

Autologous Mygotic Cells (Mygoties™) as Totipotent/Pluripotent Embryonic Stem Cells: Overcoming iPSC Limitations and Generating All Three Lineages

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Abstract

Induced pluripotent stem cells have transformed regenerative medicine by enabling the generation of patient-specific pluripotent cells without embryo-derived starting material. However, iPSC-based systems remain limited by low reprogramming efficiency, extended manufacturing timelines, incomplete epigenetic resetting, residual somatic memory, clonal variability, genomic instability, and complex regulatory characterization requirements. Embryonic stem cells remain the benchmark for pluripotency because of their developmental origin, stable self-renewal, broad lineage potential, and comparatively robust differentiation capacity, but conventional ESCs are constrained by ethical, legal, religious, immunologic, and practical limitations.

This White Paper describes the Mygotic Process™, a proprietary platform intended to generate autologous Mygotic Cells, or Mygoties™, from somatic cells. The process is described as non-viral, non-vector-based, non-genetically engineered, and free of exogenous disease-associated or bacterial components. Mygoties™ are presented as autologous totipotent and pluripotent embryonic-stem-cell-like cells capable of expressing key pluripotency markers, including Sox2, Oct4, Nanog, SSEA-4, Tra-1-60, and Tra-1-81, while supporting differentiation into derivatives of all three germ layers. The paper reports that Mygotic clones can be generated within 2–5 days and are often ready for use by days 5–7, with preparation efficiencies of 40–70%, compared with substantially lower yields commonly associated with iPSC reprogramming.

The White Paper further presents an example of hematopoietic differentiation in which human fibroblast-derived Mygotic Cells generated hematopoietic progenitors and terminally differentiated erythrocytes within 48 hours. The resulting cells represented approximately 40% of the total cell population, demonstrated viability exceeding 90%, and expressed lineage-associated markers including CD43, CD235a, and CD71.

Together, these findings support the positioning of Mygoties™ as **a potential autologous, laboratory produced, embryonic stem cell platform** that combines attributes associated with ESCs, including developmental plasticity, lineage breadth, and self-renewal, with attributes sought in iPSC systems, including patient specificity and ethical accessibility.

Further validation, reproducibility studies, comparative benchmarking, safety testing, and application-specific functional assays have already established clinical readiness. The Mygotic Process™ may provide a new cellular starting point for regenerative medicine, cell therapy manufacturing, disease modeling, tissue engineering, organoid development, and personalized biomanufacturing.

Keywords: Autologous stem cells, Pluripotent stem cells, Embryonic-like stem cells, Cellular reprogramming, Regenerative medicine, iPSC alternatives, Non-genetic cell reprogramming, Patient-specific cell therapy, Laboratory produced embryonic stem cells, Mygotic Process™

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Preface

For years, regenerative medicine has been built on reprogramming adult cells into **induced pluripotent stem cells**.

But perhaps the field began with the wrong starting material.

Regenerative medicine has long relied on converting adult cells into induced pluripotent stem cells (iPSCs), but emerging evidence suggests the field may have chosen the wrong starting material

The goal was never to only reprogram adult cells. The goal should have been to establish the **most reliable, developmentally competent, and clinically scalable cellular starting point** for regeneration, repair, disease modeling, drug development, and personalized cell manufacturing.

This white paper argues that the future of regenerative medicine may depend on moving beyond the limitations of induced pluripotent stem cells (iPSCs) and returning to the biological logic that positioned embryonic stem cells as the benchmark in the first place: **a more complete developmental starting point, produced autologously, without conventional embryo derivation and without genetic engineering.**

On that standard, iPSCs remain an imperfect compromise. They hold considerable potential, but they are not nature's original architecture. Instead, they are engineered approximations of pluripotency generated through forced transcriptional reprogramming, often characterized by **low efficiency, residual epigenetic memory, variability, genomic instability, prolonged and costly workflows, and significant analytical and regulatory burden.** If the product originates from compromised starting material, every downstream step must compensate for that initial deficit. If it begins with a more complete cellular reset, the entire therapeutic and manufacturing architecture shifts accordingly.

The **Mygotic Process™** is designed to generate autologous **zygotic clones or Mygoties™** from somatic cells without the use of viral vectors, genetic engineering, exogenous disease-associated elements, or bacterial components. The resulting cells function as **autologous, totipotent and pluripotent, laboratory-produced embryonic-stem-cell-like cells** capable of expressing core pluripotency markers including **Sox2, Oct4, Nanog, SSEA-4, Tra-1-60, and Tra-1-81** while supporting differentiation across all three germ-layer lineages.

Embryonic stem cells (ESCs) remain the biological benchmark because they arise from the natural developmental program. They possess the **stability, plasticity, self-renewal capacity, and lineage potential** that regenerative medicine seeks. Yet conventional ESCs carry inherent limitations: they are not autologous, they originate from embryos, and they remain constrained by ethical, legal, religious, and practical barriers.

This White Paper describes Mygotic clones generated within **2-5 days**, often ready for use by **days 5-7**, with reported preparation efficiencies of **40-70%**, compared with substantially lower yields achieved through conventional iPSC reprogramming.

The implication is profound: regenerative medicine no longer needs to rely on a forced reprogramming workaround when a more **natural, autologous, rapid, and developmentally grounded starting point** is possible.

Mygoties™ represent a new class of autologous embryonic-stem-cell-like starting material: **personalized like iPSCs**, yet designed to recapture the **developmental competence, chromatin openness, epigenetic plasticity, and broad lineage potential** associated with embryonic stem cells.

This white paper further demonstrates this potential through the generation of hematopoietic progenitors and terminally differentiated erythrocytes from fibroblasts, showing reported viability above **90%** and expression of lineage-specific markers **CD43, CD235a, and CD71**.

We have established a superior Mygotic approach, validated its performance, and demonstrated its potential to reshape and advance clinical and industrial practice.

We have found a better way.

We have proven that it works.

This changes everything.

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Introduction

Embryonic Stem Cell: Pluripotency and Totipotency

Pluripotent embryonic stem cells (ESCs) derived from post-fertilization blastocysts can generate all somatic and germline lineages, enabling tissue repair, and personalized medicine¹. As a result, they have become central to regenerative medicine and cell therapy manufacturing². Totipotent stem cells, present only at the zygote and early cleavage stages, possess the highest developmental potential in mammals, capable of forming both embryonic tissues and extraembryonic supportive structures such as the placenta^{3,4}. These cells exhibit a fully open chromatin landscape (enabling transcriptional machinery to access DNA and activate early development gene programs), minimal lineage restriction, and a more complete transcriptional and epigenetic reset (including 2-cell-like transcriptional programs, and global DNA demethylation)⁵⁻⁹. This allows a single blastomere to generate an entire organism. Such properties make totipotent cells a powerful theoretical tool for investigating early embryogenesis, genome activation, and lineage segregation. However, true totipotent cells exist only during a brief developmental window, making them difficult to obtain and therefore limiting their practical utility and use within the scientific community¹⁰⁻¹³. ESCs research faces federal funding restrictions and projects are often discontinued due to ethical, legal, and religious considerations. Despite their broader biological potential, the current regenerative medicine landscape is dominated by more accessible pluripotent stem cells that provide robust, scalable, and experimentally tractable platforms driving modern biomedical science and biomanufacturing¹⁴.

ESCs vs. iPSCs: Reliability and Efficiency

ESCs remain the gold standard for pluripotent stem cell-based regenerative applications because they are considered more reliable and biologically robust than iPSCs. They originate naturally from the blastocyst inner cell mass and maintain a stable, naïve pluripotent state without undergoing reprogramming^{8,15-18}. In contrast, iPSCs are generated by forced overexpression of transcription factors such as OCT4, SOX2, KLF4, and c-MYC. This process can introduce genetic mutations, chromosomal

abnormalities, and incomplete epigenetic resetting^{17,19-22}. Therefore, iPSCs frequently retain somatic epigenetic memory that biases differentiation and contributes to variability and long term instability within the cell lines, requiring prolonged, meticulous, and expensive maintenance.^{17,18,23-25} On the other hand, ESCs exhibit robust, stable, and consistent pluripotency, more uniform expression of core markers, and greater genomic stability. ESCs differentiate into target lineages with greater consistency and efficiency while avoiding epigenetic pitfalls such as abnormal methylation patterns and the increased oncogenic risk often observed in reprogrammed cells²⁶⁻²⁸. Consequently, ESCs remain a benchmark standard despite their non-autologous nature and associated ethical, legal, and religious concerns surrounding their embryonic origin²⁹⁻³¹.

iPSC establishment and manufacturing require a complex, prolonged culture sequence and often exhibit greater genomic instability, resulting in an unfavorable long-term benefit-risk balance for patients and a more complicated regulatory approval process^{25,32,33}. Residual epigenetic memory can bias differentiation outcomes and contribute to batch-to-batch variability, while heterogeneity across donors, reprogramming methods, and clones (e.g., epigenetic state, differentiation potential, genomic stability, and expression profiles) increase the analytical burden associated with characterization, quality control, and multi-step biological lot release testing^{23,34}. Forceful reprogramming without self-correction introduces process-related risks such as epigenetic methylation defects, insertional effects, and oncogenic signatures, raising safety concerns for clinical applications³⁵. Operationally, iPSC-based workflows tend to be longer, more complex, and less predictable, with lower differentiation efficiency and higher failure rates than ESC-based processes^{29,32,36}. Regulatory agencies therefore view iPSCs as higher-risk starting materials, requiring deeper genomic, epigenomic, and functional verification and validation³⁷.

That said, iPSCs offer several advantages, particularly in ethical acceptability, patient specificity, and research flexibility³⁸⁻⁴⁰. They are commonly differentiated via embryoid body (EB) formation, without requiring the need to derive cells from embryos. The iPSCs avoid the central ethical and regulatory constraints associated with ESCs and can be produced from most donor tissue³⁹. Their patient-specific origin enables the creation of genetically matched cell lines that reduce immune-rejection risk in autologous therapies while retaining the donor's genetic background⁴¹⁻⁴³. iPSCs can also be generated in-house (enabling customized, genetically matched pluripotent lines) and expanded into diverse biobanks (derived from various donors)^{38,44,45}, supporting precision medicine and enabling broad population representation. The stem cells are becoming increasingly viable for robust, scalable manufacturing and for integration into translational and regenerative medicine workflows^{46,47}.

The Mygotes™: True Totipotent and Pluripotent ESCs

The need for a reliable cell platform that not only captures the advantages but also addresses the limitations of both ESCs and iPSCs has, for the first time in human history, led to the development of a proprietary technology known as the Mygotic Process™. The process enables the formation of autologous totipotent and pluripotent cells by relying on physical forces and naturally occurring self-correcting mechanisms to generate genetically identical zygotic clones of the host organism. The resulting zygotes provide embryonic stem cells, referred to as Mygototes™, which function as primordial totipotent cells with the capacity to differentiate into pluripotent, human embryonic stem cells, multipotent progenitor cells from all tissue layers, and terminally differentiate into lineage-specific cell types (Figs. 1A and B). The pluripotent cells naturally express major embryonic markers, such as Sox2, Oct4, Nanog, SSEA-4, Tra 1-60 and Tra-1-81.

Importantly, the Mygotic Process™ does not involve viral or any vector manipulation, genetic engineering, the use of exogenous disease-related elements, or the introduction of bacterial components. Data from previous studies demonstrates that our cells behave as true ESCs and maintain an open, chromatin-rich genome with minimal heterochromatin. This enables uniform pluripotency and high epigenetic plasticity, while selectively targeting reversible heterochromatin to silence lineage-specific genes and preserve pluripotency. Although iPSCs largely maintain the open chromatin (euchromatin) landscape of ESCs, they frequently retain regions of denser chromatin (heterochromatin) associated with transcriptionally inhibitory modifications. These clusters of incomplete epigenetic resetting can restrict access to key loci, potentially leading to inconsistent pluripotency gene activation, expression, stability, and differentiation levels^{18,48}.

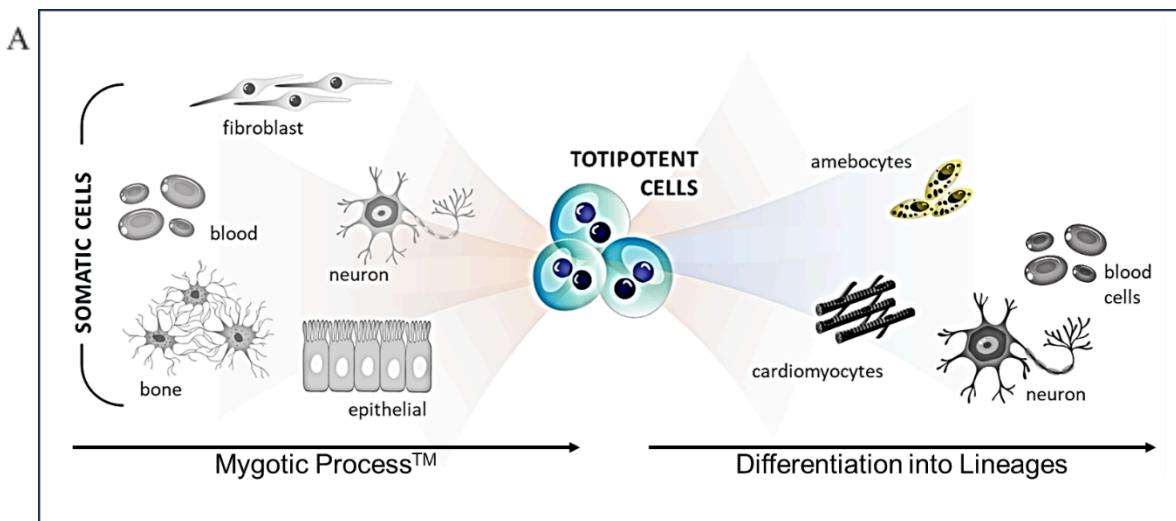
The Mygotic Process™ preserves a stable karyotype, maintains high fidelity, and enhances safety across the pluripotent stem-cell workflow. The exclusion of integrating and non-integrating reprogramming methods, together with measures that prevent their unintended use, reduces the risk of insertional mutations and reprogramming-related abnormalities while resetting epigenetic memory to generate consistent, autologous, embryo-derived cell lines. Our manufacturing process incorporates genomic screening to confirm that the cells are free of chromosomal abnormalities and supports consistent manufacturing. These advances enable the formation of more stable, predictable, and reproducible cell populations, supporting their transition from research tools to reliable platforms for drug development, large-scale manufacturing, and therapeutic applications.

iPSCs still carry inherent risks of genetic integration or retention when reprogramming relies on methods that introduce exogenous sequences or use gene editing tools with imperfect insertion controls, such as certain CRISPR-Cas approaches⁴⁹⁻⁵¹. This unintended integration can disrupt endogenous regulatory elements and compromise

gene-expression fidelity. In contrast, true Mygotic stem cells that are not subjected to genomic modifications avoid these risks entirely, maintaining full control of their native gene-regulatory information and architecture (Fig. 1C).

Mygoties™ naturally follow a defined sequence of developmental stages that occur during the natural development of pluripotent embryonic stem cells derived from the inner cell mass (ICM) of clonal blastocysts. Emerging colonies exhibiting characteristic ESC morphology are subsequently passaged and expanded to establish a stable line capable of indefinite growth under controlled culture conditions and stored to create master cell banks.

iPSC clones require 2-4 weeks to develop and can be used after this maturation period, with some workflows extending to 8 weeks or more. Reliance on naturally occurring self-correcting mechanisms allows Mygotic clones (Fig. 1D) to be generated within 2-5 days and are often ready for use by days 5-7, offering a substantially faster turnaround. The efficiency gap between the two systems is significant. iPSC reprogramming yields are extremely low (reaching approximately 2%), whereas Mygotic cell preparation can reach efficiencies of 40-70%. This notable difference highlights the practicality and scalability offered by Mygotic cell platforms compared to conventional iPSC reprogramming methods⁵².



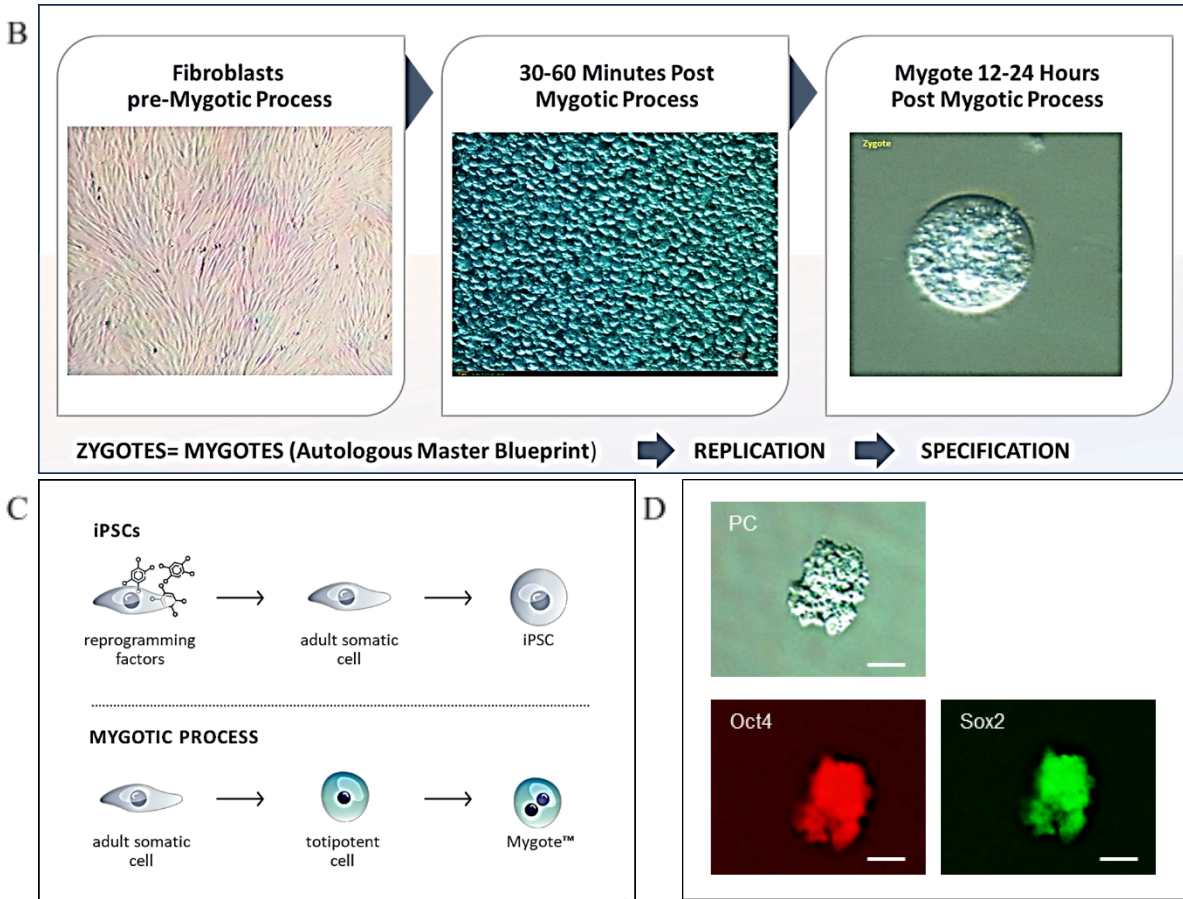


Fig. 1. The Mygotic Process™: **A.** Diagram illustrating the development of Mygotes™ from a variety of somatic cell types, transitioning through totipotent stage and subsequent terminal differentiation into all three lineages. The process was also demonstrated on non-human tissues (amebocytes). **B.** Microscopic images showing the morphological progression of somatic cells (fibroblasts) as they transform into Mygotes. **C.** Illustration comparing the reprogramming stages of somatic cells into iPSCs with the transformation of somatic cells into Mygotes™. **D.** Immunofluorescence Staining of a Mygote colony expressing the self-renewal markers Oct4 and Sox2 (PC:Phase Contrast)

The Mygotic Cells in Regenerative Medicine

Mygotes™ can support organ regeneration due to their ability to reach totipotent and pluripotent stages, allowing them to differentiate into any cell type in the body. These cells exhibit unique natural developmental capacities such as the formation of zygotes, embryonic and extraembryonic lineages, zygotic genome activation, self-correcting mechanism during cell development, tri-lineage separation, and epigenetic programs restored to a naïve state. In regenerative medicine, under proper conditions, these

pluripotent stem cells (ESCs) can self-renew indefinitely and can be differentiated *in vivo* or *in vitro* into all somatic cell types, including cardiomyocytes, neurons, chondrocytes, pancreatic cells, kidney progenitors, and blood cells using defined growth factors and developmental cues to generate replacement tissue and cell-based therapies. The fully functional autologous Mygotic Process™ cells can integrate into host tissues through direct injection or embedded within scaffolds to create transplantable constructs.

Embryonic cells derived from Mygoties™ can not only replace existing cells but also serve as a source of trophic (e.g., extracellular matrix) and paracrine (e.g. FGF, VEGF) factors, secreting molecules that promote local endogenous repair, create a rejuvenating environment, and release anti-inflammatory mediators that modulate the immune response. Advances in organoid and tissue-engineering technologies further enable the autologous cells to self-organize into 3D structures that model organ development and serve as building blocks for future personalized regenerative therapies. These capabilities position the Mygotic Process™ as a powerful platform for restoring tissues and organs damaged by injury, disease, or aging.

Example: Regenerating Differentiated Red Blood Cells from Fibroblasts

There is a global gap between blood demand and eligible donor supply. This shortage is driven by increased surgeries, trauma cases, and infectious agents limiting donor eligibility. Securing safe, high-quality cultured red blood cells (RBCs) and components remains a challenge. A fully functional artificial substitute for RBCs has yet to be developed. However, Mygogenesis, by utilizing its platform (Fig 2. A-C) produced human autologous hematopoietic stem cells (Fig 2. D), which further differentiated into progenitors, generating millions of terminally differentiated erythrocytes (RBCs) within 48 hours (Fig 2. E). These cells ranged in size from 5-8 μm , representing approximately 40% of the total cell population and exhibiting viability exceeding 90%. The cells expressed lineage-specific markers such as Sialophorin (CD43), Glycophorin A (CD 235a), and Transferrin (CD 71) receptors. Besides producing autologous blood cells and blood-derived components for transfusion, the platform enables generation of scalable allogeneic blood banks, including the rare O-negative subtype for a range of clinical applications.

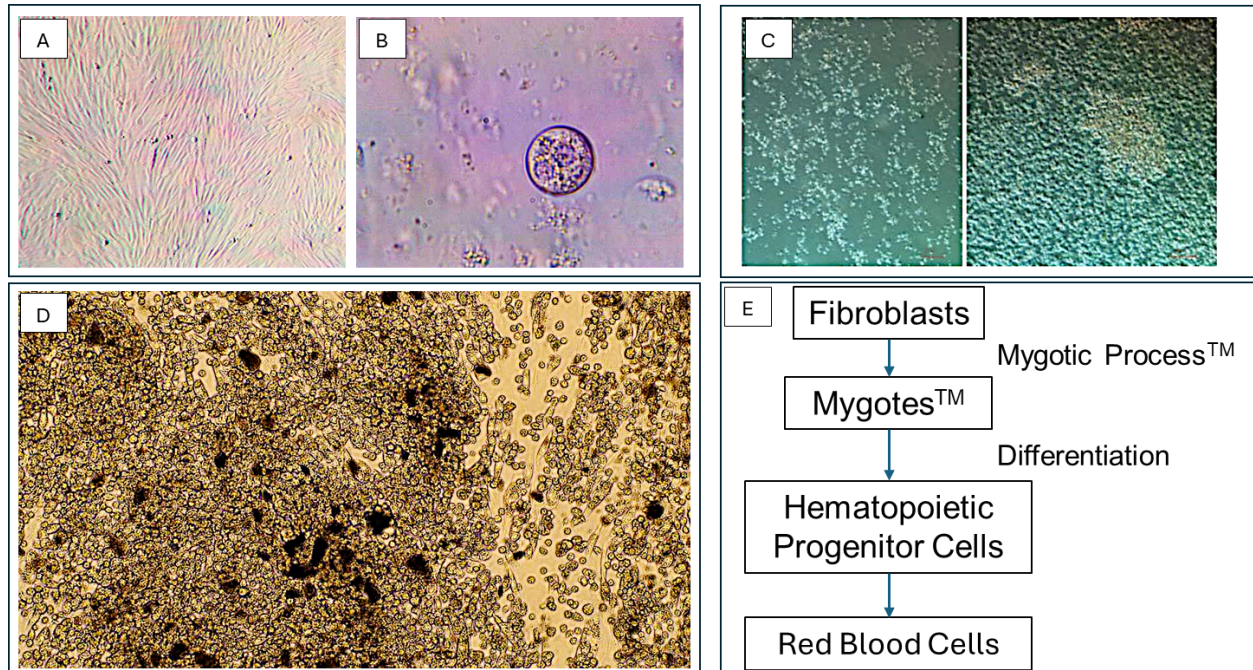


Fig. 2. Human Mygote™ and RBCs Formation: **A.** Fibroblasts (pre Mygotic Process). **B.** Mygote™ (post Mygotic Process™- day 1). **C.** Embryonic stem cells colonies, **D.** Hematopoietic progenitor cells. **E.** A diagram illustrating the formation of RBCs from fibroblasts via the Mygotic Process™ and the generation of Mygotes™.

Conclusion

While iPSCs offer clear advantages in patient specificity and ethical accessibility, their low reprogramming efficiency, variable quality, and risks of genomic alterations continue to limit their reliability for large-scale or clinical applications. ESCs remain the benchmark for pluripotency, exhibiting greater stability with more robust and predictable lineage commitment and terminal differentiation, while facing ethical constraints and limited availability. These findings highlight the significance of the Mygogenesis autologous embryonic stem cell platform, developed through the Mygotic Process™, which combines high genomic fidelity, pluripotency, and reproducibility of ESCs with the accessibility and personalization associated with iPSCs. Mygotes™ formation can be generated from somatic cells by resetting their epigenetic memory, generating true ESCs with the capacity to differentiate into all three germ-layer lineages when provided with appropriate cues. High efficiency and lineage breadth not only position them as an excellent option for clinical and biotechnology applications, but also open new avenues for developing targeted and personalized regenerative therapies.

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