



CASE REPORT

# Comparison of Natural Multipotent Stem Cell and Induced Pluripotent Stem Cell Therapeutic Applications: Benefits and Challenges

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## ABSTRACT

Natural Multipotent Stem Cell preparation is unique and safe when compared with other methods. Using this technology, American Stem Cell Base Dr. Wang has treated more than 100 kinds of diseases, made thousands of transplantations, with excellent cure rate (> 90% cured or great improvement per clinical end point measurement) and most importantly, there are no significant side effects. In 2012, the Nobel Prize-winning medical technology, Induced Pluripotent Stem Cell, invigorated stem cell research as it showed that Induced Pluripotent Stem Cell has the potential to produce every type of cell and tissue in the body. However, the inherited properties of Induced Pluripotent Stem Cell were known as tumorigenicity, immunogenicity, and heterogeneity. In his 2024 review article, Dr. Yamanaka indicated that he had dedicated two decades of research aimed at overcoming these three difficulties. Given the potential for these cells to become cancerous stem cells, the widespread application of the technology in treating various clinical diseases might require collaborative research by scholars, scientists, and clinicians and potentially could take decades to resolve. Natural Multipotent Stem Cell, on the other hand, is a mature biotechnology with specialized technologies and capabilities for mass production. It has successfully treated over 100 long-standing and intractable diseases, potentially providing widespread relief to millions afflicted with these diseases. This study provided a side-by-side comparison of two leading and promising stem cell therapy candidates, natural Multipotent Stem Cell and Induced Pluripotent Stem Cell, in clinical applications and present the challenges and promises in stem cell therapy.

## Abbreviations:

**MSC:** Mesenchymal Stem Cell

**nMS:** Natural Multipotent MSC

**G-MSC:** Gingival Mesenchymal Stem Cell

**iPSC:** Induced Pluripotent Stem Cell

**nPS:** Natural Pluripotent Stem Cell

**hPSC:** Human Pluripotent Stem Cell

**hUC-MSC:** Human Umbilical Cord MSC

**ASC:** Adult Stem Cell

**ISCT:** International Society for Cellular Therapy

## Introduction:

Stem cells have self-renewing abilities and the capabilities to differentiate into cells with specialized functions. They serve as a reserved repair system for the body. They are used to regenerate tissues and cells in the body that have been damaged or destroyed by disease. Stem cells come in three different varieties: adult stem cells, embryonic stem cells and induced pluripotent stem cells (iPSCs).<sup>1</sup>

The process of isolating embryonic stem cells has been controversial and raises ethical concerns as it results in the destruction of the embryo. On the other hand, adult stem cells (ASCs) represent an ethically acceptable source of extremely rare stem cells, which might be lower than 1% of a given cell population. With technology, stem cells can now be obtained and isolated from the umbilical cord, the placenta, amniotic fluid, etc.

In 2006, a Japanese team led by Shinya Yamanaka discovered that mature cells can be reprogrammed to become pluripotent stem cells. In 2012, this Nobel Prize-winning medical technology was termed induced pluripotent stem cells.<sup>1</sup> This discovery has invigorated stem cell research as it showed that iPSC has the potential to produce every type of cell and tissue in the body. Thus, iPSCs are promising candidates for tissue engineering and regenerative medicine. The treatment of human disease with iPSCs could revolutionize the health care industry with its ability to generate any cell, tissue, or even organ, "on-demand" in the laboratory.<sup>2</sup>

However, iPSC research has its share of challenges. One of the major concerns with the potential clinical application of iPSCs is their propensity to form tumors, as a result of either the inducing agents or incomplete reprogramming.<sup>3,4</sup>

At TOP IVF USA, American Stem Cell Base, Dr. Fu-Nan Wang, MD, PhD., recognized the potential benefits that stem cells have and embarked on the challenges of using allogeneic cell transplantation in stem cell therapy. When the field was still in its infancy, restrictions were placed on stem cell search making it difficult for scientists to pursue this promising medical research. However, Dr. Wang was undeterred. He envisioned that patients from around the world could safely receive allogeneic stem cell treatment at effective concentrations.<sup>5</sup>

The Natural Multipotent MSC (nMS) preparation technology is a great endeavor that can be used for clinical treatment. It has not exhibited any noticeable adverse side effects as the safety ratio was found to be close to 100%. The efficacy ratio of measurable clinical

endpoint was greater than 90% because of natural culture "adaptation" rather than that of induced stem cells. The lab has found and cataloged different types of stem cells preparation and has applied them to clinical treatment with great success. Regarding the successful clinical treatment of stem cells, examples of relevant case reports have been published in peer-reviewed medical journals.<sup>5-8</sup>

The scope of this communication is to introduce a novel stem cell isolation technique and details a science-based approach and evidence-driven clinical data, a sustainable, scalable production process over three decades, where thousands of cellular treatments were delivered against more than 100 different kinds of intractable diseases. The purpose is to provide a side-by-side comparison of two leading stem cell therapy candidates, nMS and iPSC, in clinical applications and present the challenges and promises in stem cell therapy. All iPSC data presented were obtained through PubMed literature search, published through the NIH National Library of Medicine.

## Methods:

### INDUCED PLURIPOTENT STEM CELL (iPSC)

Induced pluripotent stem cell is a type of pluripotent stem cell that can be generated directly from a somatic cell. Nobel prize awarded medical advancement demonstrated that overexpression of four transcription factors can reprogram the somatic cells to a pluripotent state by rearranging their epigenetic landscape, proving cellular identity is epigenetically regulated. These four transcriptional factors collectively were called Yamanaka factors, include Oct4, Sox2, Klf4 and c-Myc (OSKM). These cocktails of transcription factors regulate signaling pathways, epigenetic modifications, and microRNAs to establish pluripotency. Human iPSCs are autologous, are established by ectopic expression or direct delivery of certain mRNAs or proteins and free from major ethical concerns, but are prone to transcriptional and epigenetic aberrations.<sup>1,4</sup>

We searched for papers published through the NIH National Library of Medicine, the PubMed database, using the search strings [iPSC] AND [cell therapy] AND [efficacy] AND [side effect], and the search strings [iPSC] AND [clinical trial]. Relevant information in publications were cited and discussed in this manuscript.

### NATURAL MUTIPOTENT STEM CELL (nMS) PREPARATION

The study design of natural multipotent mesenchymal stem cell isolation has been researched with a comprehensive and systematic approach to elucidate the most thorough and effective stem cell isolation technique. For example, about 10 -15 cm of fresh umbilical cords is received from consenting donors. The general health examination status of stem cell donors was conducted under a comprehensive evaluation. Mesenchymal stem cells (MSC) from umbilical cords were prepared by the tissue explant method as described with minor modification.<sup>5-8</sup> Fresh umbilical cord tissue from a healthy donor was minced into small pieces and were cultured in  $\alpha$ -MEM (Thermo Fisher Scientific, Grand Island, NY, USA) supplemented with human platelet lysate (HPL, Fisher Scientific International, Pittsburg, Pennsylvania, USA). The concentration of HPL

was gradually increased to accommodate the cell growth. The medium was replaced three times a week, and adherent cells were allowed to reach 80 % - 85 % confluency before they were sub-cultured. There were no decomposing agents or digestive enzymes used during the stem cell isolation and expansion only biophysical methods such as brief cold temperature shock (4°C - 8°C) or a small brush to detach the adhesion cells from plastic surface. During the expansion process, the cell culture was incubated under a standard hypoxia condition (carbon dioxide, oxygen and balanced with dry nitrogen), and the culture was observed under an inverted microscope for cell attachment, morphology and any microbial contamination, etc. Freshly isolated stem cells were designated as P<sub>0</sub>, routine cell count, and viability assay was performed accordingly, cells passage after 7 (P<sub>7</sub>) were harvested and stored in shipping buffer. With technology, stem cells can now be obtained and isolated from many sources such as umbilical cords, the placenta, amniotic fluid, menstrual blood, gingiva, deciduous tooth, adipose tissue and skin tissue etc., except for nail, hair and keratin.

### Case Report Data:

The clinical results were captured in a real-time medical examination record, backed by laboratory diagnostic results, and the attending physicians' assessment based on established measurable clinical end points were noted, and the results were recorded in each patient's medical case summary.

### Results:

At American Stem Cell Base, our team has isolated and cataloged stem cells from bone marrow, umbilical cord tissue, adipose tissue, menses blood, and gingival tissue. These cells exhibited standard fibroblast-like morphology without significant difference in appearances under inverted microscope. We have strong evidence that different types of stem cells have specific functionalities associated with their sources. We are in preparation of a manuscript entitled "The Miraculous nMS Lineages Successfully Treating 100 Plus Intractable Diseases – Systemic Summary". Figure 1-7 illustrated the isolation and microscopic features of nMS lineage morphological images.

Natural Pluri-Potent Stem Cells (nPS stem cells), also known as embryonic stem cells (ESCs) are derived from the inner cell mass of the embryo at around the fifth day of embryonic development, also known as the Blastocyst Stage. Because they are extracted from embryonic cells, this raises ethical or sociological concerns. Pluripotent stem cells can develop into almost any cell type found in the human body, except for those that make up the placenta. This ability makes them an outstanding focus in modern biological research, offering new avenues for understanding human development and disease progression, and paving the way for advanced medical applications. The "nPS Stem Cells" differ from "iPS Stem Cells". The "i" in iPS stands for "induced," meaning they are artificially induced. The iPS cells are generated using various chemical drugs, viruses, and radiation to induce normal somatic cells into pluripotent stem cells, which are then converted into the desired types of stem cells for clinical application.

However, the major drawback and risk with iPS stem cells is the significant potential of becoming a cancerous threat.<sup>9,10</sup> Clinically, a considerable ratio of patients using iPS cells can experience various types and degrees of side effects, including the rapid induction of cancer in severe cases. iPSCs can accumulate chromosomal abnormalities, genetic instability, copy number variants and loss of heterozygosity over a period *in vitro* culture and expansion since these cells are maintained in culture for prolonged periods of time.<sup>11,12</sup> As such, tumorigenicity, immunogenicity, and heterogeneity may hamper attempts to deploy this technology therapeutically.<sup>4,13-15</sup>

On the other hand, MSC genetic stability is well documented. Cells that are cultured at physiological oxygen levels delay senescence and inhibit senescence-related genes, preventing cell cycle arrest. Even at the molecular level, microenvironmental control is multi-component and involves different players.<sup>16-18</sup> The freshly isolated cells were considered P<sub>0</sub> and they should have saved the "most primitive, original stem cells" or the "progenitor" of umbilical cord mesenchymal stem cells. It is believed that these "ancestors" were the most effective MSC of clinical treatment. Cells can be propagated for more than 20 passages and this natural preparation MSC is called "nMS". Given the fact that stem cells are so sensitive to environmental influence, the isolation process we have developed might be the most profound and effective preparation.<sup>19-22</sup>

These extensively expanded and cultured cells may lead to a gradual loss of the pluripotency of the cells and aging of the MSCs. Therefore, precise laboratory preparation environments and quality techniques are extremely important, including reducing the use of enzymes, minimizing manual laboratory procedures, etc. Many potential drawbacks have raised concerns among scientists, as the expansion of cultured cells may alter the expected biological functions of MSCs, potentially hindering their clinical therapeutic potential.

Currently, the preparation process of MSC aims to obtain "Natural Multipotent Stem Cell, nMS," which is considered the safest and most reliable technique. Although MSCs have been extensively studied, promoted, and applied in many laboratories worldwide, their isolation, expansion, and phenotypic identification standard protocols have not been fully established yet. There is not an individual biomarker that distinguishes MSCs from other types of cells. American Stem Cell Base has isolated MSC from various source and fully characterized and subjected them for medical application. For example, gingiva-derived MSC contains a population of neurocrest-derived stem cells, possess multipotent differentiation capacities and potent immunomodulatory effects, and exhibit a superior capacity for neurogeneration and are more valuable in potential applications for neurodegenerative diseases and nerve regeneration<sup>5,23</sup>. Bone marrow isolated stem cells are used in cancers, and blood disorder diseases<sup>6</sup>. We have validated morphology, spindle shaped and fibroblast-like cells, and the expression of classical surface markers on these nMS cells, isolated from each umbilical cord donor; surface clusters were conformed to the International Society for Cellular Therapy (ISCT) cluster marker display characterization

Comparison of Natural Multipotent Stem Cell and Induced Pluripotent Stem Cell Therapeutic Applications: Benefits and Challenges (CD 45<sup>-</sup>, CD 73<sup>+</sup>, CD 90<sup>+</sup>, and CD 105<sup>+</sup>). Table 1 exhibits the direct comparison between nMS and iPSC with respect to isolation technology and results of clinical applications.

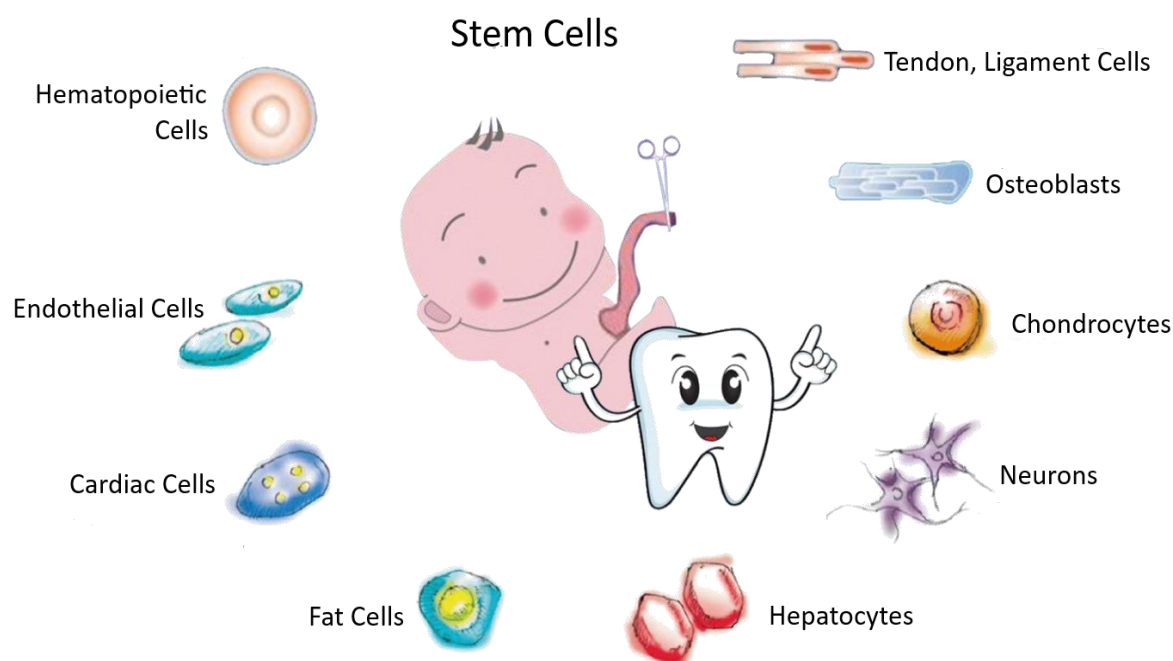
Figure 1 to Figure 3 depict a schematic presentation of stem cell isolation and culture diagram, Figure 4 to Figure 7 demonstrate the cell morphological features of the nMS

lineage culture and after subculture. Under microscopic observation these cells were pure, free of any contaminations, foreign objects, and the most important of all, these nMS lineage preparations have demonstrated outstanding efficacy in treating various intractable diseases, with thousands of transplantations administered, and displayed minimum or insignificant side effects, if any.

**Table 1:** Direct comparison between nMS and iPSC.

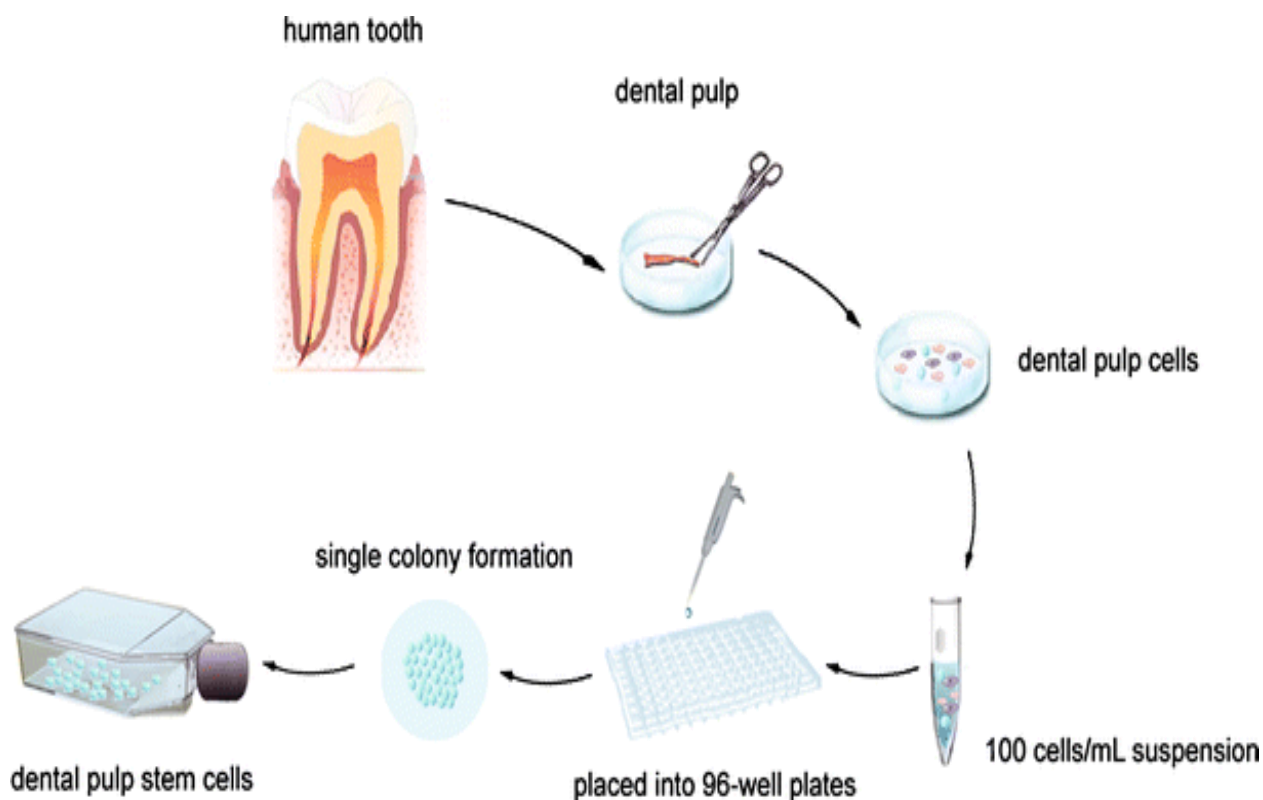
Item	Parameters	nMS	iPSC
1	Source of cell	Primary explant	Adult somatic cells <sup>1,4</sup>
2	Ethical or legal issue	None	None
3	Immunogenic limitation	None	HLA matching required
4	Isolation-culture expansion, Growth condition	Biological programming of safe culture expansion. No feeder cell, Hypoxia growth condition	Reprogramming of genome <sup>12,13</sup> Need feeder cell, Standard CO <sub>2</sub> Incubator
5	Addition of transcription factors	None	Oct4, Sox2, c-Myc, Klf4 <sup>10</sup>
6	Chemicals and enzymes used in isolation-creation	None	Yes
7	Life span	Well-controlled 60-80 generations with normal chromosome karyotype	Renew indefinitely
8	Differentiated cell types	nMS isolation from various cell types: Hematopoietic cells, osteoblasts, chondrocyte, neuron, cardiac cells, etc. (Figure 1~3)	Differentiate into many different cell types; pancreatic- $\beta$ cells, liver hepatocytes, cardiomyocytes, hematopoietic cells <sup>4</sup> , and dopaminergic neurons <sup>16-19</sup>
9	Targeted disease treatment	Almost every intractable disease, even at the end stage of colon cancer, prostate cancer, multiple myeloma <sup>6</sup>	Safety concern abound: Diabetes <sup>23</sup> , leukemia, and Parkinson's disease <sup>24,25</sup> , cancer therapy <sup>4</sup>
10	Successful cell transplantation	Successfully treated thousands of patients with excellent efficacy, without noticeable side effect	Successfully in animal models of Parkinson's disease <sup>24</sup> and liver cirrhosis <sup>4</sup> respectively
11	New drug screening	New Drug Application	Yes, with reservations
12	Roadblock to clinical: Safety	No safety concern, reliable, reproducible	Safety concern <sup>4</sup> : Immune rejection and compatibility <sup>9,10</sup>
13	Validated differentiating SOP GMP-compliant cultural SOP	Followed GMP Guidance: 21 CFR 210 & 21 CFR 211	Unknown.
14	Epigenetic memory	No adverse impact	Evidence of adverse impact <sup>14</sup>
15	Cost and Time for each treatment	Reasonable and affordable (1x10 <sup>8</sup> cells / Transplantation depending on disease status); cost is affordable even at high cumulative dose	It is too expensive and time-consuming <sup>10</sup>
16	Targeted patient	Allogeneic, autogenetic	Autogenetic
17	Tumorigenicity	Genetic stability	Teratoma and tumors <sup>25</sup> Mutation hot spot <sup>14</sup>
18	Immunogenicity	Minor or non-significant	Immune rejection <sup>26</sup> HLA Matching <sup>27-29</sup>
19	Heterogeneity	Minor or in-significant	Genetic background, integrity, impact /defect in differentiation <sup>30-32</sup>
20	Is there a psychological burden on patients and medical staff during cell transplantation?	No, safe, effective and reliable	Side effect, potential tumor formation <sup>4</sup>
21	What is the rate of disease control after treatment?	~90%	Unknown
22	Safety, sterility, efficacy	Excellent based on results of treating thousands of patients	Unknown, severe adverse side effects
23	Finished product handling	Store at ambient temperature for up to one week	Unknown or ultra-low temperature storage

**Figure 1:** A schematic illustration of Natural Multipotent cells from umbilical cord or tooth gingiva that are capable of proliferating and differentiating into various cell types.



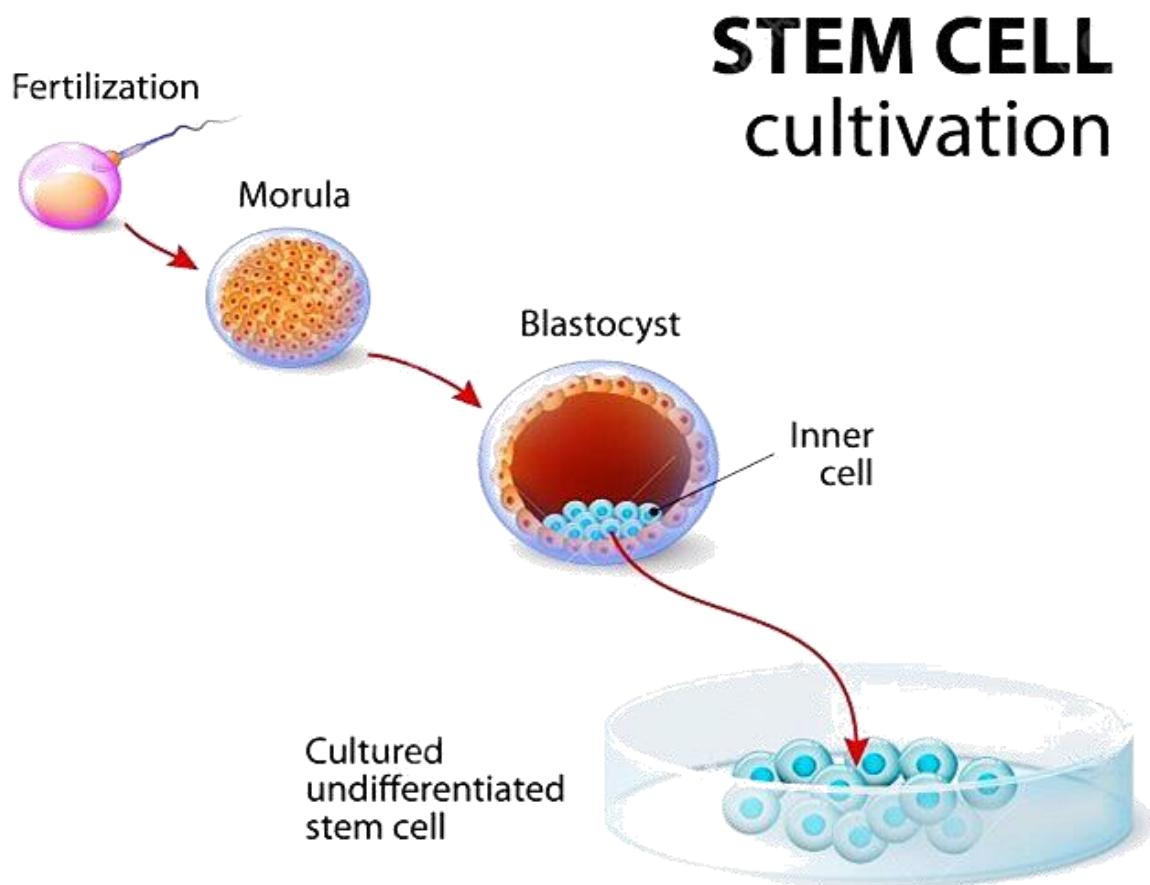
(Note: All images presented herein are for demonstration purposes only.)

**Figure 2:** A schematic diagram of dental pulp stem cell isolation. MSC isolated from gingival tissue is an excellent source to treat neurological diseases.





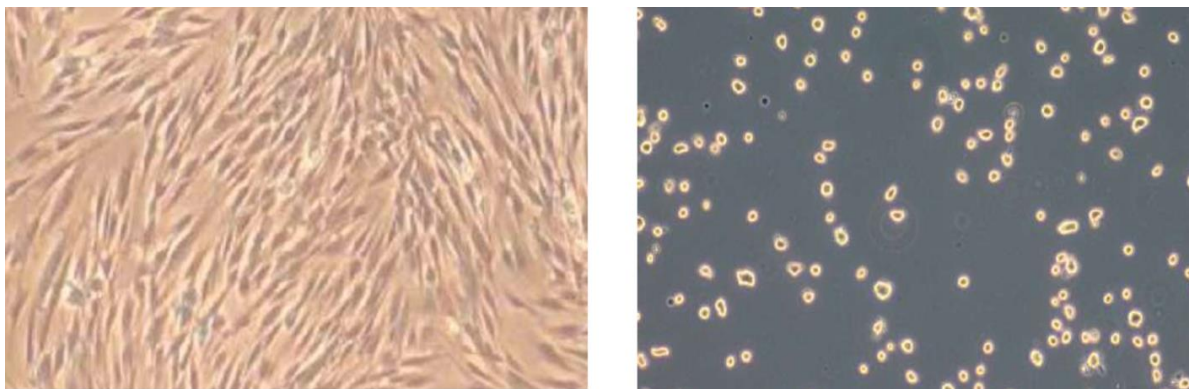
**Figure 3:** A schematic representation of pluripotent stem cell isolation.



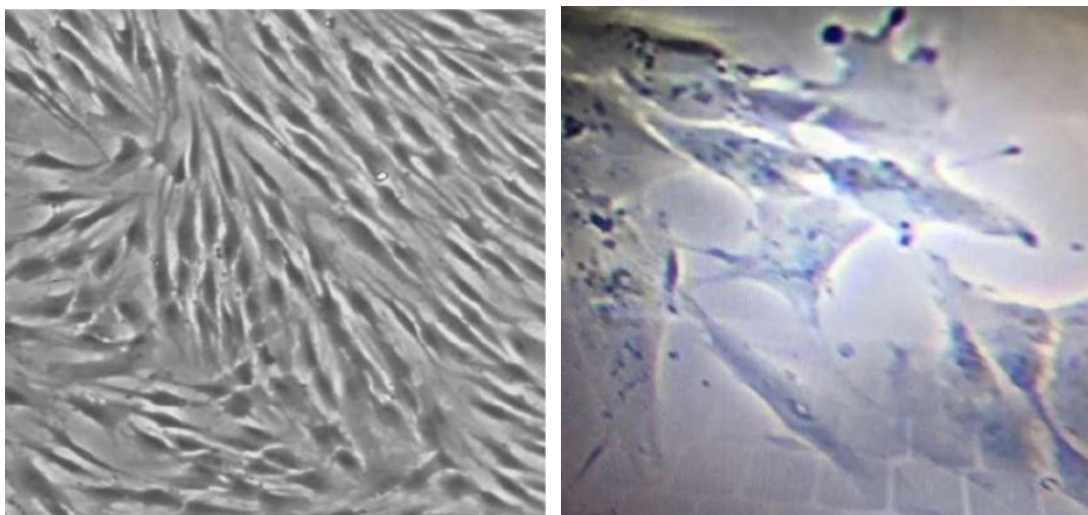
**Figure 4:** Micrograph from inverted miscopy demonstrating a kind of Natural Multipotent Stem Cell (nMS) Lineage after subculture from umbilical cord. Cells were maintained at standard hypoxia condition, under 5% CO<sub>2</sub>, 37 °C and 96% humidity incubator. The total stem cells were about 50 million on this culture dish surface, cells were fully alive, active, sterile, clean and without debris. Original magnification x 100.



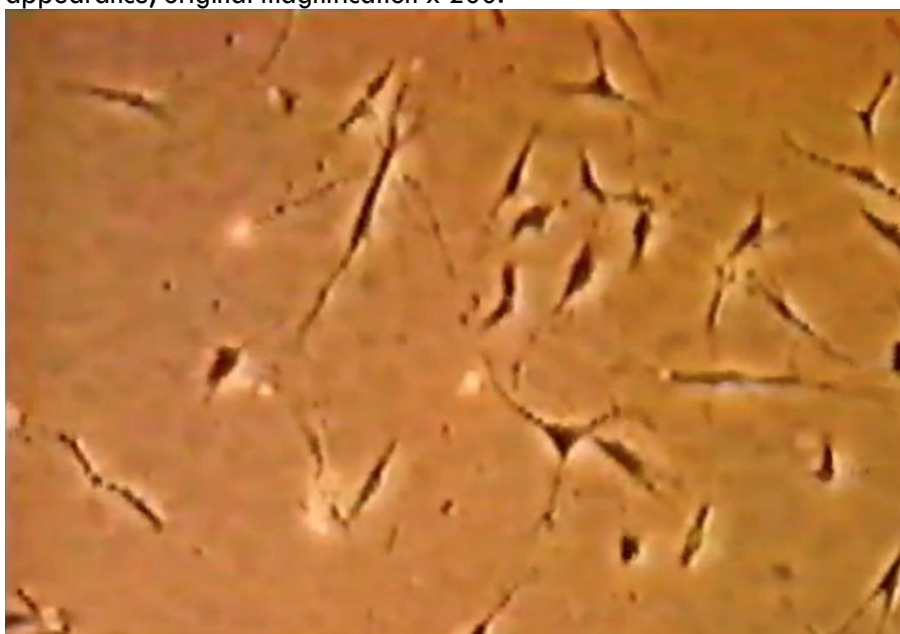
**Figure 5:** Comparison, difference, and advantages and disadvantages between nMS (left), and iPSC (right). Left: nMS stem cells were sub-cultured from a boy's deciduous tooth tissue, incubated under 5% CO<sub>2</sub>, 37 °C and 96% humidity incubator. Stem cells on the culture plate were fully alive, active, sterile, clean and without debris. No addition of any growth factors, chemical agents, effective; Right: iPSC stem cells were isolated from adult skin tissue, iPSC was a suspension culture and incubated under the same cultural condition as described above.



**Figure 6:** Top, Micrograph from inverted microscopy demonstrating the Natural Multipotent Stem Cell (nMS) Lineage after sub-culture from gingival biopsy tissue, cultural condition as described as Figure 5, cells are crawling on the plate, fully alive, active, sterile, clean and no foreign debris, free of contamination, original magnification x 300; Bottom, nMS, original magnification x 600. Harvested finished product nMS in shipping buffer, was stable at ambient temperature and general environment for up to seven days or more, without an incubator of 37 °C, CO<sub>2</sub>, O<sub>2</sub>, and fixed humidity supplies.



**Figure 7:** Micrograph from inverted microscopy demonstrating a kind of Natural Multipotent Stem Cell (nMS) Lineage after sub-culture from umbilical cord, the attachment MSC exhibits the key feature of fibroblast-like morphological appearance, original magnification x 200.



## Discussion:

iPSC medical technology has invigorated stem cell research as it shows that it has the great potential to produce every type of cell and tissue in the body. Thus, iPSCs are promising candidates for tissue engineering and regenerative medicine. The treatment of human disease with iPSCs might revolutionize the health care industry with its ability to generate any cell, tissue, or even organ, "on-demand" in the laboratory, albeit with limited success.<sup>1,4</sup>

However, iPSC research has its share of challenges. One of the major concerns with the potential clinical application of iPSCs is their propensity to form tumors, contributed by either the inducing agents, oncogenic gene set used for pluripotency induction, or incomplete reprogramming.<sup>30-33</sup> Per review articles, iPSC's tumorigenicity could be due to residual PSC, reprogramming factors or by genetical abnormality. These inherited properties of iPSC were better known as tumorigenicity, immunogenicity, and heterogeneity<sup>4</sup>. In his review article in 2024, Dr. Yamanaka indicated that he had dedicated two decades of research aimed at overcoming these three difficulties.

The main issue is the use of retroviruses to generate iPSCs as they are associated with cancer. More specifically, retroviruses can insert their DNA anywhere in the genome and subsequently trigger cancer-causing gene expression. Kamarda et al. showed that 84% of iPSCs transplanted in mice became weaker or died because of tumor development. Cancer-iPSCs have more potential risks. Their use in therapy should be used more cautiously. Stimulation or inhibition of specific factors increases the tumorigenicity risk of iPSCs.<sup>34,35</sup>

The technology of Natural Multipotent Stem Cell (nMS) preparation is unique and safe when compared with other methods. For example, tissue of gingiva or umbilical cord is processed by using biophysical technology bypassing chemicals and medicine, such as digestive enzymes (hyaluronidase or trypsin) for dissociation of the tissue, and antibiotics (Penicillin G Sodium, Streptomycin Sulfate and Amphotericin B, etc.) These nMS mesenchymal stem cell (MSC) preparations are unique and are used currently in this laboratory.<sup>5-8</sup>

After more than thirty years of research and experiment, "Dr. Wang's nMS Stem Cell Lineage" has been developed into a highly effective and efficient technique to culture stem cells with remarkable survivability and resilience. The MSC is able to survive without a fixed incubator at 37 degrees Celsius, without fixed 5% carbon dioxide, without fixed 20% oxygen, and without fixed humidity for more than seven (7) days, while maintaining physiological function for clinical application. This characteristic enables scaled nMS production, nMS bulk cells transportation and large-scale clinical administration a reality.

Dr. Wang's Team has successfully treated more than 100 diseases, made thousands of transplantations, treated just about every disease condition, with excellent treatment responses (> 90% cured or great improvement per clinical end point measurement) and most importantly,

there are no significant side effects. Dr. Wang has documented all case studies, published books and many peer-reviewed journal articles<sup>5-8</sup>.

Over the past 30 years, Dr. Wang and his team have made great strides to master unique skills. The team (1) is proficient in stem cell identification and preparation; (2) has proven efficacy in the clinical application of these stem cells; (3) has made breakthroughs in medicine and science by demonstrating nMS is a multi-target stem cell and capable of repairing damaged cells or tissues. His facility has successfully treated thousands of patients and has improved the largest variety of major and difficult human diseases via IV parenteral administration of MSCs. The records show Wang's team has broken through, greatly improved, and/or cured major intractable human diseases.

"Endogenous stem cells", the resident tissue-specific cells are unique, vital, and require special attention. They have not been fully understood or appreciated for their contributions in our daily lives, cell reproduction, cell alternation, cell repair, cell reproduction, and the aging process, but these cells continue to fulfill their role. In short, the unique and novel "Stem Cell Lineage" treatment regimen was developed, after performing thousands of stem cell transplantations. Our Stem Cell Lineage has successfully cured or significantly improved more than 100 kinds of human intractable diseases and their complications, including but not limited to, regenerative illnesses, cancer, congenital and hereditary diseases.<sup>35,36</sup>

In summary, Dr. Wang et al has discovered and taken advantage of four holistic qualities exhibited by stem cells:

1. Stem cells are "substances", they are living cells; they are visible, detectable, measurable, like a pro-drug, an active pharmaceutical ingredient circulating in the body, ready to act when call upon. Our unique nMS preparations might release many different types of normal "allogeneic groups", "biochemical substances", "signal substances", "information communication and transmission substances", many other "secretome" components and secreted hormones from normal, original stem cells. When these substances enter a diseased state of human cells, they slowly penetrate the diseased cells, subtly changing, repairing, and correcting its disease at a molecular level, thus achieving the purpose of "gene therapy".

2. Stem cells reveal "energy"; current evidence has demonstrated that in addition to growth factors and extracellular matrix cues, various metabolic energy pathways definitively provide important signals for the self-renewal and differentiation potency of stem cells. When used in a clinic setting, it is like a power charger empowering the patient with renewed active energy.<sup>1,4</sup>

3. Stem cells are "messengers", a communicator, and nMS circulates and communicate to affected niche-cells via biochemical factors or signals and then zero in to perform repair - regenerative action. It is through the combination of multiple nucleic acids and mRNA signaling that enable the precise controlled formation of functional tissues and organs via stem cell therapy. Furthermore, the ability to induce pluripotency through mRNA reprogramming has



afforded an increasing source of multipotent cells, and the same technology can be feasibly applied to efficiently induce differentiation to desired lineages in a reproducible manner, or to stimulate stem cell secretory functions.<sup>37,38</sup>

4. Stem cells represent an "electromagnetic wave", rendering an electromagnetic signal for holistic "body", "heart" and "spirit" treatment. The activity of natural healthy stem cells would emit weak "electromagnetic waves", using "electric field", "magnetic field" and "force field" to balance and interact with "body", "heart" and "spirit", that is, enabling total "body", "psychology" and "spiritual" health. Humans give off radiation<sup>38</sup>. In the brain and heart of the human body, the magnetism produced is most significant. The electromagnetic field (EMF) has an enormous impact on our body. By way of biochemical and or biophysical stimulation, it has been successfully used in physiotherapy for the treatment of bone disorders and osteoarthritic cells, as well as for cartilage regeneration or pain reduction. Stem cells reside in almost all tissues within the human body and they exhibit various electromagnetic potential and secrete growth factors to communicate with surrounding cells.<sup>39,40</sup>

The legality of stem cell therapy depends on how cells are used. Medical doctors are granted permission and privilege to treat patients with medical discovery and intervention, the US Federal "Right to Try Act". Stem cell therapy is legal in many countries, including the United States, but in the US different states have their own laws regarding stem cell research and therapy. The states of California and Massachusetts actively support stem cell research and provide funding. This has enabled the research and discovery of stem cell research. California Senate Bill 512, passed in 2017, championed by the California Institute for Regenerative Medicine (CIRM), aims to protect patients seeking stem cell treatments, with written notices about the therapy's unapproved status and potential risks. CIRM had funded clinical trials across a broad range of diseases, totaling 116 trials of which 7 were phase III trials, and conditions that include rare and genetic disorders, treatment-resistant and refractory diseases, and many forms of cancer. This has advanced both the education of regenerative medicine and the practical application of stem cell therapy.

## Conclusions:

The new medical technology of iPSCs has energized stem cell research as it shows that it has the potential to produce every type of cell and tissue in the body. Thus, iPSCs are promising candidates for tissue engineering and regenerative medicine, and could revolutionize the health care industry. However, tumorigenicity, immunogenicity, and heterogeneity may hamper attempts to deploy this technology therapeutically.<sup>4,13-15</sup> It is recommended that iPSC should be used for research purposes only and not for clinical treatment at present.

Over the last three decades, the team at American Stem Cell Base has made great efforts to develop stem cell treatment and research. The team (1) is proficient in stem cell identification and preparation; (2) has met good manufacturing practice (GMP) guidance with finished product rigorously tested to ensure sterility, potency and strength; (3) has proven efficacy in the clinical application of these stem cells; (4) has made breakthroughs in medicine and science by demonstrating nMS is potentially a multi-target or broad-spectrum stem cell lineage and capable of repairing damaged cells or tissues.

In the pursuit of frontier medicine, providing the safe, effective, affordable intervention and reproducible clinical product would be the goal and purpose of every medical researcher. It is both our duty and responsibility to report and communicate our novel nMS isolation technology, sustainable process, high quality finished products, affordable treatment regimen, and outstanding treatment results, as one of the most advantageous options available to the stem cell therapy community. Further, the harvested finished product nMS stored in shipping buffer remains active and effective for at least one week at ambient temperature and general environment, without a fixed 37 °C incubator, fixed CO<sub>2</sub> and O<sub>2</sub> and humidity control. There is solid evidence that depicts the effectiveness of nMS cells for regenerative therapies and increasing evidence supports their effectiveness in regeneration and repair, as such that makes nMS the gold standard of stem cell therapy for patients.<sup>41</sup>

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