

From Cord to Cure: Repurposing Biological Waste for UAE's Health Revolution with **Umbilical Cord Stem Cell Therapy**

إعادة استخدام بقايا الخلايا الجذعية من الحبل السرى كوسيلة علاجية أحداث نهضة علمية في مجال الصحة الإماراتي

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In the UAE, current hospital policies mandate the disposal of biological waste, such as umbilical cords. However, this tissue represents a valuable source of therapeutic material like mesenchymal stem cells (MSCs) and their secretome. The disposal of this valuable therapeutic material imposes a significant burden on public health. In the United States alone, approximately 18,000 people per year are diagnosed with diseases that could be ameliorated with stem cell therapy. These individuals often remain untreated due to the lack of available stem cells, as current methods for MSC obtention, such as Bone Marrow-MSCs, require an invasive bone marrow aspirate procedure, which is painful and can pose risks to donors, including infection and prolonged recovery times. This paper advocates for policy reform to facilitate the collection, storage, and utilization of umbilical cords. By addressing regulatory barriers and implementing standardized protocols, hospitals in the UAE can not only contribute to advancements in regenerative medicine but also solidify the nation's position as a leader in this emerging field, ultimately improving patient outcomes and reducing the disease burden both locally and regionally. This is particularly relevant given the significant burden of cardiovascular diseases and type 2 diabetes mellitus (T2DM) in the UAE, where 17.3% of the population aged 20 to 79 is affected with T2DM. Cardiovascular diseases and T2DM are few of the many disorders that can benefit from MSC therapy. Utilizing umbilical cord biowaste for such diseases can further build the UAE's status as a hub for medical tourism and accentuate it's growing prominence in the field of regenerative medicine.

الملخص

إن استخدام تقنيه الحلايا الجذعية المستخرجة من بقايا الحبل السرى قد يحدث ثورة في طريقة الرعاية الصحية و العلاج للعديد من الامراض المزمنة في دولة الإمارات العربية المتحدة. و تبدأ هذه التقنية بأصدار التعليات للمستشفيات لضرورة الاحتفاظ ببقايا الحبل السرى لما تتحويه من الحلايا الجذعية واستخدام هذه التقنية المستحدثة سيساعد على تقليل الضغط على المستشفيات في علاج و متابعه الحالات المرضية المزمنة ففي الولايات المتحدة الأمريكية سنويًا يتم علاج اكثر من ١٨٠٠ حالة مرضية مزمنة باستخدام تقنية الحلايا الجذعية و المستخرجة في الغالب من نخاع العظم و التي تتميز بالتكلفة العالية ولا تخلو من حصول بعض المضاعفات مثل العدوى الجرثومية و المكوث في المستشفى للمتابعة السربرية. ومن المقرر وضع خطة باستخدام تقنية عالية الكفاءة عن كيفية حفظ بقايا الحبل السري وكيفية الحصول على الخلايا الجذعية و طرق حفضها و تخزينها لاستخدامها في أوقات لاحقة لعلاج بعض الحالات المرضية و خاصة المزمنة منها كأمراض القلب و الأوعية الدموية و امراض السكر من النوع الثاني. وذألك لزيادة عدد المصابين بالسكر حيث هناك حوالي ١٧.٣٪ من المصابين بالسكر من عدد السكان في دوله الامارات. وأخيرا إن استخدام تقنيه الخلايا الجذعية سوف لا يقتصر على علاج أمراض القلب المزمنة والسكر، بل سوف يتم استخدام هذه التقنية في علاج العديد من الأمراض الأخرى. وهذا بالتأكيد سيعطى دعما متزايدا للرعاية الطبية المتميزة في دولة الإمارات م سيزيد من السياحة الطبية في دولة الإمارات لغرض العلاج والمتابعة الطبية.

Keywords: Regenerative therapy, Mesenchymal stem cells (MSCs), Umbilical cord, Biomedical waste الكلمات المفتاحية: الكلمات المفتاحية: العلاج التجديدي، الخلايا الجذعية، الحبل السري، النف



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1. Introduction

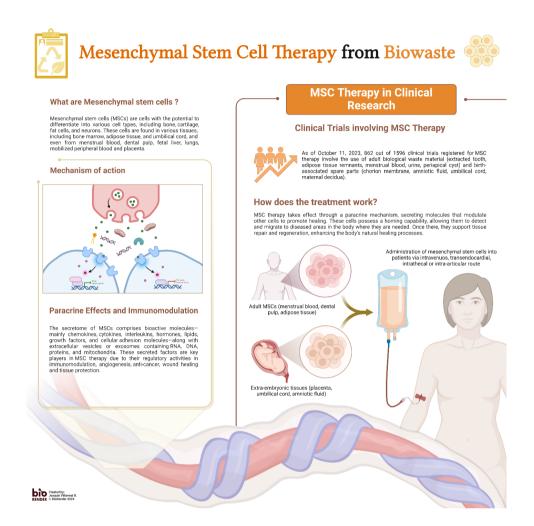
Biowaste is defined as any biodegradable organic material originating from vegetable, animal, or human sources, generated domestically and industrially, such as the food industry (Jiménez-Rosado et al., 2023) and healthcare facilities. Medical waste, defined by the World Health Organization, includes needles, syringes, diagnostic samples, blood, chemicals, pharmaceuticals, medical devices, and body parts. These body parts or discarded tissues include skin and fat tissues from abdominoplasty procedures, aborted fetuses, extra-embryonic tissues like the placenta, umbilical cord, and amniotic fluid, as well as human physiological waste such as urine, menstrual blood, hair, and deciduous teeth. These biomedical wastes represent a sustainable cell source for mesenchymal stem cells (MSCs) therapy (Wan Kamarul Zaman & Abdullah, 2023; Figure **1**).

MSCs are multipotent stromal cells capable of differentiating into various cell types, including bone, cartilage, fat cells, and neurons. These cells are found in various tissues, including bone marrow (BM), adipose tissue (AT), and umbilical cord (Musiał-Wysocka et al., 2019), and even from menstrual blood (Uzieliene et al., 2018), dental pulp (Kawashima et al., 2017), fetal liver (Fan et al., 2019), lungs (Hostettler et al., 2017), mobilized peripheral blood (Wiegner et al., 2018) and placenta (De La Torre et al., 2019). MSC therapy holds great potential due to its paracrine effect, homing capability, and immunomodulatory activity. These are effective in treating conditions like spinal cord injuries (Xia et al., 2023), autoimmune diseases (Galderisi et al., 2022; Mezey, 2022), and neuroinflammatory disorders such as Parkinson's and Alzheimer's Disease (Mattei & Delle Monache, 2024). However, due to the issues related to cell engraftment or homing to the site of injury post transplantation, current research is also focused on developing MSC-based cell-free therapies by investigating the paracrine factors (or the secretome) through which MSCs exert their effect in healing responses (Yu et al., 2023). The survival rate of MSCs after transplantation has been shown to be <5%, which critically impacts the therapeutic outcome, as the paracrine and immunoregulatory functions of MSCs are dependent on their viability (Garcia-Sanchez et al., 2019). Similarly, homing capabilities are also constrained by various factors, including reciprocal interactions between cells, the extracellular matrix, and bioactive factors (Noronha et al., 2019).

The MSC secretome comprises bioactive molecules—mainly chemokines, cytokines, interleukins, hormones, lipids, growth factors, and cellular adhesion molecules—along with extracellular vesicles (EVs) or exosomes containing RNA, DNA, proteins (Han et al., 2022; L. et al., 2019), and mitochondria (Liu et al., 2024). These secreted factors are key players in MSC therapy due to their activities in immunomodulation, angiogenesis, anti-cancer, and tissue protection (Javan et al., 2019). The primary mechanisms driving MSC immunomodulation and angiogenesis include direct cell-to-cell contact and paracrine signaling, which are activated by cytokines, chemokines, EVs, and inflammatory stimuli (Song et al., 2020). The angiogenic modulation by MSC-derived secretome is achieved through a complex synergistic interaction among various bioactive molecules carried by EVs, including microRNA (miRNA), transfer RNA (tRNA), long noncoding RNA (IncRNA), growth factors, proteins, and lipids (Maacha et al., 2020). UC-MSC secretome has been shown to significantly reduce cell viability and proliferation, inhibit migratory behavior, and suppress PI3K/AKT activation in prostate cancer (Sousa et al., 2023).

Figure 1

Mesenchymal stem cell therapy from biowaste.



1.1. MSC therapy in clinical trials

From 1995 to 2020, 1014 clinical trials have been registered for MSC therapy on the US National Institute of Health–ClinicalTrials database (http://clinicaltrials.gov) (Jovic et al., 2022). While some have ended prematurely, others have been completed and are about to reach Phase III of their clinical trials. These clinical trials cover various conditions, with many related to cardiovascular diseases, brain and neurological disorders, muscle, bone, and cartilage diseases, lung and bronchial diseases, wounds and restorations, and immune system diseases.

For brain and neurological disorders, a Phase-II clinical study (NCT02166021) by Petrou *et al.* explored the therapeutic effects of BM-MSCs in treating multiple sclerosis (MS). These patients were injected either intrathecally or intravenously. The results indicated a favorable tolerance for the treatment, as only three serious adverse events were reported, none of which were related to the treatment. Two events were associated with MS relapses, and one involved an upper respiratory infection, which was resolved with a dose of antibiotics. Results also included short-term health benefits such as changes in the Expanded

Disability Status Scale (EDSS) score. The study was more effective for the intrathecal injection showing more effectiveness than intravenous administration(Petrou et al., 2020). However, a Phase-III study is still needed to further assess these conclusions.

For immune system diseases, a clinical study with patients suffering from autoimmune refractory epilepsy treated them with autologous AT-MSCs (NCT03676569). These patients underwent liposuction followed by enzymatic isolation of the AT-MSCs, which were later administered via intrathecal injection. The study proved safe and showed clinical improvement, demonstrating enhanced social functions and intellectual performance in these patients (Szczepanik et al., 2020).

In cardiovascular diseases, the SENECA trial (StEm cell iNjECtion in cAncer survivors; NCT02509156) explored the use of allogenic BM-MSCs to improve cardiac performance in cancer survivors with anthracycline-induced cardiomyopathy (AIC), proving safe and effective in Phase I. However, Phase II and III clinical studies are needed to properly assess efficacy (Bolli et al., 2018).

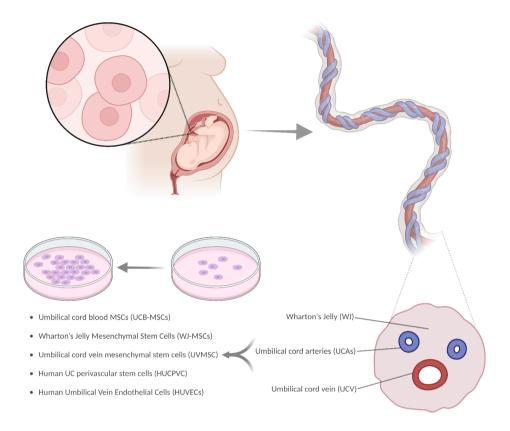
Regarding muscle, bone, and cartilage diseases, the JOINTSTEM study (NCT02658344) used autologous adipose-derived mesenchymal stem cells (AD-MSCs). Twenty-four patients were treated using MSCs extracted from their own lipoaspirates obtained from abdominal subcutaneous fat to treat knee osteoarthritis. These patients were injected intra-articularly and followed for six months to assess clinical efficacy. The results showed functional improvement and pain relief without causing any adverse effects (Lee et al., 2019).

Similarly, the secretome from MSCs has been explored in a clinical setting. In a Phase-I single-arm clinical trial called MEXVT (NCT04313647), 24 healthy volunteers received a nebulized form of human adipose-derived MSC-EVs (haMSC-EVs) to assess its safety for future clinical applications to treat lung injury diseases. This clinical study proved safe for the volunteers, and in a preclinical model with mice suffering from lung injury due to exposure to *Pseudomonas aeruginosa*, this treatment reduced lung inflammation and the histological severity of the disease (Shi et al., 2021). After the success of this clinical study, seven severe COVID-19 related pneumonia patients presenting acute respiratory distress syndrome (ARDS) were enrolled in a phase-II clinical trial (NCT04276987) to receive the nebulized haMSC-Exos. Within seven days, these patients presented a safety profile followed by CT imaging improvement (Zhu et al., 2022).

Most of these clinical trials have used both allogenic and autologous sources of BM-MSCs and AT-MSCs. However, recent research and clinical trials have shifted toward using umbilical cord-derived MSCs (UC-MSCs) due to their longer-lasting paracrine effects (Hoseini et al., 2024) and their richness in angiogenic factors (Farkhad et al., 2021) compared to other MSC sources. Additionally, these cells are easier to harvest and pose no health threats when collected, making them an ideal alternative candidate (Mebarki et al., 2021).

Figure 2

Composition of the umbilical cord.



1.2. Cell sources from the umbilical cord

As of October 11, 2023, 451 out of 1596 clinical trials registered for MSC therapy involved umbilical cord blood MSCs (UCB-MSCs), and Wharton's Jelly Mesenchymal Stem Cells (WJ-MSCs) due to their higher proliferation capacity (Vieira Paladino et al., 2019), lifespan, and differentiation ability (Liau et al., 2020; Mastrolia et al., 2019). However, these cells are not the only type obtainable from umbilical cords.

The vascular system of the umbilical cord comprises two umbilical arteries (UCAs) and one umbilical vein (UCV) embedded inside mucous tissue known as Wharton's Jelly (Medina-Leyte et al., 2020; Figure **2**). Umbilical cord vein mesenchymal stem cells (UVMSC) have been studied for regenerative applications, including genetic manipulation to enhance their therapeutic power (Nowakowski et al., 2016).

The umbilical cord consists of several main components: arteries, a vein, and Wharton's Jelly. Various cell types can be found within these structures, including UCB-MSCs, WJ-MSCs, UVMSC, human umbilical cord perivascular stem cells (HUCPVC), and human umbilical vein endothelial cells (HUVECs).

Another type of UC-MSCs are unrestricted somatic stem cells (USSC), which are in a state between embryonic stem cells (ESCs) and terminally differentiated cells. These cells hold the potential to differentiate into cell types from all germ layers (Schorn et al., 2019), making them ideal alternative candidates for ESC research to avoid the ethical issues related to the use of ESCs. These cells offer

similar advantages and hold as much promise as Multilineage Differentiating Stress Enduring (MUSE) cells, another cell type derived from extra-embryonic tissues like the umbilical cord (Leng et al., 2019). MUSE cells are regarded as pluripotent stem cells capable of differentiating into all germ layers, and they do not require HLA matching, making them an excellent candidate for regenerative therapy (Yamashita et al., 2021). Furthermore, MUSE cells exhibit superior properties compared to other somatic cells that claim to be pluripotent, such as very small embryonic-like (VSEL) stem cells found in UCB, which have been shown to lack some key stem cell characteristics (Danova-Alt et al., 2012).

In the context of treating challenging skin defects, HUCPVC have been studied as a potential alternative to BM-MSCs due to their higher proliferative rate and frequency. These cells demonstrated accelerated wound healing, proving to be ideal candidates for dermal tissue engineering (Azari et al., 2022).

Another important model system for regenerative therapy is HUVECs. HUVECs, easily accessible and cultured, express numerous key endothelial cell (EC) markers, junctional proteins, and inflammatory proteins, serving as a model for in vitro validation studies and drug validation (Hauser et al., 2017). HUVECs are noted for their angiogenic capabilities, which are useful in revascularization strategies like bioprinting technologies (Shafiee et al., 2021). In fact, in addition to their application for in vitro studies of vasculature and angiogenesis, HUVECs are one of the most commonly employed mature ECs in vascularized bone engineering (Kocherova et al., 2019; Pirosa et al., 2018).

Derived from the umbilical cords of healthy mothers and babies, HUVECs offer an ideal model for studying primary human ECs, enhancing the translational potential of research beyond traditional animal studies or nonhuman cell lines. They possess inherent properties, including proliferation and differentiation, angiogenesis, and immunomodulatory abilities, that are crucial for treating cardiovascular diseases, wound healing, and ischemic conditions where restoring blood flow and tissue perfusion is essential (Qu et al., 2020).

The HUVEC model has proven especially valuable for studying the impact of hemodynamic forces on the endothelium and atherosclerotic plaque formation. This model allows researchers to expose ECs to shear stress under controlled flow conditions, effectively mimicking the blood flow conditions found in vivo (Alhawarat et al., 2019; Jia et al., 2017). HUVECs have been useful in studying an array of biological processes and diseases, such as inflammation, diabetes, cardiovascular conditions, cancer, and regenerative medicine, offering advantages in accessibility and therapeutic potential (Alhawarat et al., 2019; Cao et al., 2017; Di Tomo et al., 2021; Yin et al., 2022).

1.3. Clinical trials with UC-MSCs

Current trends in MSC therapy clinical trials have shifted toward the use of UC-MSCs, covering a wide range of diseases. One example relevant to the UAE context is the use of UC-MSCs for treating diabetes. Several studies have been launched to treat this disease using different cell sources of UC-MSCs. In China, a clinical study involving 29 patients recently diagnosed with type 1 diabetes mellitus treated them with WJ-MSCs, with follow-ups for two years. The study confirmed no major side effects and demonstrated

that the therapy could restore the functionality of islet β cells over a long observational period, positioning the treatment as a potentially effective strategy for type 1 diabetes (Hu et al., 2013).

The use of UC-MSCs has also demonstrated promising results in the treatment of spinal cord injuries. Two clinical trials (NCT01046786 and NCT01354483) used UCB mononuclear stem cells to treat 20 patients suffering from chronic spinal cord injuries. Patients received intramedullary injections and were followed up for 12 months. By the end of the study, patients exhibited improvements in their motor function, walking index of SCI (WISCI), and spinal cord independence measure (SCIM) scores. They also no longer required assistance for bladder or bowel management (Zhu et al., 2016).

The transplantation of UCB has also shown promising results in cancer treatment. A multicenter clinical trial by Eapen *et al.* compared 503 leukemia patients who received BM and umbilical cord transplants, finding that those who received UCB transplants had a lower risk of transplant-related mortality due to better human leukocyte antigen (HLA) matching. This study underscores the need for larger-scale banking of UCB to increase HLA diversity (Eapen et al., 2007).

Clinical trials with UC-MSCs reveal that these cells are as effective as BM-MSCs and AT-MSCs in treating various diseases and possess superior properties. UC-MSCs have higher HLA matching compatibility (Eapen et al., 2007), a lower risk of teratoma formation, and less immunogenicity with a better immunosuppressive ability for clinical use (Abbaspanah et al., 2021; Medina-Leyte et al., 2020; Tesarova et al., 2020). All these factors make UC-MSCs a more suitable candidate for regenerative therapy.

1.4. Future perspectives

Despite UC-MSCs being a better and more sustainable alternative for MSC therapy and research, obtaining these cells is still hindered by regulations in several countries and hospital policies that mandate discarding this valuable material as medical waste (Atala et al., 2018), missing an opportunity to leverage these biological resources and to bridge the gap between the demand for stem cell therapies and the available supply. This policy commentary highlights the importance of umbilical cords for MSC extraction and proposes policy changes to facilitate their collection and use in the UAE.

2. Existing Policies

2.1. Current policies in the UAE

In the UAE, umbilical cords are typically treated as medical waste and discarded after delivery. This practice is common across many hospitals in the region, where hygiene and safety protocols often precede potential medical benefits. Hospitals are required to have a specialized company regularly collect, transport, and destroy medical waste materials in accordance with the Public Health Department (Dubai Health Authority DHA, 2021). While these protocols aim to prevent contamination and ensure patient safety, they unintentionally limit innovative medical practices.

2.2. Alternatives and international models

In 2006, the Dubai Cord Blood and Research Centre (DCBRC) was established as a government entity, functioning as a hybrid public–private cord blood bank. The center successfully secured over 8000 cord blood units. Although the DCBRC initially launched as a public biobank, it eventually transitioned into a private cord blood bank and no longer offers public biobanking. Currently, M42 Healthcare in the UAE is undertaking an initiative to establish a new cord blood bank. However, this effort is limited in scope, focusing solely on cord blood and overlooking the potential of umbilical cord tissue and other biowaste from healthcare institutions that could be repurposed for research and therapeutic applications. Additionally, private cord blood banking is available in the UAE, however, the financial responsibility falls on the parents, and public awareness about these services remains low as there is insufficient comprehensive information to educate parents on the benefits. In contrast, private cord blood banking is prohibited in countries like France and Italy (Beltrame, 2019).

Internationally, the UK and Spain have succeeded in establishing public cord blood banking institutions supported by national health policies. These programs highlight the viability and advantages of systematic umbilical cord collection and storage. For instance, Spain's national health system incorporates cord blood banking into standard prenatal care, ensuring a consistent supply of umbilical cords for research and therapeutic purposes. Additionally, the United States launched the Stem Cell Therapeutic and Research Act in 2005, which supports the National Cord Blood Program and ensures the collection of 150,000 cord blood units (Kapinos et al., 2017).

3. Policy Recommendations

3.1. Create a national umbilical cord bank

To guarantee a sustainable and fair supply of MSCs, the UAE should consider establishing a national umbilical cord bank. This facility would handle the collection, processing, and storage of UCB and tissue, thereby making MSCs accessible for therapeutic applications. This initiative would also foster research and development in stem cell therapy, driving the field forward.

The creation of this bank should follow international models for public cord blood banking to adhere to international standards and regulations. However, this bank should also utilize all cells present in the umbilical cord and not just the cord blood, which is often a common practice for private biobanking. Therefore, the tissue should be used to harness all stem cells, such as WJ-MSCs and HUCPVC.

3.2. Incentivize private sector participation

Provide grants for private companies to establish and maintain umbilical cord banks. These incentives would encourage private-sector investment in umbilical cord cell banking, expanding the available infrastructure.

Encourage public–private partnerships to expand collection and storage capacity. By collaborating with private companies, public health institutions can leverage additional resources and expertise, enhancing the overall effectiveness of umbilical cord cell banking programs.

3.3. Facilitate collection and storage of Umbilical Cord MSCs

Implementing hospital-based programs for umbilical cord collection can ensure a steady and dependable supply. Integrating these programs into existing prenatal and delivery care routines would minimize disruption and ensure a seamless collection process. Medical staff can be trained to manage collections effectively without interrupting standard procedures. Establishing standardized collection, processing, and storage protocols in hospitals across the UAE is crucial. Access should be granted for following the chain of identity and chain of custody through appropriate channels.

3.4. Streamline regulatory approvals for MSC therapies

It is essential to collaborate with medical professionals, regulatory bodies, and bioethicists to develop standardized, evidence-based protocols that incorporate best practices from international models. These guidelines should cover consent, privacy, and ethical issues to build parental trust and ensure ethical and transparent collection practices. Simplifying the regulatory framework for stem cell therapies in the UAE would facilitate MSC-based treatments' approval and adoption. Aligning regulatory guidelines with international standards would make the UAE a leader in regenerative medicine and attract global collaboration and investment.

3.5. Promote public awareness and education

Raising public awareness about the benefits of umbilical cord-derived MSCs is vital for the successful implementation of these policies. Educational campaigns should target expectant parents, informing them about the significance of umbilical cord donations and potential therapeutic applications. Utilizing tools such as social media platforms can enhance these efforts by reaching a broad audience. Social media can be leveraged to share informative content, success stories, and interactive resources that engage and educate parents about the benefits and procedures of umbilical cord donation. Additionally, healthcare providers should receive comprehensive training on the benefits and procedures of umbilical cord collection, equipping them with the necessary skills and knowledge. They should be prepared to offer accurate information and guidance to parents contemplating umbilical cord donation, complementing the information shared through digital platforms.

3.6. Pilot programs

Initiate a pilot program involving collaboration between an academic lab and a hospital to refine processes and demonstrate feasibility. Such programs can gather valuable data on collection rates, costs, and outcomes, which can inform broader implementation strategies. Thorough data analysis will identify potential challenges and optimize the collection process.

4. Conclusion

Effectively utilizing umbilical cord MSCs offers a unique opportunity to address the growing demand for stem cell therapies in the UAE and beyond. By adopting policies that support the collection, storage, and use of umbilical cords, the UAE can ensure a sustainable and equitable supply of MSCs. This strategy not only promises to enhance patient outcomes but also positions the UAE as a leader in regenerative medicine. The country's significant burden of diseases such as T2DM, underscores the urgent need for advanced treatment options. With the potential to alleviate conditions that are currently difficult to manage with existing therapies, umbilical cord-derived MSCs could play a crucial role in improving health outcomes.

By implementing collection and storage of biowaste policies in hospitals, the UAE can drive forward MSC research and treatment, solidifying its role as a leader in this emerging field. Policymakers must act promptly to harness the potential of umbilical cord-derived MSCs and propel advancements in stem cell therapy. Discarding umbilical cords represents a missed opportunity for progress in regenerative medicine, making the establishment of hospital-based collection programs with clear protocols and training essential for unlocking the full medical potential of these valuable resources.

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Competing Interests

The authors declare no conflict of interest.

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Joaquín is currently pursuing a PhD in Biomedical Engineering at Khalifa University, focusing on stem cell research. He completed his MSc in Bioengineering at King Abdullah University of Science and Technology in Saudi Arabia, with a project focused on neuroscience. With experience in the healthcare industry, he has been involved in clinical research projects and worked to establish a clinic for stem cell treatment in Mexico. His advanced research in Stem-Cell Secretome Therapies and Regenerative Medicine aims to develop innovative solutions for unmet clinical needs by bridging the gap between laboratory science and clinical translation.

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Dr. Kohli, an Assistant Professor at Khalifa University since 2022, holds a PhD in Biomedical Science from Aston University, UK, where she earned several awards, including the Best Young Investigator Award at EORS 2012. Her postdoctoral work at RAFT in London led to a patented biomaterial for bone defect healing, now being commercialized. At Imperial College London, she established a preclinical testing facility for 3D-printed implants that employed a multidisciplinary approach to enhance implant testing. Her research focusses on stem cell secretome therapies, regenerative medicine, and 3D biomaterials, aiming to translate innovative laboratory findings into practical clinical solutions.

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