



Exploring Novel Cell Sources to Overcome Limitations in Current Modalities

*Abdulkader Rahmo PhD
President SMSbiotech*

Cell Therapies Recent Attempts to Treat COPD

CLINICAL Studies

Safety

- No obvious safety issues including
- No infusional toxicity (cell emboli)
- No significant adverse effects for follow up period of 2 years

Efficacy

- No significant changes to pulmonary function
- No improvement of quality of life
- Lower CRP, T cells

Explanation

- MSC low engraftment
- Cell death
- Source of cells: aged, frozen
- Dose and timing
- Patient severity of disease
- Difficult delivery to distal alveoli septa

Very little evidence that MSC is recruited to lung; treatment is artificial rather than an augmentation.

Documented Clinical Trials

ClinicalTrial.gov	Intervention	Amount of Cells	Starting Date
NCT00683722	Allogenic BM-MSC four monthly infusions	1.3M/kg/infusion	2008
NCT01110252	Autologous BMMC single infusion	Not clear	2010
NCT01306513	Autologous BM-MSC three infusions	10-30k/kg/infusion	2011
NCT02216630	Autologous Ad-MSC	Not available	2014
NCT02348060	Autologous Ad-MSC	Not available	2015
NCT03909750	Autologous Ad-MSC	Not available	2019
NCT04047810	Allogenic, intravenous, once	0.5- 2 million cells/kg	2020

Regenerative Cell Therapy: Disappointment!

MSC Cell Therapy

Category	Approximate Count
MSC clinical trials	~1,600+ worldwide
MSC Phase III	~70–90
Approved MSC Worldwide	~12 products
MSC products (U.S.)	1 (Ryoncil)

Category	Obstacle
Scientific / Biological	Cell heterogeneity
	Poor engraftment or persistence
	Unclear mechanism of action
	Immune rejection (allogeneic)
	Tumorigenicity risk
Manufacturing / CMC	Scalability
	Lot-to-lot variability
	Potency assay development
Clinical / Operational	Open manufacturing systems
	High cost of goods (COGs)
	Delivery method limitations
	Patient selection
	Endpoint selection
Ethical / Perception	Long-term safety monitoring
	Donor sourcing concerns

Introducing: Small Mobile Stem Cells (SMS)

SMSbiotech has discovered, developed, and patented Small Mobile Stem cells

In collaboration with multiple associates, we have found SMS cells to be a **safe and superior therapeutic**

- Regenerative medicine develops methods to **regrow, repair, or replace damaged or diseased cells, organs or tissues**
- **Stem cells are central to healing;** cells that have a high capacity to regenerate themselves and other human cells

EXCEPTIONAL CELL CHARACTERISTICS

- **Robust** proliferation and **scalable** production
- **Small** cell size
- Fast **motility**
- **Robustness** and sturdiness
- **Native** to peripheral blood
- **MHC** deficient
- **Strong** cell-to-cell binding
- **Selective** cell binding

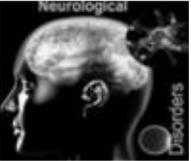
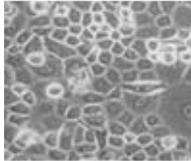
THERAPEUTIC VALUE

- **Allogeneic**, off-the-shelf cell therapy
- **First** cell therapy for a **major** indication
- **Non-immunogenic**
- **Anti-inflammatory**
- **Multi-targeting** for orchestrated tissue regeneration
- **Regenerative capacity** mainly through host stem/progenitor cell activation
- **Easy and localized administration**
- **Economic storage** and transportation at 4°C / 39°F for 26 days

Our First Stem Cell Therapy Target: **Chronic Obstructive Pulmonary Disease (COPD)**

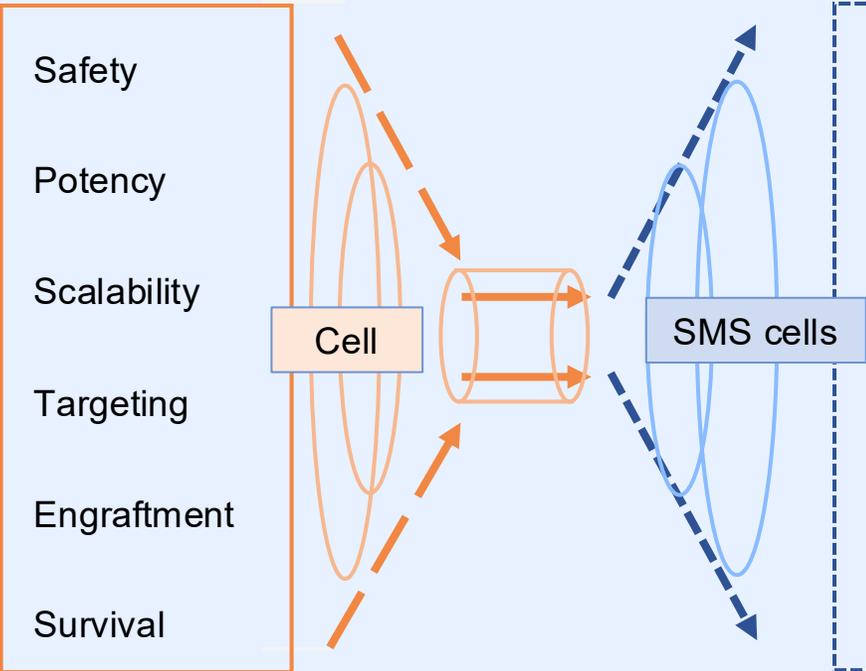
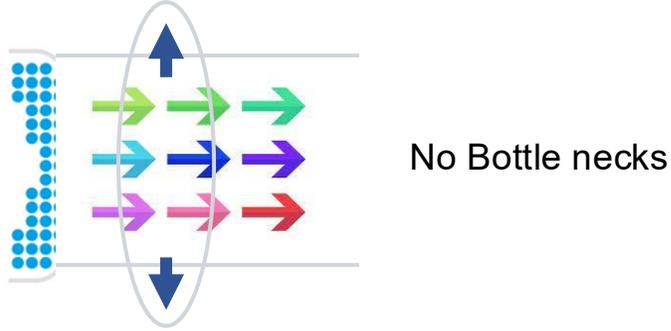
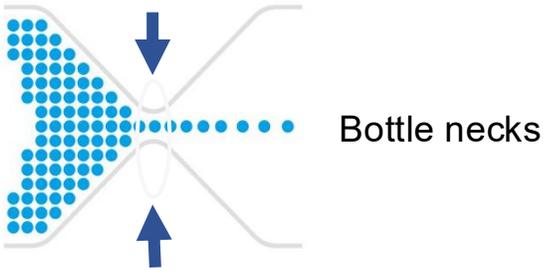
SMS Cell Platform Technology: Opportunities and Verticals

Data related to cellular interactions, omics, and animal disease models' studies support SMS cell mechanisms for targeting tissue and organ regeneration, which leads to potential applications in many indications that include (but are not limited to) multiple conditions and diseases such as:

NEUROLOGIC	PULMONARY	CELL & TISSUE ENGINEERING	ADJUVANT CANCER THERAPIES	CARDIOVASCULAR SYSTEM	MAJOR ORGAN DISEASE	MAXILLO-FACIAL & DENTAL	WOUND/SURGICAL	COSMECEUTICAL
 <ul style="list-style-type: none"> Alzheimer's Parkinson's disease Dementia Traumatic brain injuries Ischemic Brain Injury 	 <ul style="list-style-type: none"> COPD Covid-19 Viral infections ARDS Pneumonia Pulmonary HTN IPF/ Cystic Fibrosis 	 <ul style="list-style-type: none"> Organ engineering & banking Extra cellular matrix engineering & banking Structured prosthesis, film, sutures, adhesive, tape, glue, & foam hydrogel 	 <ul style="list-style-type: none"> Adjunctive regenerative therapies Change cancer-cell micro-environment Enhance immune system 	 <ul style="list-style-type: none"> Cardio Myopathy Stroke Myocardial infarction Atherosclerosis Coronary artery disease 	 <ul style="list-style-type: none"> Kidney Disease Liver Disease Ophthalmic Diseases Skin Diseases Gastro-intestinal 	 <ul style="list-style-type: none"> Temporomandibular and post-excision structural regeneration Osteonecrosis Gingival Regeneration 	 <ul style="list-style-type: none"> Chronic wounds (diabetic, venous, radiation, pressure, surgical, traumatic) Intra-operative: faster tissue healing Joint regeneration/ joint replacement adjunct 	 <ul style="list-style-type: none"> Companion therapies with aesthetic procedures Skin anti-aging treatments Scar mitigation
	ACTIVE PROJECT			ACTIVE PROJECT			ACTIVE PROJECT	ACTIVE PROJECT

Phase 1 safety study will open the door to testing for many other indications, including longevity.

SMSbiotech discovery of Small Mobile Stem cells Resolves Critical Cell Therapy bottle necks



- Cells isolated from adult human; No genetic manipulation.
- Multi-targeted Orchestrated unique mode of action.
- Cell biomanufacturing is highly scalable.
- Strong selective and direct binding to endogenous cells.
- Cells administered directly to the lung; non-invasively.
- Resilient, small, and low immunogenicity.



Small Mobile Stem (SMS) Cells vs Other Stem Cells

	SMS Cells	Adult Stem Cells	Embryonic Stem Cells	iPSC
Supply	High capacity for sustained proliferation	No techniques to produce large quantities in culture; donor-reliant	Limited; acquired through ethically dubious sourcing methods	Reproducibility and maintenance uncertain
Quality	Stable genome and few mitochondria reducing potential damage	Less likely to be rejected if used for specific tissues, loses ability to differentiate after multiple cell duplications (passages)	Difficult to control. Can cause tumors and cancer, likely to be rejected in certain applications	Can cause tumors and cancer
Availability	Simple and safe cell harvesting procedure	Scarce in native tissues; difficult to extract	Process to generate ESC inefficient	Created in lab environment, though require somatic cells from donor
Identification	Unambiguous due to morphological and functional characteristics	Repopulation or cell culture growth and cell markers to identify	No agreement on identification	Heterogenous cells based on source; Same methods as adult stem cells
Lifespan	Grown over years remaining actively dividing	Cannot be grown for long periods in culture	May grow for a year or more in culture	Ability to continuously divide after pluripotent transformation
Flexibility	Extremely responsive to cellular induction	Partially responsive to cellular induction	Somewhat responsive	A multi-stem process to reprogram cells then induce
Differentiation	Ability to differentiate into specialized cells	Ability to partially differentiate but limited to early proliferation	Potential to generate most cell types	Uncertain
Fragility	Exceptionally resilient and robust	Not durable	More durable than ASC, but can produce uncontrolled results	Highly fragile qualities
Summary	<ul style="list-style-type: none"> SMS cells are better than Embryonic Stem Cells (ESC) and Induced Pluripotent Stem Cells (IPSC) because of safety and ethical concerns Better than adult stem cells because of continued potency Better than both because of resilience and small size 			

Summary Comparison Table

Mesenchymal Stem Cells (MSC) vs Small Mobile Stem (SMS) cells

		Mesenchymal Stem Cell based therapy	Small Mobile Stem Cell based therapy (SMSbiotech)
Type of therapy	Adult cells	Yes	Yes
	Genetically manipulated	No	No
	Allogenic	Yes, but requiring multiple donors	Yes, single donor is possible
	Off the shelf	Yes, with limitations	Yes, no limitations
	Autologous	Yes	No
Access and availability	Tissue origin	Bone marrow, solid tissue	Peripheral blood
	Size of dose	Highly limited	Little to no limitations
	Potency	Lasts until 4-6 passages of cell culture	Stable for >27 passages of cell culture
	Transport temperature	-112°F to -321 °F (-80°C to -196°C)	39°F (2°C to 8°C)
	Mechanical/chemical stability	Low	High
	Stability in suspension	Hours to 2 days	3 weeks, guaranteed
	Delivery state	Frozen	Fluid
	Administration	Injections of thawed cells	Injection or inhalation of suspended cells, no thawing required
In vivo activity	Clogs capillaries	Yes (large size)	No (small size)
	Immunogenicity	Appears low but present	Appears very low to absent
	Post-injection Inflammation	Transient inflammation most likely occur	SMS do not produce transient inflammation
	Fast motility	No	Yes
	Homing to disease location	Yes	Yes
	Binding to other cells	Absent	Strong and selective binding
	Multiple indications	Yes	Yes
	Engraftment	Minor to absent	Strong binding to cells/tissue
	Stimulation of MSC cells	N/a	Yes
	Angiogenesis (blood vessel formation)	Yes	Yes
	Mechanism of action	Appears mainly as secretions	Appears multiple (direct binding and secretions, gene expression changes)
	Effectiveness	Low	High
	Infusion time	~30 minutes (due to larger size)	5–6 minutes (rapid infusion due to small size)
	Persistence in body	Short-lived; cleared relatively quickly	Prolonged retention observed in preclinical studies

Endogenous cell therapy

MSCs as Targets of Therapy NOT Vehicles

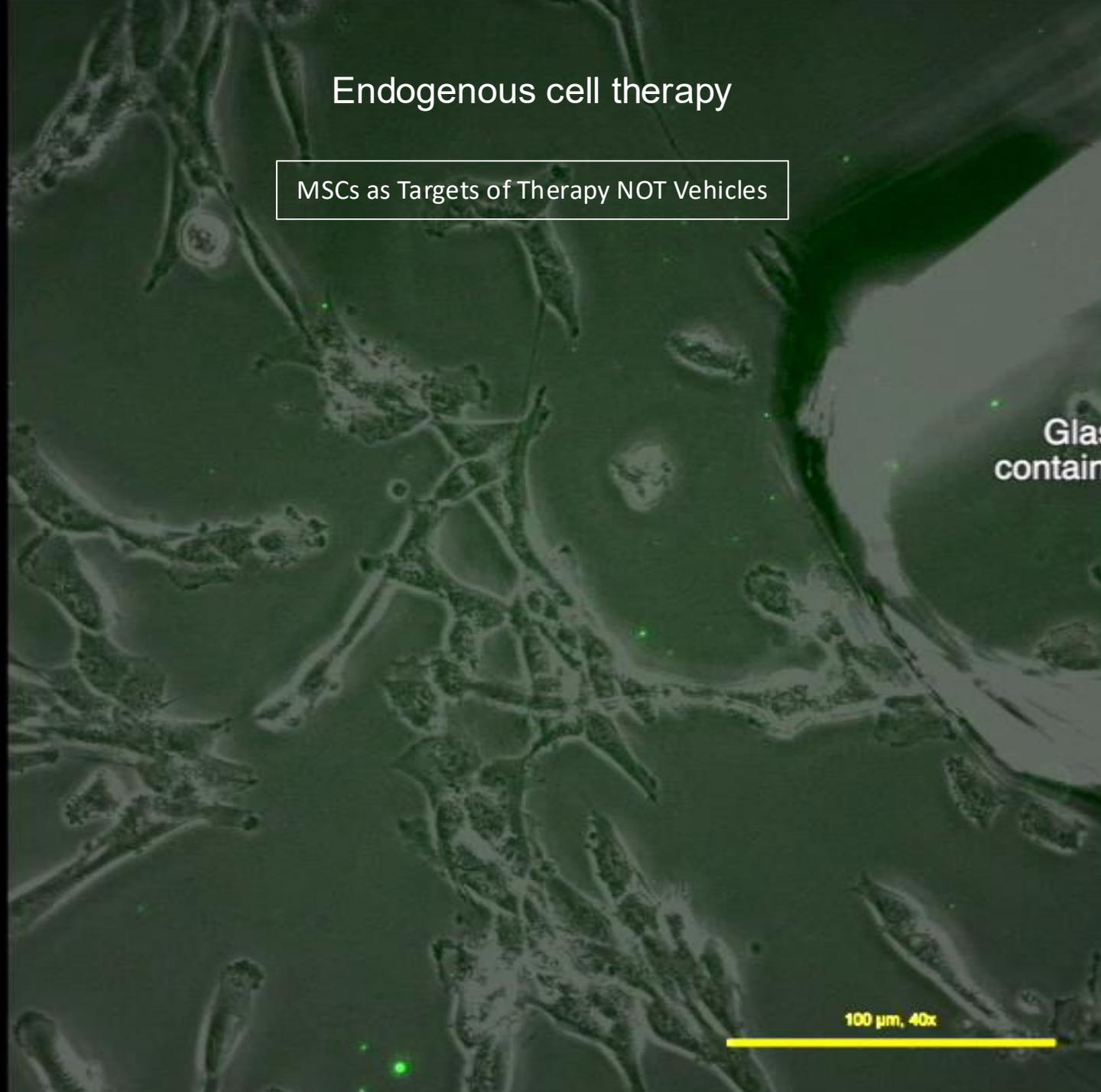
Patented
Regenerative
Platform
Technology
Promoting
Cell and
Tissue
Regeneration

Glass capillary
containing SMS cells

Fluorescent SMS cells
binding to Lung MSCs

Duration: 25 Hours

100 μ m, 40x



SMS cell Extracellular Matrix stimulating blood vessel formation

SMSbiotech proprietary technology

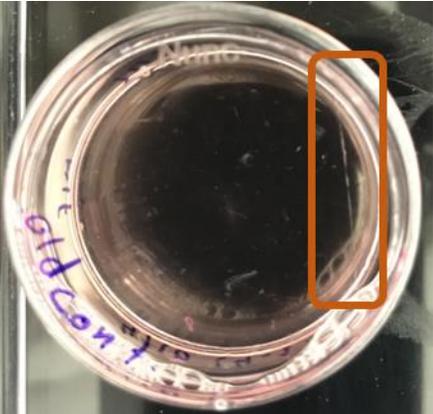
Extracellular matrix
from SMS Cells:

Exceptional
Regenerative
Properties



Date Recorded: 9/9/19-9/13/19

Hanging Vessel

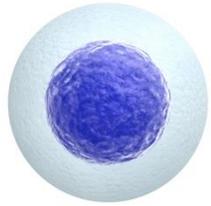


Duration: 71 Hours

2019-09-09 @ 16:53:44.12

20 μm, 10x

SMS Cell Multimodal mechanism of action: Multitargeted Orchestrated Regeneration MOR



Small Mobile Stem cell

Selective binding to multiple cells: stimulating/inhibiting cell proliferation and gene expression

- **Fibroblasts** inhibition of proliferation change in gene expression
- **Mesenchymal stem cells** stimulation of proliferation, modifying gene expression
- **Endothelial cells** differentiation and restructuring
- **Alveolar type 2 progenitor cells** stimulation of proliferation, modifying gene expression
- **Chondrocytes** modifying gene expression
- **Tenocytes** modifying gene expression

General

Specific

TMAM

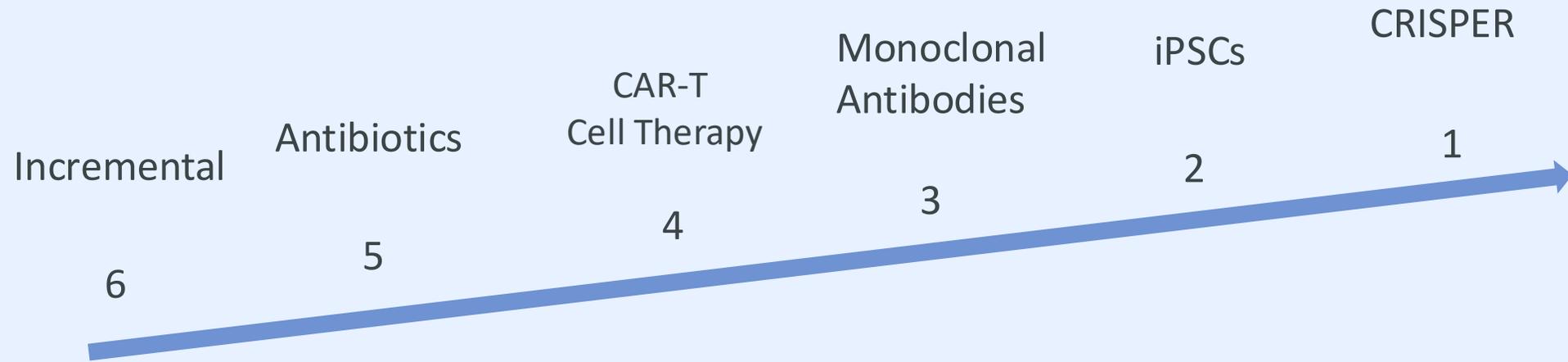
Secretion of matrix, matrix associated & non associated proteins/peptides (US Patent App. 17/766,164)

- **Talin** is a mechanosensitive cytoskeleton protein.
- **Complement C3** protective role in the lungs in the early stage of infection
- **Vitronectin** is part of the protein scaffolding that promotes cell anchorage and migration. has a positive effect in radiation-induced lung toxicity and it protects alveolar macrophages from silica toxicity.
- **Hsp90 secreted form** involved in repair of injured tissues and organs
- **Thrombospondin-1** deficiency leads to inflammation and alveolar barrier permeability during the acute phase of injury and defective alveolar type II epithelial regeneration
- **Dermcidin** Is a protein originally found in human sweat, which produces antibacterial peptides

Other mechanisms: tissue structuring and remodeling (described in patent published:

WHAT IS THE RANKING OF THE DISCOVERY OF SMALL MOBILE STEM CELL THERAPY?

AI Ranking of Major Recent Biomedical discoveries:



- Scientific Novelty
- Clinical Potential
- Platform / Translational Value
- Paradigm Shift
- Historical Impact

SMS Cell Therapy

The only platform that combines:

- Stability
- Mobility
- Small Size
- Targeting
- Gene modulation
- Adult-cell safety
- Manufacturability

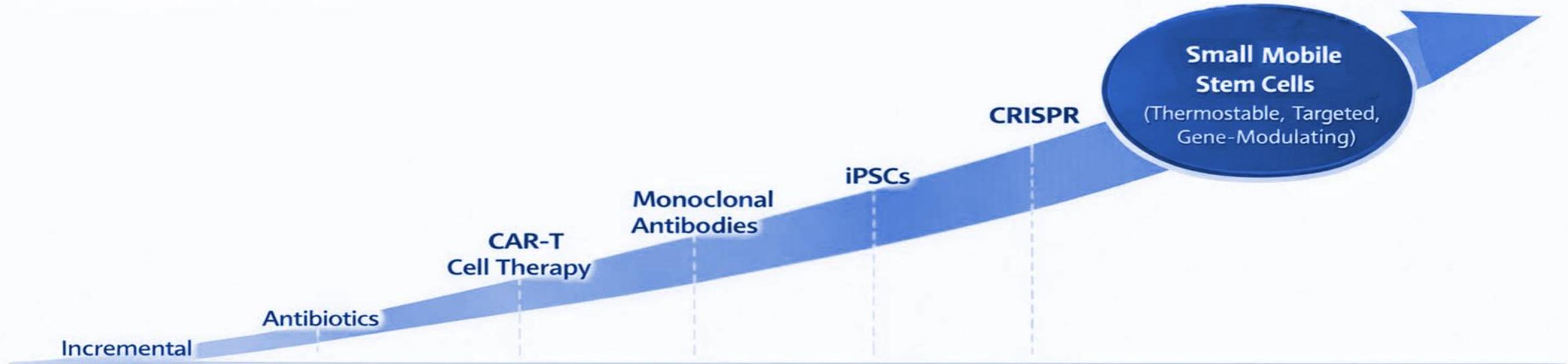
WHAT IS THE RANKING OF THE DISCOVERY OF SMALL MOBILE STEM CELL THERAPY?

Dimension	Combined Characteristics
Scientific novelty	Very High (truly new class of functional adult stem cells)
Clinical potential	Very High (systemic, precise, multi-indication, feasible worldwide)
Platform / translational value	Very High (one platform could replace multiple biologics / cell therapies)
Paradigm shift	High to Revolutionary (cells now programmable, stable, and modular)
Historical impact	High / Potentially transformative, comparable to iPSCs or CRISPR in potential long-term influence

WHAT IS THE RANKING OF THE DISCOVERY OF SMALL MOBILE STEM CELLS?

THE AI ANSWER:

Ranking of Scientific & Medical Discoveries



Enhanced Small Mobile Stem Cells Combine Multiple Breakthrough Innovations

- ✓ **Thermostability** (50°C, 1 Month Refrigerated)
- ✓ **Highly Stable** Binds Selectively to Cells
- ✓ **Changes Gene Expression** of Target Cells
- ✓ **Precise Target Therapeutic Effects**
- ✓ **Modular, Programmable** Cellular Therapy

Small Mobile Stem Cells

- ▶ Thermostable
- ▶ Targeted
- ▶ Gene-Modulating



www.smsbiotech.com

**On a mission to democratize the application
of stem cell technologies for human health**

Access Our Resource Library



Inquiries

SMSbiotech, Inc.
San Diego, California

+1-760-290-3406
Info@smsbiotech.com
www.smsbiotech.com
