res Ther, 2024. 15(1): p. 447.
9. Choi, K.N. and W.B. Liu, Driving the future of iPS-cell-based therapy in Japan: government strategies, regulatory review and clinical development. Drug Discov Today, 2026. 31(1): p. 104562.
10. Hakariya, H., et al., Japan's Conditional/Time-Limited Early Approval System in Regenerative Medicine: A Case Study of Rise and Falls of Autologous Skeletal Myoblast Sheets. Clin Pharmacol Ther, 2025. 117(5): p. 1171-1174.

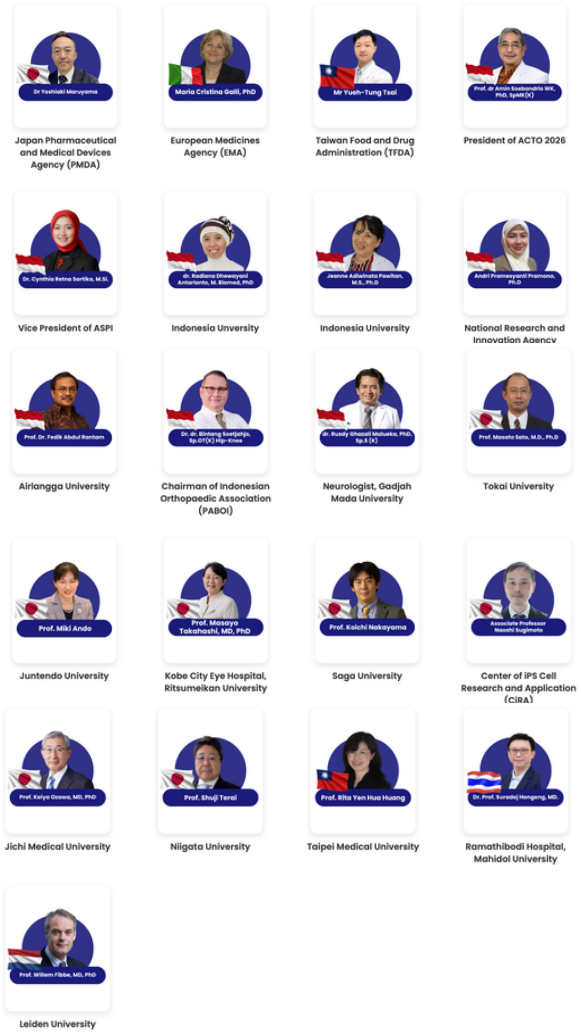
17th annual meeting of ACTO will be held in Jakarta, Indonesia

"Advancing Research & Clinical Translation of Cell-Based Therapies: Academician, Business, Clinician, and Government"

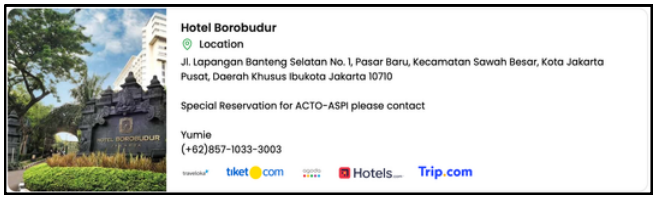
The 17th Annual Meeting of the Asian Cellular Therapy Organization (ACTO), in collaboration with the Indonesian Stem Cell Association (ASPI), will be held on 26–28 August 2026 in Jakarta, Indonesia. The meeting will bring together experts in cellular therapy, regenerative medicine, and translational biomedical science to discuss recent scientific developments, clinical applications, and regulatory perspectives shaping the future of cell-based therapies in the Asia-Pacific region.

Registration period :

- Early Bird Registration: 1 March – 15 June 2026
- Normal Registration: 16 June – 26 August 2026



Registration Pricing				
Category	Local (Early)	Local (Normal)	International (Early)	International (Normal
Academia / Clinician	Rp 3.800.000	Rp 5.000.000	$ 300	$ 400
Corporate	Rp 5.000.000	Rp 6.500.000	$ 400	$ 500
Student	Rp 2.500.000	Rp 3.300.000	$ 200	$ 300



Registration:
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ACTO 2026 Indonesia

D. Renovaldi, M.Sc.
Editorial Office, The ACTO Times
International Ph.D Program in Medicine, Taipei Medical University, Taiwan

IMAGE FROM CANVA.COM

Discover Indonesia through ACTO Annual Meeting 2026 in Jakarta

Welcome to Indonesia

Indonesia, the world's largest archipelago, is a vibrant nation consisting of more than 17,000 islands, rich in cultural diversity, natural beauty, and warm hospitality. Home to hundreds of ethnic groups, languages, and traditions, Indonesia offers visitors a unique blend of heritage, modernity, and unforgettable experiences.
From breathtaking tropical beaches and volcanic landscapes to historical temples and world-renowned cuisine, Indonesia has become one of Asia's most attractive destinations for international travelers, researchers, and professionals.

Jakarta: The Dynamic Capital City

As the capital city of Indonesia, Jakarta is a thriving metropolitan hub that combines modern infrastructure with rich cultural heritage. Jakarta serves as the country's center for business, education, innovation, and international collaboration, making it an ideal host city for the ACTO Annual Meeting 2026.

The city offers excellent international accessibility through Soekarno–Hatta International Airport, with direct connections to many major cities worldwide. Participants can enjoy a wide range of accommodations, transportation systems, shopping centers, and culinary destinations throughout the city.

Beyond the conference venue, Jakarta presents numerous attractions for visitors, including:

- National Monument (Monas), the iconic symbol of Indonesia
- Kota Tua (Old Town Jakarta), showcasing colonial-era architecture and museums
- Beautiful cultural performances and traditional Indonesian arts
- Diverse culinary experiences representing flavors from across the Indonesian archipelago
- Modern lifestyle destinations, shopping malls, and entertainment centers

Experience Indonesian Hospitality and Culture

Attending the ACTO Annual Meeting 2026 is not only an opportunity for scientific exchange and international networking, but also a chance to experience the warmth and hospitality of Indonesia.

Participants will have the opportunity to connect with colleagues from different countries while enjoying Indonesia's rich traditions, multicultural environment, and welcoming atmosphere. Visitors may also extend their stay to explore famous Indonesian destinations such as Bali, Yogyakarta, Lombok, Labuan Bajo, and many other remarkable locations.

Join ACTO Annual Meeting 2026 in Jakarta

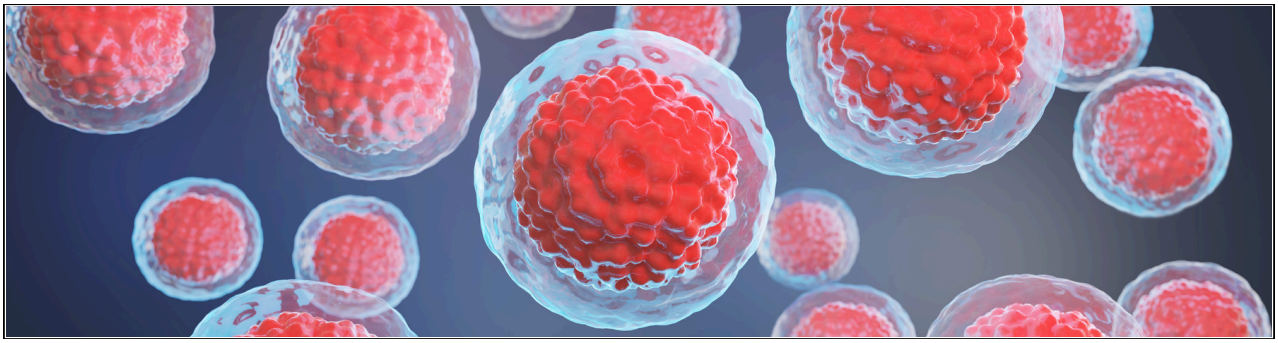
The ACTO Annual Meeting 2026 in Jakarta aims to bring together researchers, clinicians, academics, and professionals from across the world in an inspiring and collaborative environment.

We warmly invite participants from all regions and countries to join this exciting international gathering in Jakarta, Indonesia. Together, let us advance scientific collaboration while experiencing the beauty, culture, and hospitality that Indonesia has to offer.

We look forward to welcoming you to Jakarta in 2026.

Tzu-Yu Chen, Yu-Xiu Lin, &
Thai-Yen Ling, Ph.D.

Graduate Institute of Pharmacology, College of Medicine
National Taiwan University, Taipei, Taiwan



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The 20-year journey of induced pluripotent stem cells (iPSCs) in regenerative medicine

Human induced pluripotent stem cells (iPSCs) are pluripotent stem cells generated through the reprogramming of differentiated somatic cells into an embryonic stem cell-like state via the ectopic expression of defined transcription factors. Due to their unlimited self-renewal capability and multilineage differentiation potential, iPSCs have emerged as one of the most important advances in regenerative medicine and stem cell biology over the past two decades [1]. In 2006, Kazutoshi Takahashi and Shinya Yamanaka first demonstrated that differentiated somatic cells could be reprogrammed into a pluripotent state through the ectopic expression of four transcription factors, OCT4, SOX2, KLF4, and c-MYC.

This pioneering discovery fundamentally transformed stem cell research by providing a novel strategy for generating pluripotent stem cells from adult somatic cells. Following this milestone, human iPSCs were independently established by Yamanaka's group and James Thomson's group in 2007, further accelerating the development of regenerative medicine and personalized therapeutics [2]. Compared with embryonic stem cells (ESCs), iPSCs provide an alternative source of pluripotent stem cells while largely avoiding the ethical concerns associated with embryo destruction. Similar to ESCs, iPSCs possess the ability to differentiate into cell types derived from all three germ layers, including ectoderm, mesoderm, and endoderm.

Due to these unique biological characteristics, iPSCs have become highly promising platforms for disease modeling, drug discovery, toxicological studies, regenerative medicine, and personalized therapy.

Unlike conventional immortalized cell lines, patient-derived iPSCs retain the donor's genetic background, allowing researchers to better investigate disease pathogenesis, genetic heterogeneity, and patient-specific therapeutic responses. Consequently, iPSC-based disease models have been widely applied in studies of neurodegenerative diseases, cardiovascular disorders, metabolic diseases, liver diseases, and inherited genetic disorders [3].

Furthermore, advances in directed differentiation technologies have enabled the efficient generation of various functional cell types from iPSCs, including cardiomyocytes, hepatocytes, neurons, pancreatic β cells, retinal cells, and mesenchymal stromal cells [4]. These developments have substantially expanded the translational potential of iPSC-derived products in tissue engineering, organ regeneration, and cell replacement therapies.

In parallel with advances in differentiation technologies, considerable efforts have also been devoted to improving the safety and clinical applicability of iPSC-based platforms. Early reprogramming strategies primarily relied on integrating viral vectors, which raised concerns regarding insertional mutagenesis and genomic instability. To overcome these limitations, several non-integrating approaches, including episomal plasmids, Sendai virus, synthetic mRNA, microRNAs, and small molecules, have subsequently been developed to enhance reprogramming efficiency and biosafety [5].

Moreover, continuous improvements in large-scale cell manufacturing, quality control systems, and standardized differentiation protocols have further facilitated the clinical translation of iPSC-derived therapeutics.

Importantly, the clinical development of iPSC-based therapies has recently achieved a major milestone. In 2026, Japan granted conditional approval for the world's first iPSC-derived therapeutic products, including iPSC-derived dopaminergic progenitor cells for Parkinson's disease and iPSC-derived cardiomyocyte patches for ischemic heart failure treatment [6].

These landmark approvals highlight the growing feasibility and translational potential of iPSC-based regenerative medicine in clinical settings. Nevertheless, several challenges still remain before the widespread clinical implementation of iPSC-derived therapies can be fully realized, including tumorigenicity, immune rejection, incomplete differentiation, genomic instability, batch-to-batch variability, and large-scale manufacturing limitations. Therefore, further studies are still required to improve the safety, stability, reproducibility, and standardization of iPSC-derived products for future biomedical and clinical applications.

References

1. Qu, X., Liu, T., Song, K., Li, X., & Ge, D. (2012). Induced pluripotent stem cells generated from human adipose-derived stem cells using a non-viral polycistronic plasmid in feeder-free conditions. PloS one, 7(10), e48161. https://doi.org/10.1371/journal.pone.0048161
2. Cerneckis, J., Cai, H., & Shi, Y. (2024). Induced pluripotent stem cells (iPSCs): molecular mechanisms of induction and applications. Signal Transduction and Targeted Therapy, 9(1), 112. https://doi.org/10.1038/s41392-024-01809-0
3. Liu, C., Oikonomopoulos, A., Sayed, N., & Wu, J. C. (2018). Modeling human diseases with induced pluripotent stem cells: from 2D to 3D and beyond. Development, 145(5), dev156166. https://doi.org/10.1242/dev.156166
4. Ye, Z., Zhao, H., & Ye, X. (2025). Application potential of induced pluripotent stem cells in the research and treatment of autoimmune diseases. Molecular Medicine Reports, 32(6), 333. https://doi.org/10.3892/mmr.2025.13698
5. Cieślar-Pobuda, A., Knoflach, V., Ringh, M. V., Stark, J., Likus, W., Siemianowicz, K., ... & Łos, M. J. (2017). Transdifferentiation and reprogramming: Overview of the processes, their similarities and differences. Biochimica et Biophysica Acta (BBA)-Molecular Cell Research, 1864(7), 1359-1369. https://doi.org/10.1016/j.bbamcr.2017.04.017
6. Marshall, A. (2026). World's first two iPSC therapies in Japan. nature biotechnology, 44, 495-502. https://doi.org/10.1038/s41587-026-03105-4

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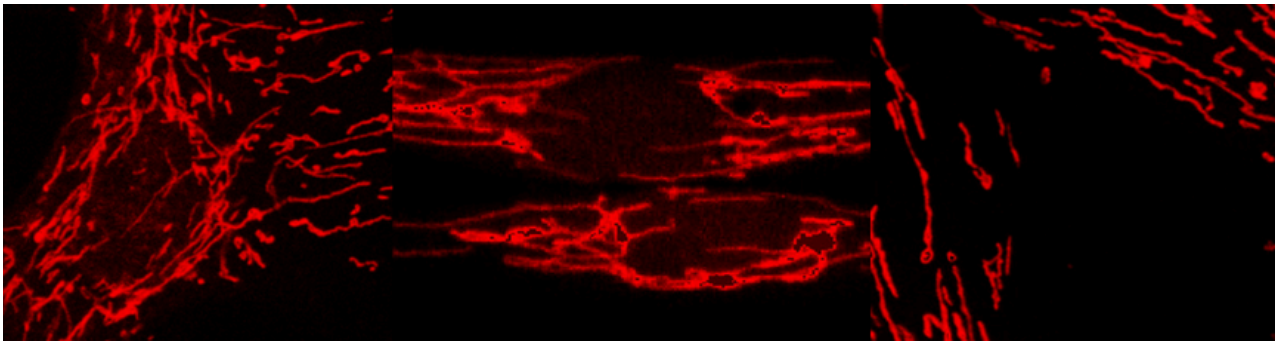

Oxidative stress-driven metabolic reprogramming failure in MERRF patient's iPSC-derived neurons: from neurodevelopmental deficits to novel therapies

Abstract

Background: Myoclonic epilepsy with ragged-red fibers (MERRF) syndrome is one of the severe mitochondrial encephalomyopathies, which are characterized by mitochondrial dysfunction and excess production of the reactive oxygen species (ROS). During neurogenesis, neural progenitor cells must switch metabolism from glycolysis to oxidative phosphorylation (OXPHOS). However, this energy metabolic reprogramming is defective and may result in an overwhelmed oxidative stress barrier that substantially impedes the commitment of induced pluripotent stem cells (iPSCs) of MERRF patients to differentiate into neural cell lineage.

Findings: This article discusses how chronic oxidative stress causes neurodevelopmental failure in the patient-derived iPSC model of the MERRF syndrome. Under sustained ROS insults and Ca^{2+} dyshomeostasis, mitochondrial networks undergo an irreversible structural collapse fueled by dysregulated fission dynamics. In cell models of MERRF patients, dysfunctional mitochondria are accumulated as a result of the stalled and maladaptive mitophagic flux. This unresolved structural and metabolic disorder ultimately precipitates in a severe bioenergetic crisis, leading to profound synaptic energy depletion and defective network connectivity in mature neurons.

Conclusion: The pathogenesis of MERRF syndrome represents an oxidative stress-driven failure of metabolic reprogramming rather than solely an insufficient supply of ATP. Crucially, targeting this oxidative bottleneck via precision interventions, including pharmacological induction of mitophagy to selectively remove dysfunctional mitochondria, mitoTALEN-mediated genome editing, repurposing of old drugs (e.g., sildenafil), and mitochondrial transplantation, offers a transformative blueprint for future treatment of MERRF syndrome and related mitochondrial diseases.

Keywords: Induced pluripotent stem cells (iPSCs), MERRF syndrome, Metabolic reprogramming, Mitophagy, Neuron, Oxidative stress

Introduction

The high energy demand of the central nervous system renders it exceptionally vulnerable to mitochondrial dysfunction.Myoclonic epilepsy with ragged-red fibers (MERRF) syndrome is predominantly caused by the m.8344A>G mutation in the $tRNA^{Lys}$ gene of mitochondrial DNA (mtDNA). This mutation impairs mitochondrial electron transport chain (ETC) function and oxidative metabolism, which leads to defects in neuronal development as well as cardiac and skeletal muscle function [1].

Prof. Yau-Huei Wei, Ph.D. is a renowned mitochondrial biologist and a pioneer in mitochondrial medicine whose research has advanced the understanding of mitochondrial diseases, aging, and mitochondrial genetics. He served as the Founding President of Mackay Medical College and currently directs the Center for Mitochondrial Medicine and Free Radical Research at Changhua Christian Hospital. Professor Wei has published extensively on mitochondrial dysfunction, oxidative stress, and mitophagy, and has played a key role in promoting mitochondrial research across Asia.

Dictated by the mutant mtDNA heteroplasmy, the severity of clinical phenotypes varies drastically according to the ratio of the mutant to wild-type mtDNA within high-energy-demand tissues and organs. However, elucidating this pathogenesis has long been hindered by the inability to obtain viable neural tissues. Fortunately, the reprogramming of patient-derived somatic cells into induced pluripotent stem cells (iPSCs) has effectively bridged this gap, which offers unprecedented opportunities to study the biochemical and molecular biological mechanisms of MERRF syndrome particularly the ROS-induced metabolic reprogramming in neural lineages [2-4].

The differentiation bottleneck: ROS and the stalling of lineage commitment

Neurogenesis is an energetically demanding process that is intimately linked to oxidative metabolism of neural tissue cells. While iPSCs rely heavily on glycolysis to maintain their stemness and minimize oxidative stress [5], they must undergo metabolic reprogramming toward oxidative phosphorylation (OXPHOS) to meet the high ATP demand for mature neurons [6].

Our previous studies established that iPSCs and derived cell lineages from MERRF patients possess an inherently impaired ROS scavenging system [2-4]. When these compromised cells attempt the shift to OXPHOS, the disrupted ETC results in electron leaks and ROS overproduction. During the transition to induced neural stem cells (iNSCs), metabolic demand spikes may lead to accumulation of ROS in MERRF iNSCs [4].

This oxidative storm profoundly alters the signaling pathways required for proper lineage commitment and acts as an active barrier against normal neurogenic programming. To overcome this ROS-induced differentiation barrier, one of our previous studies showed that the forced overexpression of specific transcription factors is required to bypass the metabolic roadblock and facilitate the sensory neural cell lineage specification [3]. This underscores how excess ROS and metabolic failure actively resist, rather than passively hinder, normal neurogenic programming.

The structural insight for metabolic reprogramming and synaptic failure

Recent advancements in mitochondrial biology have fundamentally transformed our conceptual understanding of mitochondrial structural dynamics. This includes the transient formation of a "beads-on-a-string" morphology, a ubiquitous cellular behavior conserved from yeast to mammals since its first observation in 1915.

This phenomenon now recognized as transient mitochondrial 'pearling' and characterized by localized membrane constrictions, is a cellular response to intracellular Ca^{2+} influx [7, 8]. Crucially, these constricted "pearls" serve as the precursor sites for mitochondrial fragmentation; the reversible remodeling compartmentalizes the mitochondria into discrete segments to disaggregate clustered mtDNA-containing nucleoids, ensure their precise spatial distribution, and isolate localized ROS bursts. Rather than a mere acute stress response, this spontaneous biophysical compartmentalization actively modulates cellular programming.

However, in affected tissues of patients with MERRF syndrome and other mitochondrial diseases, this mechanism is pathologically subverted [9]. Due to defective OXPHOS, compromised mitochondria lose their capacity to buffer Ca^{2+} in the cytosol. Coupled with sustained oxidative insults, this chronic stress locks the normally transient pearling process into a permanent pathological state.

Our previous observation of the highly fragmented and punctate mitochondrial networks characteristic of the cultured cells of MERRF patients [2, 11] fundamentally originated from this chronic unresolved pearling. Driven by imbalanced mitochondrial dynamics (Figure 1), downregulated fusion proteins (OPA1, Mfn1/2) fail to counteract overactivated Drp1, which permanently severs constricted mitochondrial segments and prevents the restoration of healthy tubular networks [12].

This Drp1-dependent structural collapse is a shared pathological hallmark of primary mitochondrial diseases. Although initially protective by sequestering mutant mtDNA, this remodeling ultimately drives functional decline because the clearance of compromised mitochondria is profoundly dysregulated, creating a highly conserved bottleneck of stalled mitophagy [13].

Building on the above framework, one of our recent studies demonstrated that MERRF skin fibroblasts and iPSC-derived neurons exhibit a unique ROS-driven susceptibility to PINK1-mediated mitophagy [11]. While chronic oxidative stress drives pronounced PINK1 accumulation, these hyperactive clearance attempts to remove dysfunctional mitochondria ultimately stall. Consequently, the mitochondrial network remains trapped in a persistent punctate state, accumulating dysfunctional "pearls" and failing to restore bioenergetic homeostasis. To cope with this energetic crisis, the cells undergo a profound metabolic reprogramming, actively downregulating compromised OXPHOS pathways and concurrently accelerating glycolytic flux.

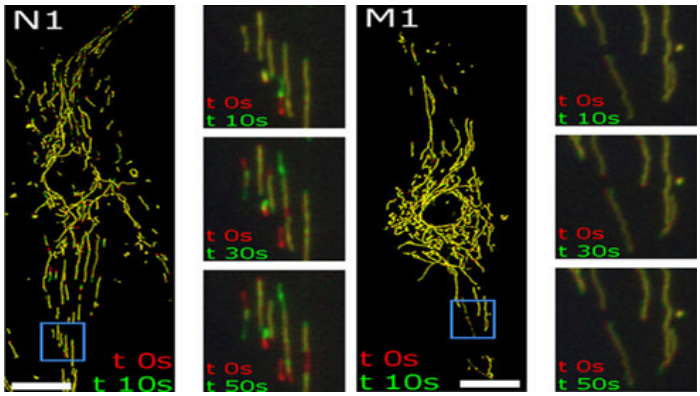

Figure 1. Representative confocal microscopy images of MitoTracker-stained skin fibroblasts demonstrating the strikingly altered mitochondrial distribution in MERRF patient-derived cells compared with controls. Live-cell imaging further reveals markedly reduced mitochondrial motility in MERRF skin fibroblasts, highlighting impaired mitochondrial dynamics associated with the disease phenotype.

Expanding on both this metabolic transition and our recent demonstration that mitochondrial impairment is coupled with synaptic defects in MERRF neurons [4], we find that the legacy of this defective metabolic reprogramming induces a significant delay in early neurite formation and maturation during the terminal stage of neuron differentiation.

Although glycolytic acceleration may sustain early survival, mature cortical neurons strictly demand immense localized ATP for the cycling of synaptic vesicles. Consequently, the unresolved mitochondrial fragmentation and bioenergetic deficit directly translate into impaired Ca^{2+} buffering in the cytosol, compromised synaptogenesis and defective neurotransmission, which can serve as a precise in vitro manifestation of the neurological disorders often observed in patients with MERRF syndrome.

Precision modeling of mtDNA heteroplasmy thresholds

Mitochondrial diseases are uniquely characterized by mtDNA heteroplasmy, the co-existence of wild-type and mutated mtDNA within a single cell. The management of mitochondrial diseases is exceptionally difficult due to the multi-copy nature of the mitochondrial genome. However, recent advancements have shifted the perspective of mitochondrial medicine, demonstrating that complete clearance of mutant mtDNA is not an absolute prerequisite for making a proper therapeutic choice. Instead, therapeutically manipulating mtDNA heteroplasmy to shift the mutant load just below a specific threshold can fundamentally restore OXPHOS capacity and prevent the ROS overproduction. A pivotal challenge in mitochondrial medicine has been to determine whether heteroplasmy shifting is viable in post-mitotic, highly energy-dependent tissues like the brain. Recent breakthrough studies in mitochondrial disease utilizing the culture cells and in vivo mouse models have successfully addressed this issue using mitochondria-targeted nucleases, specifically mitoTALENs [14].

Engineered to selectively recognize and cleave mutated mtDNA (e.g., m.8344A>G), these nucleases induce the rapid degradation of the pathogenic mitochondrial genome [15]. A recent study demonstrated that AAV-mediated delivery of mitoTALENs can effectively reduce the mtDNA mutation (m.5024C>T) load directly in mammalian neurons in vivo [16]. Because these post-mitotic cells lack robust double-strand break repair mechanisms for the mutant mtDNAs, the cleaved mutant mitochondrial genomes are degraded and the remaining wild-type mtDNAs are allowed to repopulate the mitochondrial network.

This targeted heteroplasmy shift in murine neurons successfully rescued respiratory chain defects, suppressed the ROS overproduction and restored the bioenergetic capacity required for synaptic transmission.

Building on this pivotal proof of concept, our patient-specific MERRF iPSC-derived neurons serve as an ideal preclinical platform to translate this precision gene-editing technology into clinical applications.

Clinical paradigms: from personalized diagnostics to breakthrough therapeutics

The integration of these patient iPSC-derived neurons into clinical practice establishes a powerful platform to expedite the development of personalized medicine and regenerative cell therapies.

3D organoid platforms for functional validation

While non-invasive 2D iPSC cultures provide an invaluable and highly scalable platform for dissecting cell-autonomous mechanisms and validating genetic variants, they can be further complemented to capture the broader, multicellular architecture of the human brain.

Building upon recent successes in modeling other mitochondrial encephalomyopathies, 3D iPSC-derived brain organoids are poised to extrapolate these 2D findings into a complex three-dimensional microenvironment, serving as an advanced preclinical platform for the disease modeling of MERRF syndrome. As highlighted in a comprehensive model of Leigh syndrome [17], 3D organoids bridge the evolutionary gap between lower organism models and human pathology.

Furthermore, recent studies of modeling MELAS (mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes) syndrome emphasize that brain organoids are uniquely equipped to recapitulate the complex multicellular metabolic interplay [18]. At the molecular level, these 3D organoid models have revealed that mtDNA mutations trigger hyperactive Notch signaling, which fundamentally alters neural progenitor cell proliferation and disrupts complex cytoarchitecture, giving rise to the pathological features that remain entirely invisible in standard 2D cultures.

A recent study demonstrated that targeted metabolic intervention, supplementation with the NAD^+ precursor nicotinamide riboside (NR), successfully rescued morphological defects of mitochondria and prevented large-scale neuronal loss within the organoid tissue matrix [19]. By integrating targeted interventions (e.g., mitoTALENs or metabolic modulators) into MERRF 3D organoids, researchers can definitively demonstrate how metabolic rescue at the single-neuron level translates into the restoration of the complex cytoarchitecture and network connectivity.

High-throughput screening and the therapeutic repurposing of sildenafil

The urgent need for effective treatments for mitochondrial diseases has driven the adoption of automated high-throughput screening. A recent large-scale iPSC-based screening revealed a novel therapeutic application for sildenafil [20]. Beyond its classical role as a phosphodiesterase type 5 (PDE5) inhibitor, sildenafil significantly alleviates mitochondrial disease phenotypes by attenuating intracellular oxidative stress, boosting mitochondrial biogenesis, and enhancing energy generation. Transitioning this repurposed drug into MERRF-derived neural cell models offers a highly promising strategy to restore redox homeostasis and safeguard synaptic function and structural integrity.

Bioengineered mitochondrial transplantation to overcome translational hurdle via precision organelle tuning

For patients with advanced stages of MERRF syndrome suffering from severe bioenergetic exhaustion, -regenerative medicine offers mitochondrial transplantation. The fundamental premise of mitochondrial transplantation is to physically replace the defective, mutant mtDNA-bearing organelles with healthy exogenous mitochondria to directly reboot cellular bioenergetics. The major bottleneck in translating mitochondrial transplantation into clinical practice has been the difficulty of isolating large amounts of viable, structurally intact, and highly active mitochondria. However, recent bioengineering advancements have introduced organelle-tuning conditions, allowing researchers to fabricate massive yields of functional and energetic mitochondria from donor stem cells [21]. Researchers can use a pre-conditioning environment to maximize the respiratory capacity, optimize membrane potential, and preserve the structural integrity of mitochondria prior to isolation.

The highly active mitochondria increased cellular ATP level and mitochondrial membrane potential in the chondrocytes of osteoarthritis patients. Through advanced bioencapsulation techniques, exogenous mitochondria can be delivered to prevent extracellular degradation, allowing them to be actively internalized by energy-depleted host neurons, and this transplantation strategy has been shown to effectively alleviate functional deficits in both mitochondrial and Parkinson's disease models [22].

Applying this novel bioprocessing technology to MERRF therapy is a highly promising approach to facilitate efficient cellular uptake of isolated mitochondria by energy-depleted host neurons and achieve the restoration of neural function. Once integrated, they hold the potential to reboot cellular bioenergetics, alleviate OXPHOS defects, and facilitate the electrophysiological recovery of compromised neural networks.

Concluding remarks

Moving beyond the classical paradigm of simple ATP deficiency in mitochondrial diseases, current researchers have increasingly focused on profound developmental aberrations in patients with MERRF syndrome driven by metabolic reprogramming failure. We demonstrated that dysfunctional mitochondria may be accumulated as a result of the stalled and maladaptive mitophagic flux caused by oxidative stress. This mitochondrial structural and metabolic abnormality ultimately precipitates in a severe bioenergetic crisis, leading to profound deficiency in synaptic energy and network connectivity in mature neurons.

We showed that iNSCs and mature neurons differentiated from the iPSCs of patients with MERRF syndrome can recapitulate the biochemical defects, oxidative stress and clinical pathology of the disease and may serve as a platform for the high-throughput screening of novel drugs [4,11].

Ultimately, the integration of advanced 3D organoid modeling with precision interventions, ranging from mitoTALEN-mediated mitochondrial genome editing and old drug repurposing to mitochondrial transplantation, has provided a transformative blueprint and tangible hope for the mitigation of the devastating neurological disorders of mitochondrial diseases.

Acknowledgement

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Conflict of interest

The authors declare no competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References:

1. Finsterer J, Zarrouk-Mahjoub S, Shoffner JM. MERRF Classification: Implications for diagnosis and clinical trials. Pediatr Neurol. 2018;80:8–23.
2. Chou SJ, Tseng WL, Chen CT, Lai YF, Chien CS, Chang YL, et al. Impaired ROS scavenging system in human induced pluripotent stem cells generated from patients with MERRF syndrome. Sci Rep. 2016;6:23661.
3. Chen YC, Tsai CL, Wei YH, Wu YT, Hsu WT, Lin HC. ATOH1/RFX1/RFX3 transcription factors facilitate the differentiation and characterisation of inner ear hair cell-like cells from patient-specific induced pluripotent stem cells harbouring A8344G mutation of mitochondrial DNA. Cell Death Dis. 2018;9:437.
4. Wu YT, Tay HY, Yang JT, Liao HH, Ma YS, Wei YH. Mitochondrial impairment and synaptic dysfunction are associated with neurological defects in iPSCs-derived cortical neurons of MERRF patients. J Biomed Sci. 2023;30(1):70.
5. Sinenko SA, Tomilin AN. Metabolic control of induced pluripotency. Front Cell Dev Biol. 2024;11:1328522.
6. Knobloch M, Jessberger S. Metabolism and neurogenesis. Curr Opin Neurobiol. 2017;42:45–52.
7. Landoni JC, Lycas MD, Macuada J, Stepp W, Jaccard R, Obara CJ, et al. Pearling drives mitochondrial DNA nucleoid distribution. Science. 2026; 392(6793):102–9.
8. Sturm G, Hake K, Lefebvre AEYT, Rux CJ, Ivanova D, Millett-Sikking A, et al. The biophysical mechanism of mitochondrial pearling. Mol Biol Cell. 2025;36(11): ar142.
9. Cartes-Saavedra B, Lagos D, Macuada J, Arancibia D, Burté F, Sjöberg-Herrera MK, et al. OPA1 disease-causing mutants have domain-specific effects on mitochondrial ultrastructure and fusion. Proc Natl Acad Sci USA. 2023;120:e2207471120.
10. Zhang L, Trushin S, Christensen TA, Bachmeier BV, Gateno B, Schroeder A, et al. Altered brain energetics induces mitochondrial fission arrest in Alzheimer's disease. Sci Rep. 2016;6:18725.
11. Wu YT, Tay HY, Liao HH, Yang JT, Wei YH. Role of oxidative stress in the susceptibility to mitophagy of the skin fibroblasts and iPSC-derived neurons of patients with MERRF syndrome. Mitochondrion. Published online 19 May 2026:102171. doi: 10.1016/j.mito.2026.102171.
12. Chan, DC. Mitochondrial dynamics and its involvement in disease. Annu Rev Pathol. 2020;15:235–59.
13. Lorenz C, Lesimple P, Bukowiecki R, Zink A, Inak G, Mlody B, et al. Human iPSC-derived neural progenitors are an effective drug discovery model for neurological mtDNA disorders. Cell Stem Cell. 2017;20(5):659–74.e9.
14. Zekonyte U, Bacman SR, Moraes CT. DNA-editing enzymes as potential treatments for heteroplasmic mtDNA diseases. J Intern Med. 2020;287(6):685–97.
15. Hashimoto M, Bacman SR, Peralta S, Falk MJ, Chomyn A, Chan DC, et al. MitoTALEN: A general approach to reduce mutant mtDNA loads and restore oxidative phosphorylation function in mitochondrial diseases. Mol Ther. 2015;23(10):1592–9.
16. Bacman SR, Barrera-Paez JD, Pinto M, Van Booven D, Stewart JB, Griswold AJ, et al. mitoTALEN reduces the mutant mtDNA load in neurons. Mol Ther Nucleic Acids. 2024;35(1):102132.
17. Henke MT, Prigione A, Schuelke M. Disease models of Leigh syndrome: From yeast to organoids. J Inherit Metab Dis. 2024;47(6):1292–321.
18. Winanto, Khong ZJ, Soh BS, Fan Y, Ng SY. Organoid cultures of MELAS neural cells reveal hyperactive Notch signaling that impacts neurodevelopment. Cell Death Dis. 2020;11(3):182.
19. Hong Y, Zhang Z, Yangzom T, Chen A, Lundberg BC, Fang EF, et al. The NAD^+ precursor nicotinamide riboside rescues mitochondrial defects and neuronal loss in iPSC derived cortical organoid of Alpers' disease. Int J Biol Sci. 2024;20(4):1194–217.
20. Zink A, Dai DF, Wittich A, Henke MT, Pedrotti G, Heiduschka S, et al. Pluripotent stem-cell-based screening uncovers sildenafil as a mitochondrial disease therapy. Cell. 2026;189(6):1656–79.e42.
21. Chen X, Zhou Y, Yao W, Gao C, Sha Z, Yi J, et al. Organelle-tuning condition robustly fabricates energetic mitochondria for cartilage regeneration. Bone Res. 2025;13(1):37.
22. Du S, Long Q, Zhou Y, Fu J, Wu H, Yang L, et al. Transplantation of encapsulated mitochondria alleviates dysfunction in mitochondrial and Parkinson's disease models. Cell. 2026;189(10):2821–33.e23.

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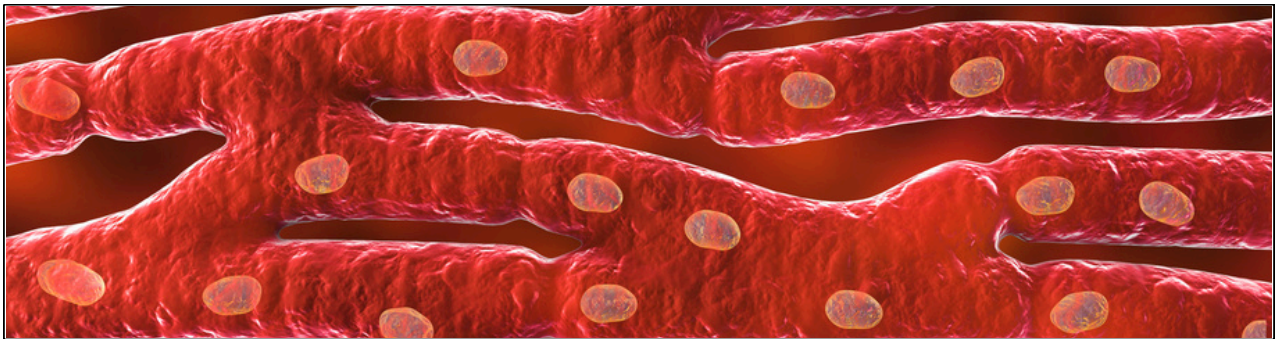

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iPSC-derived cardiac cell sheets for heart regeneration: Progress toward clinical translation

Abstract

Background: Heart disease remains the second leading cause of death worldwide. Currently, heart transplantation is considered the only definitive treatment for severe heart failure due to the poor heart regeneration after injury. Adult cardiomyocytes lose their proliferative ability after birth, leading to insufficient compensation for the infarcted myocardium. Therefore, to complete heart regeneration continues to present a major challenge in cardiac therapy.

Findings: Following the discovery of induced pluripotent stem cell (iPSC) technology, iPSC-derived cardiomyocytes (iPSC-CMs) have been generally considered as a promising cell source for cardiac regeneration. However, direct cell injection is associated with poor cell survival and limited engraftment efficiency. To overcome these limitations, cell sheet technology was developed and subsequently combined with iPSC-CMs to provide direct contractile contribution and partial myocardial replacement. ReHeart/RiHeart, which integrates cell sheet engineering with iPSC technology, has become the first conditionally approved iPSC-derived cardiac regenerative therapy worldwide. Nevertheless, to achieve true long-term remuscularization of the injured myocardium remains a major challenge.

Conclusion: ReHeart/RiHeart represents a major step forward in translational cardiac regenerative medicine and provides an important foundation for the future development of clinically effective heart regenerative therapies.

Keywords: iPSC, ReHeart/RiHeart, Cell sheet, Heart regeneration

Introduction

Heart regeneration has long been considered impossible because cardiac myocytes lose their proliferative capacity after cardiac injury. To date, heart transplantation remains the gold-standard therapy for end-stage heart failure; however, the severe shortage of donor hearts continues to limit its clinical application[1]. Recent advances in induced pluripotent stem cell

(iPSC) technology have provided new hope for heart regeneration[1,2]. Notably, the first conditionally approved clinical application utilizes iPSC-derived cardiomyocyte (iPSC-CM) sheets, known as ReHeart/RiHeart, developed by Osaka University in collaboration with Cuorips[3,4].

This achievement represents a major step forward in the field of cardiac regeneration. In this review, I first introduce the major milestones in the development of cell sheet technology for cardiac repair after injury and further summarize the different cell types that have been applied to generate cardiac cell sheets.

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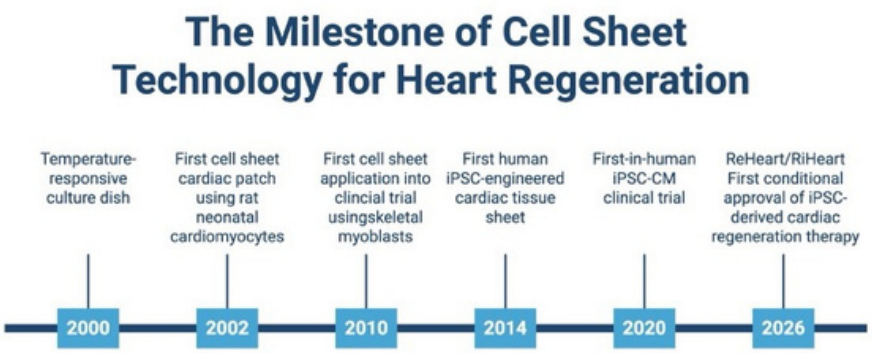

Figure 1. The milestone of cell sheet technology for heart regeneration. Created in BioRender. Cheng, Y. (2026) https://BioRender.com/1yhi233.

Finally, ReHeart/RiHeart is highlighted as a representative example to illustrate both the significant advances achieved and the remaining challenges that still need to be overcome in clinical cardiac regeneration.

The history of cell sheet technology for heart regeneration

Cell sheet is a tissue engineering technique that utilizes a contiguous layer of cells with preserved extracellular matrix (ECM)[5]. It can be harvested and transplanted without enzyme digestion. The development of cell sheet technology can be traced back to the early 2000s, when researchers discovered that extremely low cell retention after direct cell injection[6]. Dr. Teruo Okano's group developed a temperature-responsive culture dish to generate intact cell sheets[7]. When the temperature is reduced to 20 ℃, the culture surface becomes hydrophilic to enable the cells spontaneously detach as an intact sheet rather than as dissociated single cells.

Through this harvesting method, the ECM, cell-cell junction, and surface proteins are largely preserved to generate tissue-like cell sheets. In 2002, Drs. Shimizu and Okano group published the first cardiac cell sheet generated from primary neonatal rat CMs cultured on temperature-responsive culture dishes[8]. Importantly, these layered cell sheets exhibited synchronous contraction and electrical coupling between layers[8]. However, the first clinical application of cell sheet technology in cardiac repair utilized skeletal myoblast sheets, pioneered by Dr. Yoshiki Sawa's group in Japan in 2010[9,10].

Autologous skeletal myoblast sheet transplantation demonstrated improved cardiac function and symptoms in patients with severe heart failure, including reduced hospitalization rates.

Nevertheless, the limited electrical integration and non-CM nature of skeletal myoblasts remained major concerns. To overcome these limitations, mesenchymal stem cell (MSC)-based and iPSC-derived cardiac cell sheets were subsequently developed[11,12]. In 2012, human iPSC-engineered cardiac tissue sheets were first generated and transplanted into infarcted rat hearts, resulting in improved cardiac function[12].

After that, the clinical-grade production and translational application of cardiac patches rapidly advanced, ultimately leading to the first conditional approval of an iPSC-derived cardiac regeneration therapy, ReHeart/RiHeart[3,4]. Figure 1 summarizes the major milestones in the development of cell sheet technology for cardiac regeneration.

Cell sources to generate cell sheets for heart regeneration

The first cell source used for generating cell sheets for heart regeneration was skeletal myoblasts. Autologous transplantation, ischemic resistance, and high proliferative capacity made skeletal myoblasts an attractive candidate for early cardiac cell sheet studies[10,13] (Figure 2). Initial studies demonstrated that skeletal myoblast-derived cell sheets improved heart function after myocardial infarction (MI) by enhancing systolic function, reducing left ventricular wall thickness, and promoting neovascularization[10,13].

Furthermore, combining the omentum with skeletal myoblast-derived cell sheets significantly enhanced cell engraftment within the infarct area of the injured hearts[14,15]. Even more encouragingly, obvious functional recovery was observed in patients suffering from dilated or ischemic cardiomyopathy[14,15]. However, the limited CM differentiation potential and poor electrical integration with resident CMs restricted the clinical application of skeletal myoblast-derived cell sheets for cardiac regeneration[13,16].

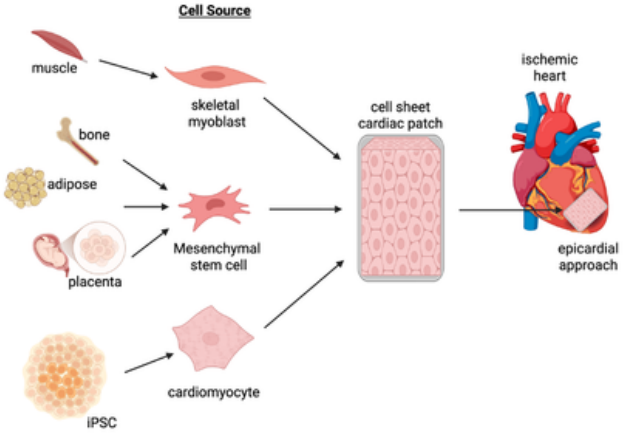

Figure 2. Various cell source to generate cell sheet cardiac patch for heart regeneration. Created in BioRender. Cheng, Y. (2026) https://BioRender.com/zuyt9z9.

Due to their ease of isolation and autologous availability, MSC subsequently emerged as another promising cell source for cardiac cell sheet generation[11]. MSCs can be isolated from bone marrow, adipose tissue, and placenta, and their therapeutic benefits are largely attributed to paracrine signaling that supports vascularization and cardiac protection after injury[17]. MSC-derived cell sheets were reported to attenuate adverse cardiac remodeling and reduce fibrosis in mouse and rat MI models[11,18]. However, because MSCs exhibited limited capacity to differentiate into functional CMs[19,20], their practical application in true myocardial regeneration remains constrained.

Through the discovery of iPSCs by Dr. Shinya Yamanaka in 2006[2], a promising cell source for cardiac regeneration became available. Due to their pluripotency and self-renewal capacity, iPSCs exhibit strong potential to differentiate into CMs and therefore emerged as an ideal cell source for generating cardiac cell sheets[21].

In 2012, human iPSC-CM sheets were successfully generated with high differentiation efficiency by Drs. Masumoto and Sawa, and colleagues at Osaka University[12]. Importantly, transplantation of these iPSC-CM sheets improved cardiac function by enhancing neovascularization, attenuating LV remodeling, and promoting cardiomyogenesis in rat MI models[12]. Subsequently, in 2013, human iPSC-CM sheets combined with an omental flap were further shown to enhance graft survival and engraftment within infarcted regions, which resulted in additional improvement of cardiac function in porcine MI models[22].

Building upon these findings, a clinical-grade allogeneic cardiac patch platform, ReHeart/RiHeart, was developed by Osaka University in collaboration with Cuorips[3,4]. This platform successfully advanced to clinical trials and ultimately became the first conditional approved iPSC-derived cardiac regenerative therapy worldwide.

Advantages and limitation of iPSC-derived cardiac patch ReHeart/RiHeart

Unlike direct cell injection, cell sheets preserve cell-cell junctions and surface proteins to enhance cell survival and function[5]. These properties facilitate CM maturation and electrical coupling with host tissue, which may greatly reduce the risk of arrhythmia[6]. In addition, epicardial patch transplantation provides a less invasive and less damaging alternative to direct intramyocardial injection[22,23]. The sheet-based structure also improves cell survival and engraftment and can be layered to generate thicker tissues constructs for enhanced cell retention[8,24]. Moreover, the use of iPSC-CMs offers the potential for direct contractile contribution and partial myocardial replacement[25,26]. Collectively, these advantages enabled ReHeart/RiHeart to successfully advance through clinical trials and become the first conditional approved iPSC-derived cardiac regenerative therapy in Japan[3,4] (Table 1).

Nevertheless, several important limitations remain. Increased tissue thickness in multilayered cells sheets can lead to insufficient vascularization and reduced long-term cell survival[24,27]. Although sheet transplantation improves engraftment, the maturation of iPSC-CMs remains incomplete, resulting in immature electromechanical integration with host CMs[28,29]. Most importantly, definitive evidence demonstrating true long-term remuscularization of the injured myocardium is still lacking[1,30].

Advantages	Limitations
Increase cell survival and engraftment	Long-term survival
Attenuate arrythmia risk	Mature electromechnical integration with remnant cardiomyocyte
Layer to form thick tissue	Incomplete vascularization
	Remuscularization

Table 1. The advantages and limitations of ReHeart/RiHeart for cardiac regeneration. Created in BioRender. Cheng, Y. (2026) https://BioRender.com/2ixgd8m.

Overall, although significant challenges remain, the development of cardiac cell sheet technology and ReHeart/RiHeart represents a major milestone in translational cardiac regenerative medicine and provides a promising foundation for future strategies aimed at achieving true myocardial regeneration and functional heart repair[4,31].

Conclusion

In this review, I summarized the historical development of cell sheet technology for cardiac regeneration and highlighted the major milestones that have driven progress in the field. The various cell sources were discussed to be used for generating cardiac cell sheets and the combination of iPSC technology with cell sheet engineering was presented as a promising strategy for heart regeneration. In addition, the major advantages and therapeutic potential of the current ReHeart/RiHeart platform were outlined, while the remaining limitations and challenges were addressed to be overcome to achieve true remuscularization and functional heart regeneration after injury. In conclusion, ReHeart/RiHeart represents a major step forward in translational cardiac regenerative medicine and provides an important foundation for the future development of clinically effective heart regeneration therapies.

Acknowledgement

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Conflict of interest

There is no conflict of interest.

References:

1. Eschenhagen T, Bolli R, Braun T, et al. Cardiomyocyte regeneration: a consensus statement. Nat Rev Cardial. 20117;14(9):563-579.
2. Takahashi K, Yamanaka S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Cell. 2006;126(4):663-676.
3. Miyagawa S, Sawa Y. Building a new strategy for cardiac regeneration therapy using induced pluripotent stem cells. J Cardiol. 2018;72(6):445-448.
4. Miyagawa S, Domae K, Yoshikawa Y, et al. Transplantation of human induced pluripotent stem cell-derived cardiomyocyte patches for ischemic cardiomyopathy. JACC Case Rep. 2022;4(7):396-400.
5. Yang J, Yamato M, Nishida K, et al. Cell delivery in regenerative medicine: the cell sheet engineering approach. J Control Release. 2006;116(2):193-203.
6. Zhang M, Methot D, Poppa V, Fujio Y, Walsh K, Murry CE. Cardiomyocyte grafting for cardiac repair: graft cell death and anti-death strategies. J Mol Cell Cardiol. 2001;33(5):907-921.
7. Okano T, Yamada N, Sakai H, Sakurai Y. A novel recovery system for cultured cells using plasma-treated polystyrene dishes grafted with poly(N-isopropylacrylamide). J Biomed Mater Res. 1993;27(10):1243-1251.
8. Shimizu T, Yamato M, Kikuchi A, Okano T. Cell sheet engineering for myocardial tissue reconstruction. Biomaterials.2003;24(13):2309-2316.
9. Sawa Y, Miyagawa S, Sakaguchi T, et al. Tissue engineered myoblast sheets improved cardiac function sufficiently to discontinue LVAS in a patient with DCM: report of a case. Surg Today. 2012;42(2):181-184.
10. Memon IA, Sawa Y, Fukushima N, et al. Repair of impaired myocardium by means of implantation of engineered autologous myoblast sheets. J Thorac Cardiovasc Surg. 2005;130(5):1333-1341.
11. Miyahara Y, Nagaya N, Kataoka M, et al. Monolayered mesenchymal stem cells repair scarred myocardium after myocardial infarction. Nat Med. 2006;12(4):459-465.
12. Masumoto H, Matsuo T, Yamamizu K, et al. Pluripotent stem cell-engineered cell sheets reestablish cardiac function in a rat myocardial infarction model. Circ Res. 2012;111(3):e8-e14.
13. Menasché P. Skeletal myoblasts for cardiac repair. Expert Rev Cardiovasc Ther. 2005;3(1):21-27.
14. Sekiya N, Matsumiya G, Miyagawa S, et al. Layered implantation of myoblast sheets attenuates adverse cardiac remodeling of the infarcted heart. J Thorac Cardiovasc Surg. 2009;138(4):985-993.
15. Shudo Y, Miyagawa S, Fukushima S, et al. Novel regenerative therapy using cell sheet with omentopexy for damaged myocardium. J Thorac Cardiovasc Surg. 2013;145(5):1188-1196.
16. Leobon B, Garcin I, Menasché P, et al. Myoblasts transplanted into rat infarcted myocardium are functionally isolated from their host. Proc Natl Acad Sci U S A. 2003;100(13):7808-7811.
17. Gnecchi M, He H, Liang OD, et al. Paracrine action accounts for marked protection of ischemic heart by Akt-modified mesenchymal stem cells. Nat Med. 2005;11(4):367-368.
18. Hamdi H, Planat-Bénard V, Bel A, et al. Epicardial adipose stem cell sheets result in greater post-infarction survival than intramyocardial injections. Cardiovasc Res. 2011;91(3):483-491.
19. Murry CE, Soonpaa MH, Reinecke H, et al. Haematopoietic stem cells do not transdifferentiate into cardiac myocytes in myocardial infarcts. Nature. 2004;428(6983):664-668.
20. Gnecchi M, Zhang Z, Ni A, Dzau VJ. Paracrine mechanisms in adult stem cell signaling and therapy. Circ Res.2008;103(11):1204-1219.
21. Burridge PW, Keller G, Gold JD, Wu JC. Production of de novo cardiomyocytes: human pluripotent stem cell differentiation and direct reprogramming. Cell Stem Cell. 2012;10(1):16-28.
22. Kawamura M, Miyagawa S, Fukushima S, et al. Enhanced survival of transplanted human induced pluripotent stem cell-derived cardiomyocytes by the combination of cell sheets with the pedicled omentum in a porcine heart. Circulation. 2013;128(11 Suppl 1):S87-S94.
23. Haraguchi Y, Shimizu T, Yamato M, Okano T. Regenerative therapies using cell sheet-based tissue engineering for cardiac disease. Cardiol Res Pract. 2011:845170.
24. Shimizu T, Yamato M, Isoi Y, et al. Fabrication of pulsatile cardiac tissue grafts using a novel 3-dimensional cell sheet manipulation technique and temperature-responsive cell culture surfaces. Circ Res. 2002;90(3):e40.
25. Chong JJH, Yang X, Don CW, et al. Human embryonic-stem-cell-derived cardiomyocytes regenerate non-human primate hearts. Nature. 2014;510(7504):273-277.
26. Laflamme MA, Murry CE. Heart regeneration. Nature. 2011;473(7347):326-335.
27. Sekine H, Shimizu T, Yang J, Kobayashi E, Okano T. Pulsatile myocardial tubes fabricated with cell sheet engineering. Circulation. 2006;114(1 Suppl):I87-I93.
28. Yang X, Pabon L, Murry CE. Engineering adolescence: maturation of human pluripotent stem cell-derived cardiomyocytes. Circ Res. 2014;114(3):511-523.
29. Lundy SD, Zhu WZ, Regnier M, Laflamme MA. Structural and functional maturation of cardiomyocytes derived from human pluripotent stem cells. Stem Cells Dev. 2013;22(14):1991-2002.
30. Laflamme MA, Murry CE. Heart regeneration. Nature. 2011;473(7347):326-335.\
31. Matsuura K, Shimizu T. Cardiac cell sheet engineering for regenerative medicine and tissue modeling. Prog Mol Biol Transl Sci. 2023;197:127-154.

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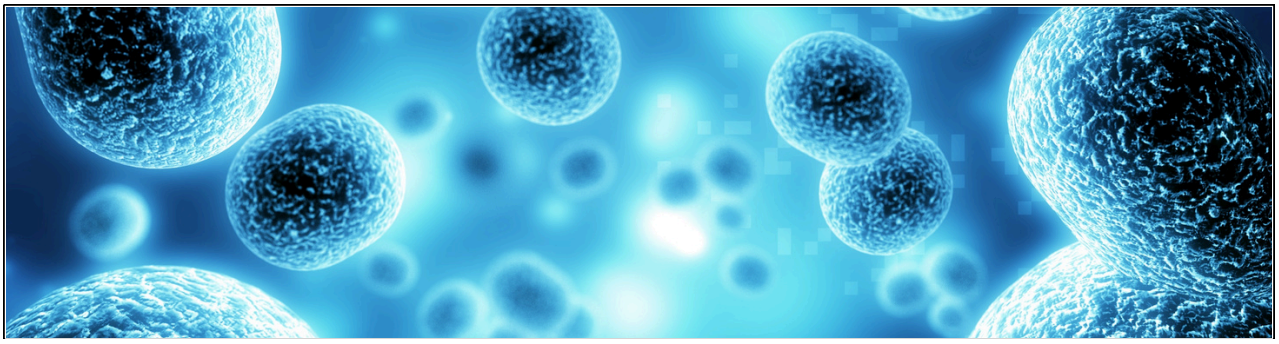


IMAGE FROM CANVA.COM

Therapeutic potentials of induced pluripotent and mesenchymal stem cell-derived exosomes

Introduction

Mesenchymal stem cells (MSCs) have long been at the forefront of regenerative medicine due to their multipotency and immunomodulatory properties[1, 2]. However, direct stem cell transplantation is often limited by challenges such as donor-to-donor heterogeneity, diminished viability post-transplantation, potential immunogenicity, and the risk of teratoma formation[1, 2]. To circumvent these hurdles, induced pluripotent stem cells (iPSCs) and iPSC-derived mesenchymal stem cells (iMSCs) have emerged as powerful alternatives, providing a highly scalable and patient-specific cellular source. Concurrently, it has become evident that the regenerative benefits of stem cells are largely mediated by paracrine factors rather than direct cellular engraftment[2, 3]. Chief among these paracrine effectors are exosomes—nanoscale extracellular vesicles that inherit the therapeutic properties of their parental cells but offer a safer, cell-free therapeutic modality without the risk of tumorigenesis or severe immune rejection[1, 2].

Biogenesis, Composition, and Mechanisms of Action

Exosomes, typically ranging from 30 to 180 nm in diameter, are formed through the endosomal pathway, wherein multivesicular bodies (MVBs) fuse with the plasma membrane to release vesicles into the extracellular space[2, 4]. The lipid bilayer of exosomes is enriched with cholesterol and sphingomyelin, which protects their internal cargo from enzymatic degradation.

Exosomes carry a complex and highly specific payload consisting of lipids, proteins (such as tetraspanins CD9, CD63, and CD81, and heat shock proteins like HSP70), and nucleic acids, most notably microRNAs (miRNAs)[2, 4].

Upon release, exosomes communicate with target cells through endocytosis, direct membrane fusion, or receptor-ligand interactions[1, 2, 4]. By transferring their bioactive cargo, stem cell-derived exosomes (SC-Exos) can alter gene expression in recipient cells, activating critical intracellular signaling cascades—such as the PI3K/Akt, Wnt/β-catenin, and ERK1/2 pathways—which drive cell survival, proliferation, and tissue regeneration.

Cardiovascular Diseases and Ischemic Repair

Cardiovascular diseases (CVDs) remain the leading cause of global mortality[3]. While engineered cardiac tissues and iPSC-derived cardiomyocytes offer potential for heart remuscularization, these cellular approaches are sometimes complicated by low engraftment rates and the induction of ventricular tachyarrhythmias. Consequently, exosome-based therapies are gaining traction as a safer alternative. Exosomes derived from iPSCs, iMSCs, and iPSC-derived cardiomyocytes have demonstrated profound cardioprotective effects following myocardial infarction (MI). By delivering specific cardioprotective miRNAs, such as miR-21 and miR-210, these exosomes reduce cardiomyocyte apoptosis, attenuate oxidative stress, and decrease fibrotic remodeling[4].

Beyond the heart, exosome therapy significantly enhances angiogenesis in peripheral ischemic conditions. For instance, in models of hindlimb ischemia, exosomes from iPSC-derived endothelial cells heavily enriched with miR-199b-5p were shown to promote microvessel density and blood perfusion by upregulating the vascular endothelial growth factor receptor 2 (VEGFR2) pathway[2, 4].

Orthopedics and Musculoskeletal Regeneration

In the musculoskeletal system, iMSC-derived exosomes and SC-Exos facilitate robust bone and cartilage repair. For bone defect therapies, combining exosomes with tricalcium phosphate (β-TCP) scaffolds significantly accelerates osteogenesis by activating the PI3K/Akt signaling pathway in endogenous bone marrow MSCs[2, 4]. Furthermore, in conditions like glucocorticoid-induced osteonecrosis of the femoral head, iMSC-derived exosomes prevent bone loss and promote local vascularization[1, 2, 4].

Exosomes also present a promising disease-modifying strategy for osteoarthritis (OA). Interestingly, exosomes derived from iMSCs have been shown to outperform those from adult synovial membrane MSCs, exerting superior effects in stimulating chondrocyte proliferation and migration while inhibiting matrix-degrading enzymes and cellular apoptosis[1, 2].

Neurology and Neurodegeneration

The therapeutic application of exosomes in the central nervous system spans both acute injuries and chronic neurodegenerative diseases. In ischemic stroke and traumatic brain injury (TBI), exosome administration reduces infarct volume, suppresses neuroinflammation, and promotes neurogenesis[1]. iPSC-derived neural stem cell exosomes (iNSC-Exos) have also shown remarkable ability in restoring motor function and improving structural outcomes post-stroke[4].

In Alzheimer's disease (AD), exosome therapies have demonstrated the ability to clear amyloid-beta plaques and rescue synaptic dysfunction[1]. However, the role of exosomes in neurodegeneration is notably dual-faceted. While healthy SC-Exos are neuroprotective, exosomes secreted by diseased neurons can act as pathogenic mediators. For example, exosomes derived from iPSC neurons bearing mutant Tau proteins have been shown to propagate Tau pathology and induce neurodegeneration in healthy neural tissues[4].

Plastic Surgery and Cutaneous Wound Healing

For cutaneous wounds, particularly recalcitrant diabetic ulcers, iMSC- and iPSC-derived exosomes accelerate healing by driving the transition from the inflammatory phase to the proliferative and remodeling phases[1, 4]. Exosome treatment upregulates the secretion of type I and III collagen and elastin, accelerating re-epithelialization and reducing overall scar formation[2, 4]. In vitro studies confirm that iMSC-exosomes enhance the migration and cell cycle progression of human dermal fibroblasts and keratinocytes (HaCaT cells) more effectively than adult MSC-exosomes, primarily via the ERK1/2 and Akt/HIF-1α pathways.

Immunomodulation: The Core of Exosome-Mediated Repair

A unifying mechanism underlying the therapeutic success of SC-Exos across these diverse tissues is their profound impact on the innate immune system. Tissue regeneration is heavily dependent on the fine-tuning of local inflammation, specifically the polarization of macrophages[3]. Following acute injury, pro-inflammatory M1 macrophages clear necrotic debris but can exacerbate tissue damage if overactive. Exosomes facilitate the critical phenotypic switch from M1 to anti-inflammatory M2 macrophages, which secrete IL-10 and TGF-β to promote wound healing, neovascularization, and organized matrix deposition. Transcriptomic studies indicate that exosomal miRNAs, such as miR-181b, are key mediators of this macrophage polarization[3].

Challenges and Future Perspectives

Despite these highly promising developments, the clinical translation of iPSC- and iMSC-derived exosomes faces several challenges. Primary among these is the low yield of exosome production in conventional cell cultures, coupled with the lack of standardized protocols for isolation, characterization, and batch-to-batch consistency[1, 2]. To address production bottlenecks, researchers are exploring exosome manipulation techniques, such as the overexpression of the ALIX protein in iPSCs, which significantly enhances exosome yield and protective protein content[4]. Another innovative solution is the generation of cell-engineered nanovesicles (CENVs) created by the serial extrusion of iPSCs, which mimic exosomal properties but allow for massive scalability[4].

Finally, while exosomes themselves are largely non-immunogenic, generating universal, "off-the-shelf" iPSC lines for both cell and exosome therapies remains a priority. Recent advances in CRISPR/Cas9 gene editing to knock out Human Leukocyte Antigens (HLA-I and HLA-II) are paving the way for hypoimmunogenic universal cells that evade immune rejection[3].

Conclusion

Induced pluripotent and mesenchymal stem cell-derived exosomes represent a paradigm shift in regenerative medicine. By harnessing the potent, multi-targeted paracrine effects of stem cells while avoiding the pitfalls of direct cell transplantation, iPSC- and iMSC-derived exosomes offer a highly versatile, cell-free platform to treat cardiovascular, musculoskeletal, neurological, and cutaneous diseases. Advancements in exosome engineering and scalable manufacturing will be crucial for realizing their full clinical potential.

References

1. Tan, F., et al., Clinical applications of stem cell-derived exosomes. Signal Transduction and Targeted Therapy, 2024. 9(1): p. 17.
2. Aldoghachi, A.F., et al., Current developments and therapeutic potentials of exosomes from induced pluripotent stem cells-derived mesenchymal stem cells. J Chin Med Assoc, 2023. 86(4): p. 356-365.
3. Germena, G. and R. Hinkel, iPSCs and Exosomes: Partners in Crime Fighting Cardiovascular Diseases. Journal of Personalized Medicine, 2021. 11(6): p. 529.
4. Wang, A.Y.L., Human Induced Pluripotent Stem Cell-Derived Exosomes as a New Therapeutic Strategy for Various Diseases. International Journal of Molecular Sciences, 2021. 22(4): p. 1769.

Wannhsin Chen, Ph.D
President of Taiwan Association for Cellular Therapy (TACT)

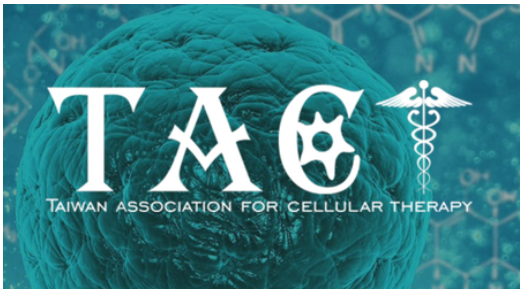
IMAGE FROM CANVA.COM

Taiwan Association for Cellular Therapy (TACT)

The Taiwan Association for Cellular Therapy (TACT; https://www.celltherapy.org.tw/) was founded in 2014 with the mission of promoting cross-sector collaboration among industry, government, academia, medical institutions, and research communities in the field of cellular therapy. The Association is dedicated to advancing cell therapy science, technology, education, clinical translation, industrial development, and the establishment and refinement of relevant regulatory frameworks.

Under the leadership of its Founding Honorary President, Professor Yao-Chang Chen, TACT established important communication channels and a collaborative platform across the cellular therapy community. It also played an active role in regulatory development, laying a strong foundation for its position in Taiwan's field of cell therapy. Through its close and long-standing partnership with the Asian Cellular Therapy Organization (ACTO), TACT has facilitated substantive Taiwan–Japan exchanges in cellular therapy across industry, government, and academia. With the continued efforts of former presidents Professor Thai-Yen Ling, Professor Deng-Chyang Wu, and Professor Chia-Ning Shen, the Association's activities and influence have steadily expanded.

Under the leadership of the current president, Dr. Wannhsin Chen, TACT has further strengthened collaboration with organizations in Malaysia and with the Asia Partnership Conference of Regenerative Medicine (APACRM) in Japan.



Taiwan Association for Cellular Therapy (TACT)

Dr. Wannhsin Chen
President of TACT

These efforts aim to support the development of cellular therapy science, clinical application, and industry in Taiwan, while connecting Taiwan with Asia and the broader international community. The establishment of TACT can be traced back to 2013, when Professor Yao-Chang Chen undertook the responsibility of organizing the ACTO Annual Meeting in Taiwan. Following the successful conclusion of that meeting, Professor Chen was encouraged by ACTO's operating model and by its Chairperson, Dr. Akihiro Shimosaka, to establish a dedicated organization in Taiwan.

Figure 1. Documentation of some TACT activities

In June 2014, he invited 33 experts from industry, government, academia, medical, and research institutions to serve as founding members and preparatory committee members. After extensive discussions on the Association's structure, mission, implementation framework, and articles of association, the inaugural assembly and first general meeting were held on December 5, 2014. At the time of its founding, the Association was named the Taiwan Association for the Promotion of Cellular Therapy. In 2018, as the field of cell therapy in Taiwan began to take shape and gain momentum, it was renamed the Taiwan Association for Cellular Therapy.

In its early years, TACT focused on building a platform for professional exchange through symposia, forums, and annual meetings. This period coincided with the Ministry of Health and Welfare's efforts to establish regulatory frameworks for cellular therapy. TACT supported exchanges and site visits to Japan, while several of its board directors and supervisors served as members of the Regenerative Medicine Advisory Committee. These members actively contributed to the formulation and revision of related regulations, as well as the review of clinical cell therapy applications.

In 2015, the Formosa Fun Coast dust explosion became the most severe mass burn injury incident in Taiwan's history, resulting in 15 deaths and 484 burn injuries, with an average total burn surface area of 41% among the injured. With the approval and coordination of the Ministry of Health and Welfare, Japan Tissue Engineering Co., Ltd. (J-TEC) provided its autologous cultured epidermis product, JACE, together with technical support. Through the efforts of TACT board member Dr. Mei-Yue Huang, Mariavon Stem Cell Medical Biotechnology Co., Ltd. served as the local coordinating partner in Taiwan.

Ultimately, five patients received treatment and achieved favorable recovery outcomes. This case represented a successful example of Taiwan–Japan collaboration in regenerative medicine, jointly enabled by industry and government, with TACT playing an important coordinating role.

In 2018, Taiwan implemented the Regulation Governing the Application of Specific Medical Examination Technique and Medical Device, commonly known as the "Special Regulation" for cell therapy. Before its implementation, exchanges and site visits in Japan provided valuable insights from international experience. TACT also actively participated in the development of related regulations. To help the general public gain an accurate understanding of cell therapy, TACT worked with the Taiwan Research-based Biopharmaceutical Manufacturers Association (TRPMA) to undertake the Ministry of Health and Welfare's Cell Therapy Technology Information Portal project.

TRPMA was responsible for system architecture, while TACT board members contributed public-oriented educational articles introducing key concepts in the field. The portal continues to provide updated information on cell therapy and on institutions conducting approved treatments. It also includes proposal registration and outcome reporting functions for medical institutions implementing therapies under the Special Regulation, thereby supporting regulatory oversight.

For physicians performing cell therapy under the Special Regulation, TACT collaborated with the Taiwan Society for Stem Cell Research (TSSCR) and the Taiwan Society for Regenerative Medicine to design and launch physician training courses.

These courses were approved by the Ministry of Health and Welfare and provided certification for physicians interested in gaining a comprehensive understanding of related technologies, clinical implementation, risk considerations, and the global development of cell therapy products.

Following the implementation of Taiwan's Dual Acts on Regenerative Medicine in 2026—the Regenerative Medicine Act and the Regenerative Medicinal Products Act—TACT further developed both basic and advanced training programs, expanding the target audience to include physicians, nurses, pharmacists, and biotechnology professionals.

TACT holds an annual meeting each year to promote balanced development between northern and southern Taiwan, the meeting is generally held alternately in the north and south. To support both domestic advancement and international engagement, the Association also alternates between meetings primarily featuring domestic speakers and international conferences.

In recent years, TACT has been invited to represent Taiwan at the ACTO Annual Meeting in Singapore, meetings of the Malaysian Society for Cell Therapy, and the Asia Partnership Conference of Regenerative Medicine in Japan. Through these platforms, TACT has introduced Taiwan's regulatory framework, industry landscape, and progress in cellular therapy and regenerative medicine.

By strengthening multifaceted international collaboration with academic, clinical, industrial, and regulatory partners across Asia and beyond, the Association seeks to bring Taiwan's cellular therapy capabilities to the global stage. Through these collective efforts and cross-border partnerships, TACT aims to advance its broader vision of promoting global cooperation and helping make cellular therapy an emerging therapeutic approach and product category that is accessible and affordable to all.

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IMAGE FROM CANVA.COM

From Formosa to the world: leading the new era of regenerative medicine and cellular therapy in Taiwan

Regenerative medicine has rapidly evolved from experimental concepts into a transformative force in standard clinical care, ushering in a new era of possibilities for treating diseases that have long defied conventional therapies. In Taiwan, this field has grown exponentially, supported by a strong foundation in biotechnology, clinical excellence, and, most importantly, proactive policy evolution.

The Formosa Association of Regenerative Medicine (FARM), which proudly takes its name from the historical appellation for Taiwan meaning "beautiful island", established by Founding President Professor Hua-Chang Liu in 2004. Since its inception, FARM has been at the forefront of this journey, serving as a vital platform to bridge the gap between basic scientists, bioengineers, and clinical practitioners. Over the past 22 years, the association has successfully united experts from medical centers, research institutions, and the biotechnology industry to facilitate interdisciplinary dialogue and promote the safe, effective clinical application of cellular therapies.

A pivotal turning point in Taiwan's regenerative medicine landscape occurred in September 2018, when the Ministry of Health and Welfare (MOHW) announced the comprehensively amended Regulations Governing the Implementation or Use of Specific Medical Techniques, Examinations, Tests, and Medical Instruments (commonly known as the Special Regulation).

This visionary initiative established a controlled clinical governance framework that allowed specific autologous cell therapies to enter clinical practice to address urgent, unmet medical needs. This Special Regulation not only provided new hope for patients but also catalyzed the rapid growth of Taiwan's biotech ecosystem, allowing institutions to accumulate invaluable real-world clinical data and operational experience.

Formosa Association of Regenrative Medicine (FARM)

Dr. Chen-Chie Wang is a senior attending physician at the Department of Orthopedic Surgery, Taipei Tzu Chi Hospital, and the President of the Formosa Association of Regenerative Medicine (FARM). He has previously served as the President of the Taiwan Orthopaedic Foot and Ankle Society. His major interests include regenerative medicine, cellular therapy, tissue engineering, and translational research in orthopedic surgery.

FARM played an active role during this critical period, facilitating dialogue between clinicians and regulators to ensure patient safety, quality control, and the capability of being traced within this new framework. Building upon the foundational data and industry maturation fostered by the 2018 Special Regulation, the year 2026 marks a historic milestone for Taiwan with the official enactment of the Regenerative Medicine Dual Acts. This legislative breakthrough signifies a monumental shift from a technical, trial-based approach to a comprehensive product-based, full life-cycle regulatory system.

As the newly elected President of FARM, I witness firsthand how these advancements have significantly accelerated the clinical application of advanced therapies. We are seeing remarkable progress in both autologous and allogeneic cell therapies, particularly in orthopedic applications such as articular cartilage repair, where tissue-engineered scaffolds and cell cultures are yielding highly promising patient outcomes.

Furthermore, the rapid advancements in extracellular vesicles (exosomes) and organoid models are opening entirely new frontiers in targeted therapies and precision diagnostics, demonstrating Taiwan's robust capacity for medical innovation on the global stage.

However, as a practicing orthopedic surgeon, my primary vision for FARM is deeply rooted in addressing the practical realities of the "bench-to-bedside" pathway. While possessing superior cell technology is critical, the true challenge often lies in logistical execution. Specifically, this requires maintaining cell viability during cross-institutional transportation, precisely synchronizing cell delivery with surgical timing, and navigating complex interdisciplinary workflows.

To overcome these hurdles, my vision for FARM focuses on deepening translational synergy by reducing the friction between laboratory development and clinical application. We are actively advocating for the establishment of comprehensive, dedicated regenerative medicine centers within hospitals to centralize and optimize the delivery of cellular therapies.

Concurrently, FARM will continue to serve as a professional think tank, assisting regulatory authorities like the MOHW and the Taiwan Food and Drug Administration (TFDA) in refining ethical guidelines, rigorous quality control protocols, and standardized training programs for physicians to ensure patient safety remains paramount. Looking beyond our borders, the complexity and high development costs inherent to regenerative medicine dictate that no single nation can achieve ultimate success in isolation.

As the African proverb wisely states, "If you want to go fast, go alone; if you want to go far, go together." The future of advanced therapies lies unequivocally in regional and global synergy. Moving forward, FARM is highly committed to deepening its strategic partnership with the Asian Cellular Therapy Organization (ACTO) and other regional societies.

Our collaborative focus across Asia must prioritize the harmonization of regulatory standards to lower the barriers for cross-border technology transfers, the establishment of Pan-Asian multi-center clinical trial networks to validate therapies across diverse genomic populations, and the integration of regional supply chains for biological materials.

By locking arms with ACTO and our international partners, FARM is ready to turn the immense promise of regenerative medicine into accessible, standardized treatments, building a resilient and innovative ecosystem that will ultimately deliver unprecedented hope to patients across Asia and the world.

Acknowledgment

I extend my deepest gratitude to the founding president, past presidents, board members, and the secretarial team of FARM for their decades of dedication. I also thank the ACTO Editorial Board for the privilege of sharing our vision.

Conflict of interest

The author declares no conflict of interest.

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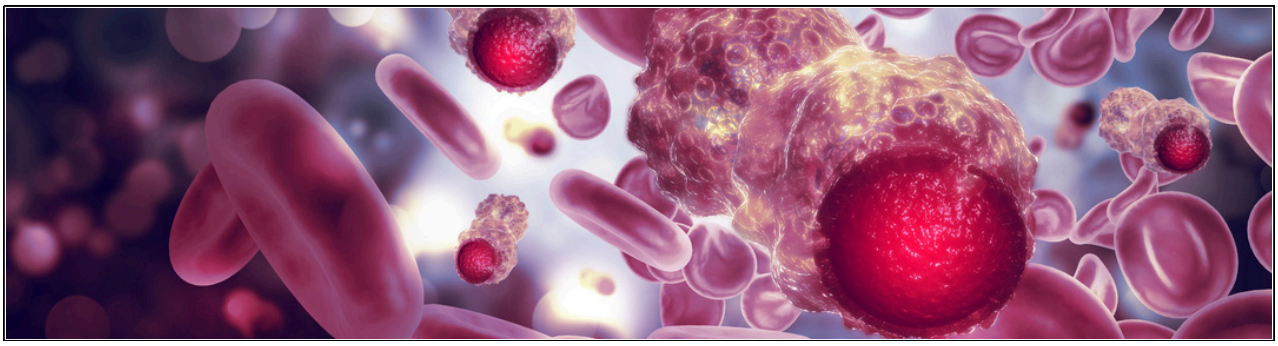

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Overcoming manufacturing bottlenecks in cell and gene therapy: The emergence of the intelligent development and manufacturing organization (IDMO) model in Asia

Abstract

The clinical efficacy of Chimeric Antigen Receptor T-cell (CAR-T) therapies has irrevocably transformed the landscape of oncology and personalized medicine. Despite these groundbreaking clinical successes, the broad accessibility of these advanced therapies is severely limited by traditional manufacturing paradigms. High production costs, reliance on manual operations, and the inherent variability of biological materials present critical bottlenecks for scaling up. To address these challenges, the industry must pivot from conventional manufacturing approaches toward highly automated, data-driven frameworks. This article explores the current manufacturing challenges in the cell and gene therapy (CGT) sector and introduces the concept of the Intelligent Development and Manufacturing Organization (IDMO). By integrating digital twin technologies, smart robotics, and closed-system automation, the IDMO model drastically enhances data efficiency, reduces contamination risks, and ensures product consistency. Furthermore, we discuss the strategic importance of establishing advanced smart manufacturing hubs in the Asia-Pacific region, which holds the potential to accelerate the commercialization of CAR-T therapies and build a robust, scalable CGT ecosystem globally.

Keywords: CAR-T therapy, Cell and Gene Therapy, CDMO, Smart Manufacturing, IDMO, Automation, Commercialization.

Introduction

Over the past decade, Chimeric Antigen Receptor T-cell (CAR-T) therapies have emerged as one of the most promising pillars of modern medicine, offering unprecedented remission rates for patients with hematological malignancies. The translational journey of CAR-T cells—from laboratory bench to bedside—has validated the potential of living drugs. However, as the industry transitions from early-phase clinical trials to large-scale commercialization, a glaring operational chasm has become evident: the manufacturing processes are struggling to keep pace with clinical demand.

Unlike traditional small-molecule drugs or biologics, the production of autologous CAR-T therapies involves complex, highly personalized, and time-sensitive procedures. The current manufacturing landscape is heavily reliant on manual, labor-intensive operations that are difficult to scale.

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Consequently, the exorbitant costs associated with manufacturing and supply chain logistics have restricted patient access, leaving a significant gap between therapeutic innovation and real-world clinical application. To bridge this gap, a paradigm shift in manufacturing strategies is urgently required, particularly in rapidly growing markets like the Asia-Pacific (APAC) region.

Current bottlenecks in CAR-T manufacturing

The manufacturing of CAR-T cells involves several intricate steps: leukapheresis, T-cell isolation and activation, genetic modification (typically via viral vectors), expansion, and final formulation. In traditional settings, these steps are performed using open or semi-closed systems that require extensive cleanroom infrastructure and highly trained personnel.

- Scalability and Reproducibility Issues

Manual handling inevitably introduces human error and operational variability, which directly impacts the reproducibility and quality of the final cell product. In autologous therapies, where the starting material exhibits significant patient-to-patient variability, maintaining consistent product quality is a monumental challenge. Scaling out (multiplying the number of production units) rather than scaling up (increasing the volume of a single batch) is necessary, yet doing so with manual processes leads to an unsustainable exponential increase in labor and infrastructure costs.

- High Production Costs

The cost of goods sold (COGS) for CAR-T therapies remains prohibitively high. A substantial portion of this cost is driven by the stringent requirements of Good Manufacturing Practice (GMP) facilities, expensive raw materials (such as viral vectors), and the extensive quality control (QC) testing required for release. Without technological intervention, these financial barriers will continue to impede the widespread adoption of cell therapies.

The "IDMO" solution: redefining cell manufacturing

To overcome the inherent limitations of traditional Contract Development and Manufacturing Organizations (CDMOs), a new conceptual framework has emerged: the Intelligent Development and Manufacturing Organization (IDMO). The IDMO model represents a fundamental evolution from standard contract manufacturing to a comprehensive, digitally integrated ecosystem.

- Automation and Closed Systems

The cornerstone of the IDMO model is the transition to fully closed, automated manufacturing systems. By minimizing manual interventions, automated platforms drastically reduce the risk of contamination and batch failure. This standardization is crucial for ensuring that complex cellular products meet the rigorous quality attributes demanded by regulatory bodies.

- Digital Twins and Smart Robotics

Advanced IDMO facilities integrate "Digital Twin" technologies—virtual representations of the physical manufacturing processes that allow for real-time simulation, monitoring, and optimization. Coupled with smart robotics, these facilities can achieve continuous operation with unparalleled precision. This synergy allows for the early detection of process deviations, enabling preemptive corrections before product viability is compromised.

- Data Efficiency and AI Integration

In the IDMO framework, data is treated as a critical asset. "Data Efficiency" refers to the ability to continuously capture, analyze, and leverage massive datasets generated throughout the manufacturing cycle. By applying artificial intelligence (AI) and machine learning algorithms to this data, manufacturers can optimize culture conditions, predict cell expansion trajectories, and streamline QC processes. This data-centric approach not only accelerates batch release times but also drives continuous process improvements.

Strategic advantages of an Asian CGT hub

The APAC region is currently experiencing an explosive growth in CGT clinical trials, driven by a large patient population, increasing investments, and supportive regulatory pathways. However, the region has historically faced a shortage of commercial-scale GMP manufacturing capacity, often necessitating cross-border logistics that add both cost and time to the therapeutic delivery.

Establishing an IDMO-driven smart manufacturing hub in Asia—such as the state-of-the-art facilities in Taiwan—offers a strategic solution. Taiwan's unique geographic position, combined with its world-class information and communication technology (ICT) infrastructure, makes it an ideal nexus for biopharmaceutical innovation. By leveraging high-degree automation and international standards (PIC/S GMP), an Asian CGT hub can serve as a reliable manufacturing partner for global biotech firms, significantly lowering production costs and shortening turnaround times.

Furthermore, deep integration with international ecosystems, through partnerships with leading technology and equipment providers in Japan, Europe, and the U.S., ensures that the regional hub remains at the forefront of global manufacturing standards. This collaborative approach is vital for fulfilling large-scale commercial orders and ensuring supply chain resilience.

Conclusion

The future of CAR-T and other advanced cellular therapies relies unequivocally on our ability to industrialize their manufacturing processes. The transition from traditional, manual production to the automated, data-driven IDMO model is not merely an operational upgrade; it is a strategic necessity for the survival and expansion of the CGT industry. By embracing smart robotics, digital twins, and AI-driven data efficiency, the IDMO framework effectively shatters the existing bottlenecks of cost and scalability. As advanced manufacturing hubs continue to take root in Asia, they will play an indispensable role in democratizing access to life-saving therapies, ultimately translating the promise of cellular medicine into accessible clinical realities for patients worldwide.

Acknowledgement

The author would like to express profound gratitude to the entire team at Locus Cell Co., Ltd. for their relentless dedication to advancing smart manufacturing in cell therapies, and to our international strategic partners for their collaborative efforts in building a robust CGT ecosystem.

Conflict of interest

The author declares no conflict of interest.

References

1. Levine BL, Miskin J, Wonnacott K, Keir C. Global manufacturing of CAR T cell therapy. Mol Ther Methods Clin Dev. 2017;4:92-101.
2. Vormittag P, Gunn R, Ghorashian S, Veraitch FS. A guide to manufacturing CAR T cell therapies. Curr Opin Biotechnol. 2018;53:164-181.
3. Tyagarajan S, Spencer T, Smith J. Optimizing CAR-T cell manufacturing processes during pivotal clinical trials. Mol Ther Methods Clin Dev. 2020;16:136-144.
4. Müller F, et al. CD19 CAR T-Cell Therapy in Autoimmune Disease — A Case Series with Follow-up. N Engl J Med. 2024;390:687-700.
5. Wang X, et al. Allogeneic CD19-targeted CAR-T therapy in patients with severe myositis and systemic sclerosis. Cell. 2024;187:4890-4904.
6. Schett G, et al. CAR T-cell therapy in autoimmune diseases. Lancet. 2023;402:2034-2044.
7. Granit V, et al. Safety and clinical activity of autologous RNA chimeric antigen receptor T-cell therapy in myasthenia gravis (MG-001): a prospective, multicentre, open-label, non-randomised phase 1b/2a study. Lancet Neurol. 2023;22:578-590.
8. Yang C, et al. TyU19 CAR-T cells induce remission in 4 SLE patients. Cell Res. 2025. DOI: 10.1038/s41422-025-01128-1.
9. Schett G, et al. Nat Rev Rheumatol. 2024;20:531-544. Rubin SJS, et al. B-cell-targeted therapies in autoimmune disease. Nat Rev Rheumatol. 2019;15(5):303-315.
10. Barnas JL, et al. B cell targeted therapies in autoimmune disease. Curr Opin Immunol. 2019;61:92-99.
11. Kurata H, Ishino T, Ohshima Y, Yohda M. CDMOs Play a Critical Role in the Biopharmaceutical Ecosystem. Front Bioeng Biotechnol. 2022;10:841420.
12. Ferreira RS, Morales MM, Barretti P, Barraviera B. Launching a CDMO in Brazil aiming to develop biopharmaceuticals for clinical trials. J Venom Anim Toxins Incl Trop Dis. 2022;28:e20220017.
13. Baghbaderani BA. Commercialization of Cell Therapies: A CDMO Perspective. Adv Exp Med Biol. 2025;1486:137-145.

17TH ACTO ANNUAL MEETING

The 17th Annual Meeting of the Asian Cellular Therapy Organization (ACTO), held in collaboration with the Indonesian Stem Cell Association (ASPI).

Programme Highlights :

- Advancing research and clinical translation of cell-based therapies
- Multidisciplinary sessions involving academicians, clinicians, industry, and government
- Scientific, regulatory, clinical, and public sessions
- Organization and networking meetings

More information:
https://acto-hq.org/acto-2026-in-jakarta/

ISSCR - iPSC 20th Anniversary Symposium

The discovery of induced pluripotent stem cell (iPSC) technology has revolutionized biomedical research and regenerative medicine. To celebrate the 20th anniversary of this transformative breakthrough, the ISSCR is bringing together the global stem cell community in Kyoto, the birthplace of iPS cells, for a three-day symposium. This program will reflect on two decades of remarkable progress and explore the future of the field.

More information:
https://www.isscr.org/upcoming-programs/2026-kyoto-international-symposium

ISSCR 2026

Leaders in stem cell research and regenerative medicine gather annually for the ISSCR Annual Meeting, and you're invited to be part of it! Join nearly 3,500 scientists from across the world at ISSCR 2026 for a 4-day event highlighting the most important breakthroughs in the field.

More information:
https://www.isscr2026.org

ISCT ASIA 2026 REGIONAL MEETING

The International Society for Cell & Gene Therapy (ISCT) Asia 2026 Regional Meeting will be held on September 2–5, 2026, at the Suntec Singapore Convention & Exhibition Centre, Singapore. This premier event will bring together researchers, clinicians, industry leaders, and regulators to discuss the latest advances in cell and gene therapy.

More information:
https://www.isctglobal.org/isctasia2026singapore/home-2026

APSEV 2026

This year's meeting will be held in conjunction with APSEV 2026, organized by the Asia Pacific Society for Extracellular Vesicles.
Building upon Japan's pioneering achievements in extracellular vesicle (EV) research from basic science to applied studies, we aim to send a strong message to the world about the future of EV research from Japan, as leading researchers across the Asia-Pacific region gather together. Accordingly, the joint conference theme is "Beyond Exosome."

More information:
https://www.ace-enterprise.jp/apsev-jsev2026/en_index.html

CGT WORLD ASIA 2026

As the region emerges as a global leader in regenerative medicine, Cell & Gene Therapy World Asia 2026 (#CGTAsia2026) returns as Asia's most anticipated CGT knowledge-sharing conference for the 9th year! Designed to connect and empower stakeholders from the cell and gene therapy ecosystem, the event provides an unparalleled platform to explore the latest advancements in cell therapies, gene therapies, and CAR-T technologies.

More information:
https://www.imapac.com/events/cell-gene-therapy-world-asia-2026

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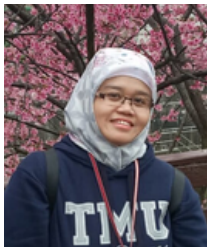

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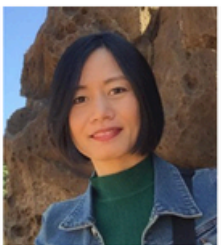

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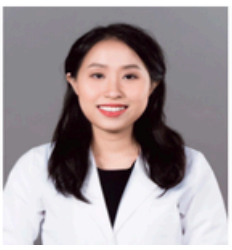

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