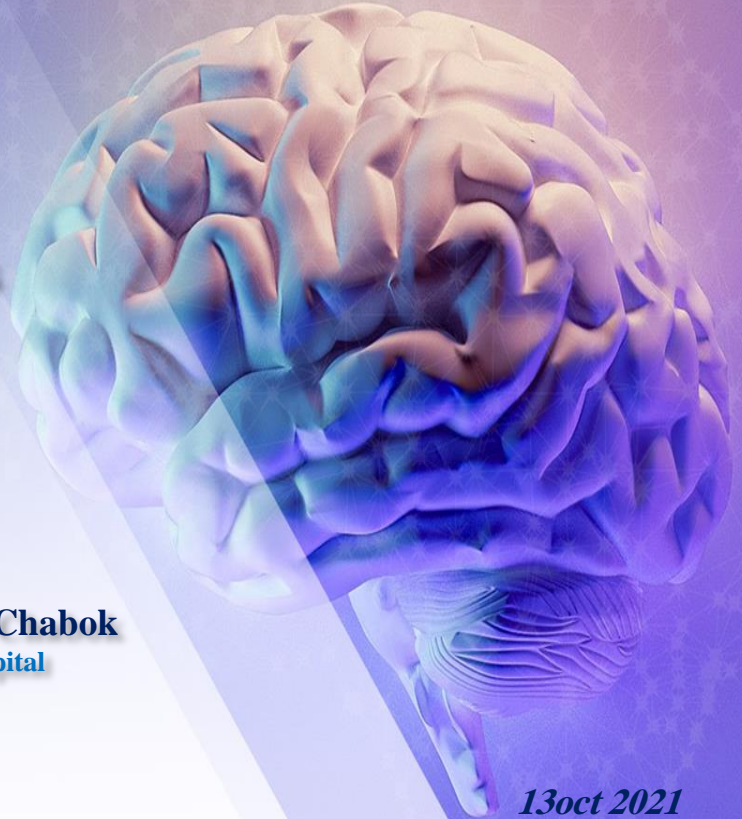




Gene & Cell Therapies Targeting CNS Disorders Market: Iran Research Insights & Global Landscape

Presented by Shahrokh Yousefzadeh Chabok
Professor of Neurosurgery in Poursina Hospital



13oct 2021

Today's Talk



Introduction

Products & Clinical Trials

Global Landscape

Current Status in Iran

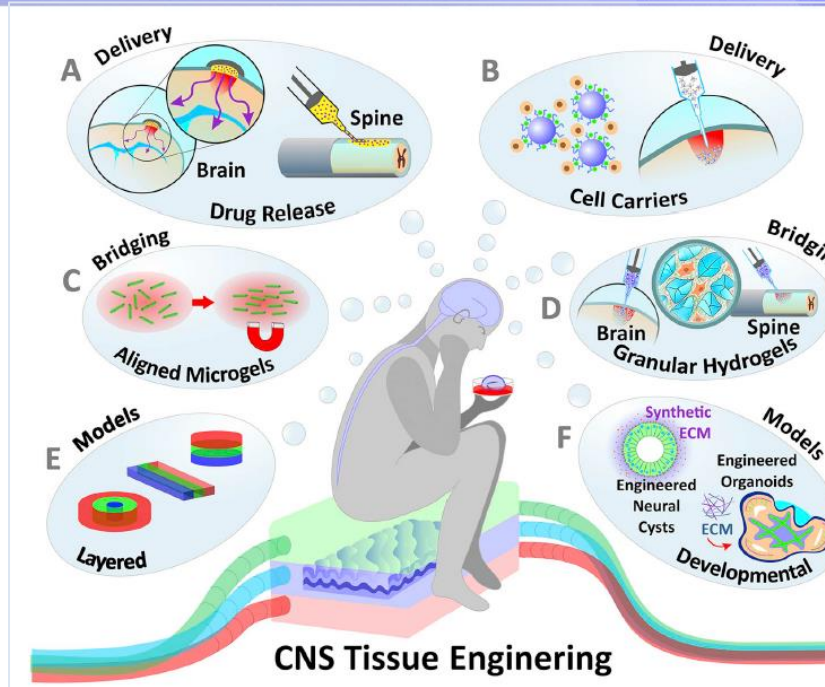
Introduction

- **Burden on Health Care Systems**
- **Restoration of Lost Neuronal Function**
- **Impact Patient's Physical, Psychological**
- **Still Remains a Considerable Challenge**

- ✓ **Spinal cord injury**
- ✓ **Traumatic brain injury**
- ✓ **PNS injury**
- ✓ **Brain tumors**
- ✓ **Stroke**
- ✓ **MS**
- ✓ **other Neurodegenerative disease**



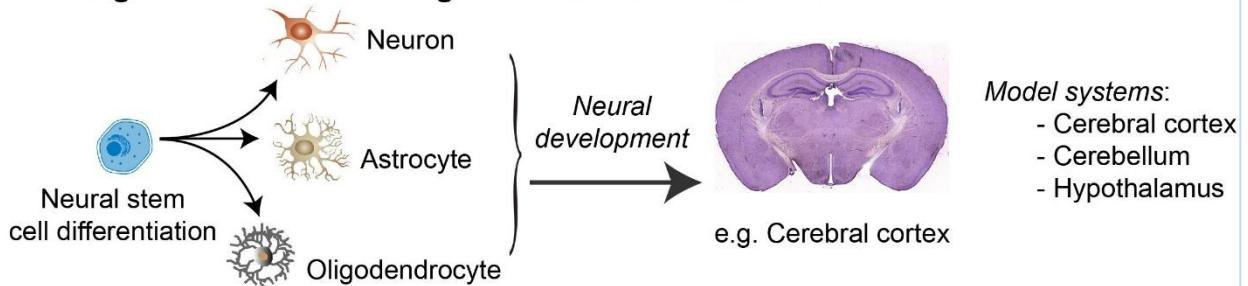
CNS Regenerative Approaches



Neural tissue engineering with structured hydrogels in CNS models and therapies, *Biotechnology Advances*, Volume 42, 2020,107370

Stem Cells Research Programs in Neural Tissue Engineering

Program 1: Understanding the drivers of neural stem cell differentiation



Program 2: Identifying how abnormal neural stem cell biology contributes to disease

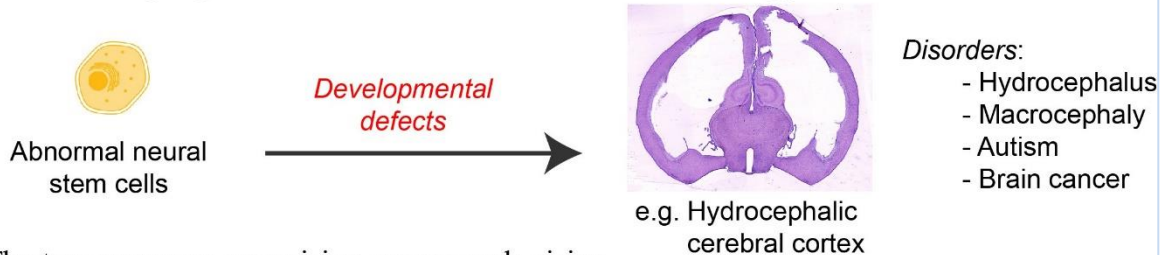


Figure 1: The two programs comprising my research vision



RM Products & Clinical Trials

Attractive Opportunities in the Cell & Gene Therapy Market



The growth of the APAC market is attributed to the increasing pharmaceutical R&D spending, the growing trend of outsourcing drug discovery services, growing life sciences research, and increasing government initiatives for healthcare research.



APAC

7.7 USD Billion
2021-e

13.8 USD Billion
2026-p

CAGR of
12.4%

The global cell & gene therapy manufacturing services market is projected to reach USD 13.8 billion by 2026 from USD 7.7 billion in 2021, at a CAGR of 12.4% during the forecast period.



Growth in this market is primarily driven by the high incidence of cancer and other target diseases, increasing investments in pharmaceutical R&D, investments in advanced technologies by CDMOs, and increasing partnerships & agreements between pharmaceutical companies and CDMOs.



The rising demand for cell & gene therapies and increasing number of cell & gene therapy clinical trials are expected to offer growth opportunities for players operating in this market.

1,001+

Regenerative medicine and advanced therapy companies worldwide, including gene, cell, and tissue-based therapeutic developers

For the first time, there are now more than 1,000 active regenerative medicine and advanced therapy developers worldwide, of these companies, 415 are in the clinical stage of development.



9 Country / Regulatory Body	No.
Australia (TGA)	1
Canada (Health Canada)	2
China (CSFDA)	1
Europe (EMA)	8 + 1
India (DCGI)	4
Japan (PMDA)	4
New Zealand (MEDSAFE)	1
South Korea (MFDS)	14
United States (FDA)	16 + 1
Total	51 + 2
Unique products	44 + 2



TOTAL GLOBAL FINANCING
\$10.7B
 raised in H1 2020
 120% increase YoY from H1 2019
 \$3.2B raised in Q1 2020
 \$7.5B raised in Q2 2020



GENE & GENE-MODIFIED CELL THERAPY
\$7.9B
 raised in H1 2020
 81% increase
 YoY from H1 2019
 \$2.9B raised in Q1 2020
 \$5.0B raised in Q2 2020



CELL THERAPY
\$7.5B
 raised in H1 2020
 387% increase
 YoY from H1 2019
 \$1.8B raised in Q1 2020
 \$5.7B raised in Q2 2020



TISSUE ENGINEERING
\$84M
 raised in H1 2020
 27% increase
 YoY from H1 2019
 \$64M raised in Q1 2020
 \$20M raised in Q2 2020

Disease Type



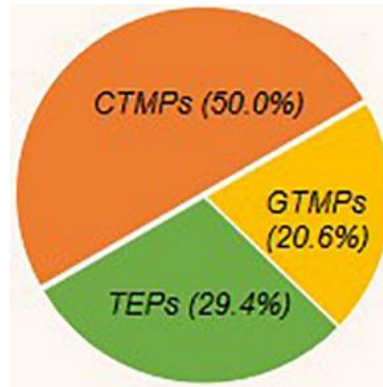
- In the ALS, the Production of Nuronata-r in January 2015

- 
- ✓ 2015 that were approximately \$1.6 million,
 - ✓ 2016 were estimated to be approximately \$4.8 million
 - ✓ 2018 were expected to reach near \$16.6 million

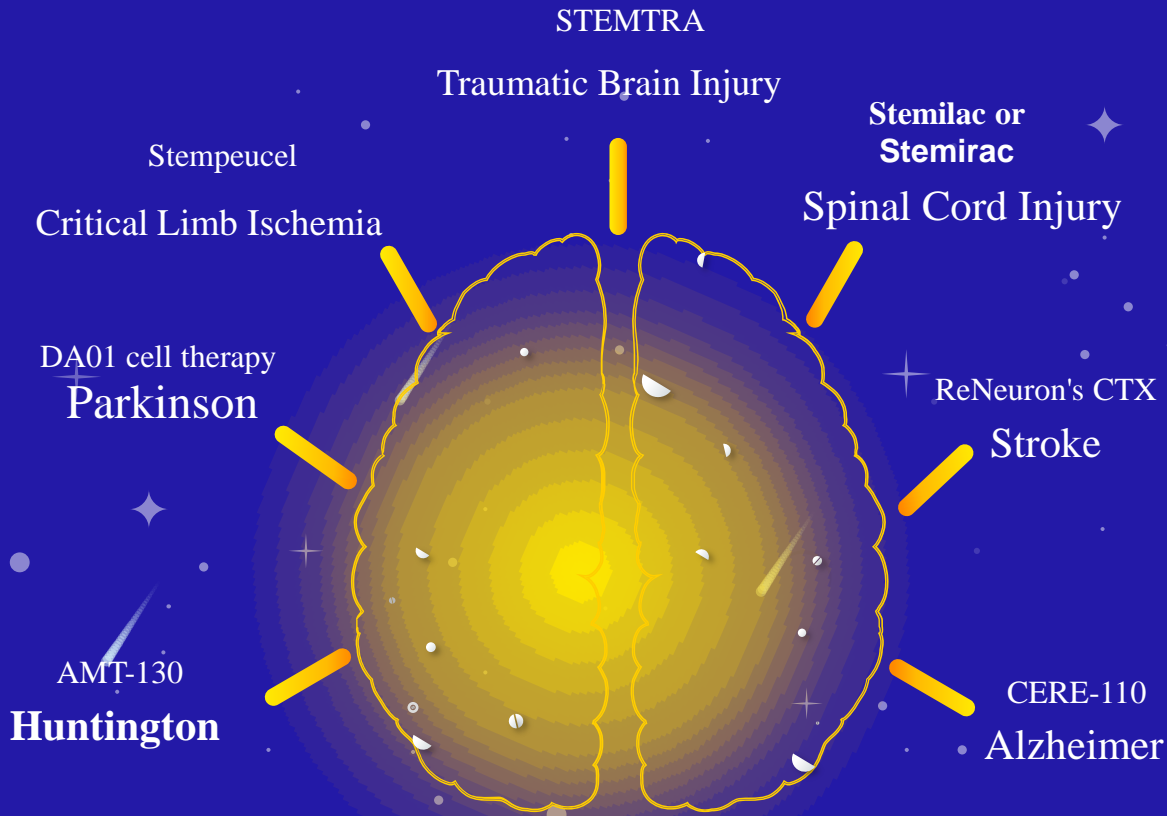
- ✓ Final number would be approximately \$37.4 million.

RM Products

- There are **64 approved ATMPs**.
- **CTMP** group, with **34 products**, is the largest class.
- The **TEP** and **GTMP** groups, with **20** and **10** products, follow in order.

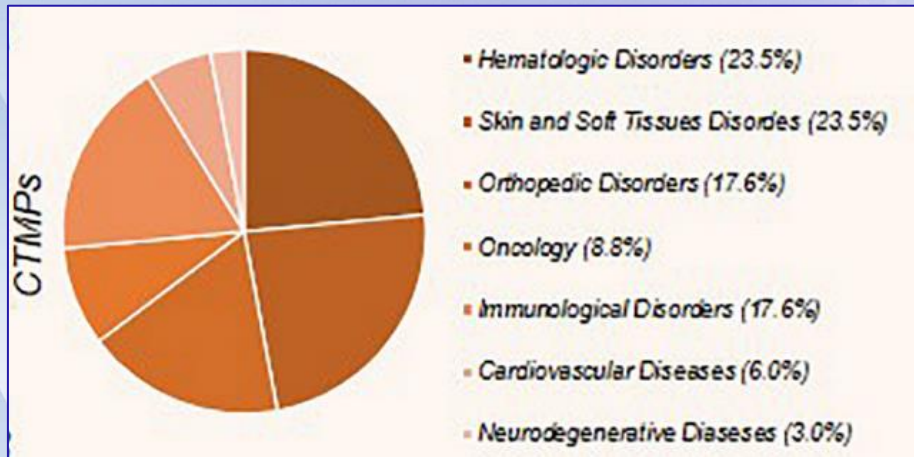


Under developed products



Cell Therapies Product

- The only related **neurological disorder** was **ALS** for which the product **Neuronata-R** (South Korea MFDS.2014) has been approved.



CTMPs & Spinal Cord Injury

- ✓ From Wheelchair to Walking Again With ANOVA IRM Stem Cell in Germany

Japanese



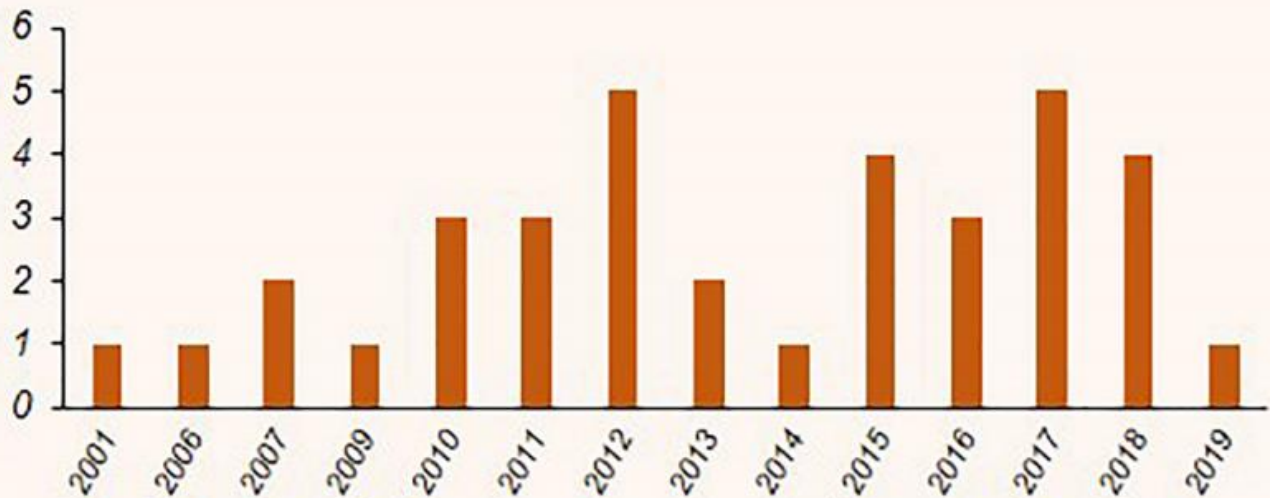
A stem-cell treatment for spinal-cord injuries will soon be available in Japan.

JAPAN

Stem-cell therapy raises concerns

Independent researchers warn that approval is premature.

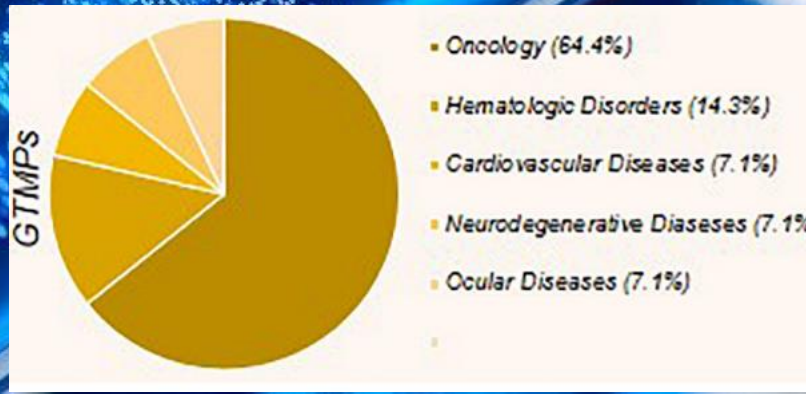
Approval Year of CTMPs



Two decades of global progress in authorized Advanced Therapy Medicinal Products: An emerging revolution in therapeutic strategies. Frontiers in Cell and Developmental Biology.

Gene Therapies Product

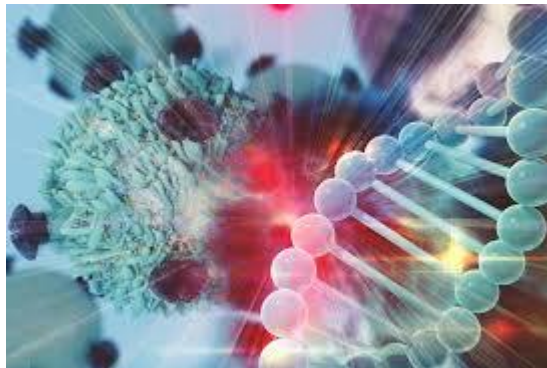
✓ Zolgensma (US FDA.2019) that enrolled 21 SMA pediatric patients with biallelic mutations in the survival motor neuron (SMN1) gene.



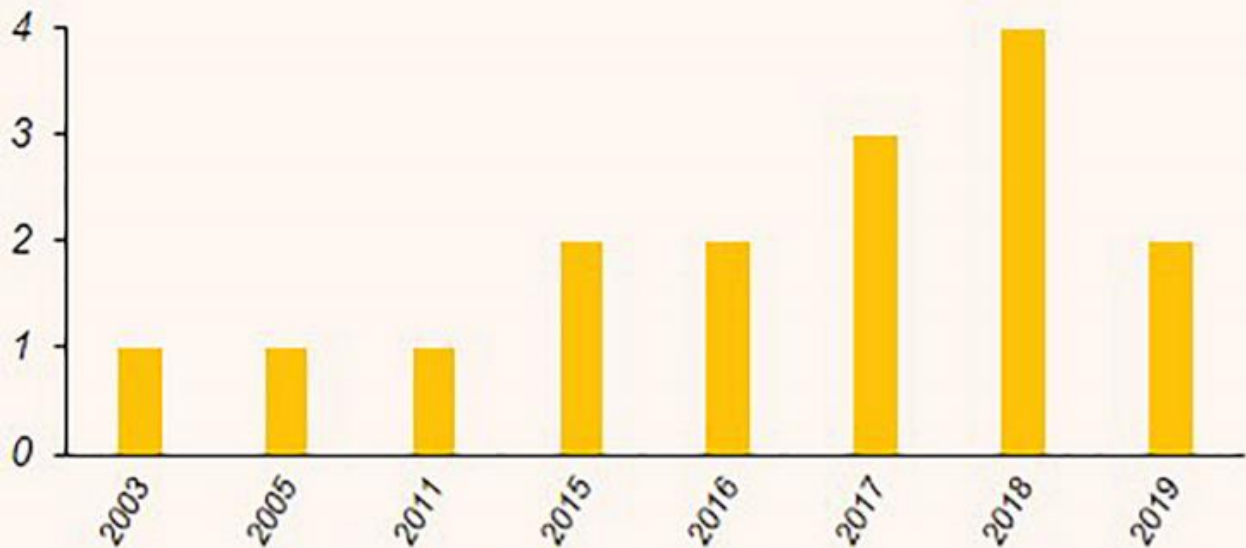
Continue

- ✓ The Ohio State team developed the gene therapy uses a viral vector to carry DNA-expressing aromatic L-amino acid decarboxylase (AADC) to the brain.

This technique could eventually be used to treat more common brain diseases, like Alzheimer's and Parkinson's



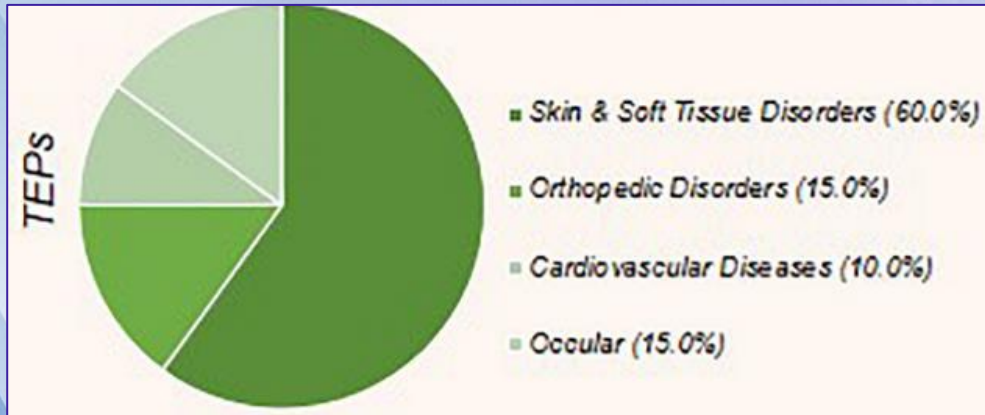
Approval Year of GTMPs



Two decades of global progress in authorized Advanced Therapy Medicinal Products: An emerging revolution in therapeutic strategies. Frontiers in Cell and Developmental Biology.

Tissue Engineering Products (TEP)

✓ Neural TEPs had the lowest amount



Dura Mater Products

Key vendor/manufacturers in the market:

- B Braun
- Johson & Johson ,...

Dural Repair Product	Collagen Source	Conformability	Suture Pull Out Strength ⁵	Leak Resistant ^{4,5}	Resorption Time ^{3,4}
DuraMatrix-Onlay® Plus	Bovine Achilles Tendon	Completely	Low ¹	Yes	8 weeks
DuraMatrix® Suturable	Intact Bovine Dermis	Highly	Very High	Yes	9 months
DuraMatrix-Onlay®	Bovine Achilles Tendon	Highly	Moderate ²	Yes	6 - 9 months
DuraMatrix®	Bovine Achilles Tendon	Moderately	High	Yes	6 - 9 months

¹ Indicated for onlay application; Suturing is not required, but tensionless, atraumatic stay sutures may be used if desired.

² Indicated for onlay application; Suturing is not required, but if desired, minimal tension sutures may be used.

³ Rabbit duraplasty study. Data on file at Collagen Matrix, Inc.

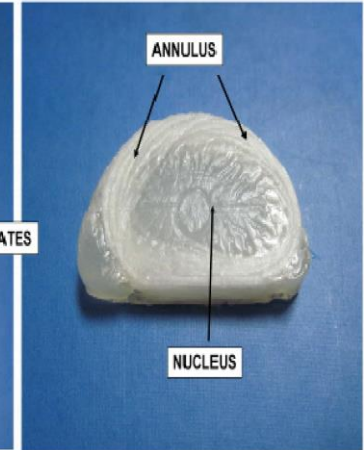
⁴ The results of pre-clinical and in vitro studies may not be indicative of human clinical outcomes.

⁵ In vitro data on file at Collagen Matrix, Inc.

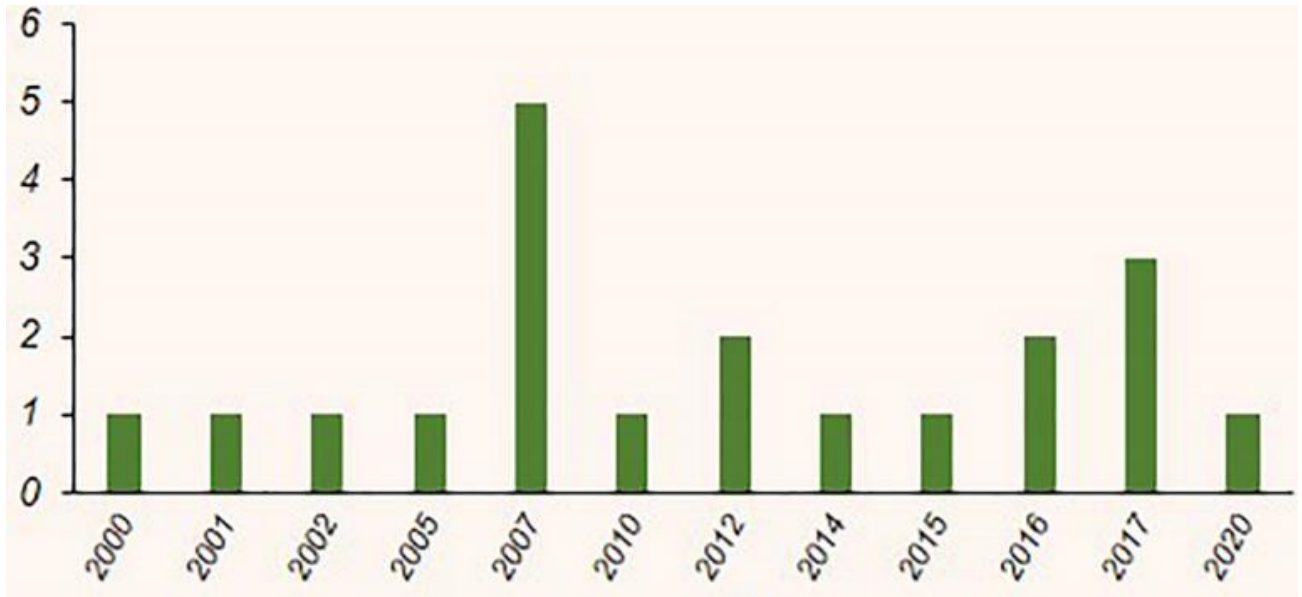


Artificial Disc

- ✓ **Market** size surpassed USD 1.6 billion in 2019 and is projected to achieve over 18.6% CAGR up to 2026.

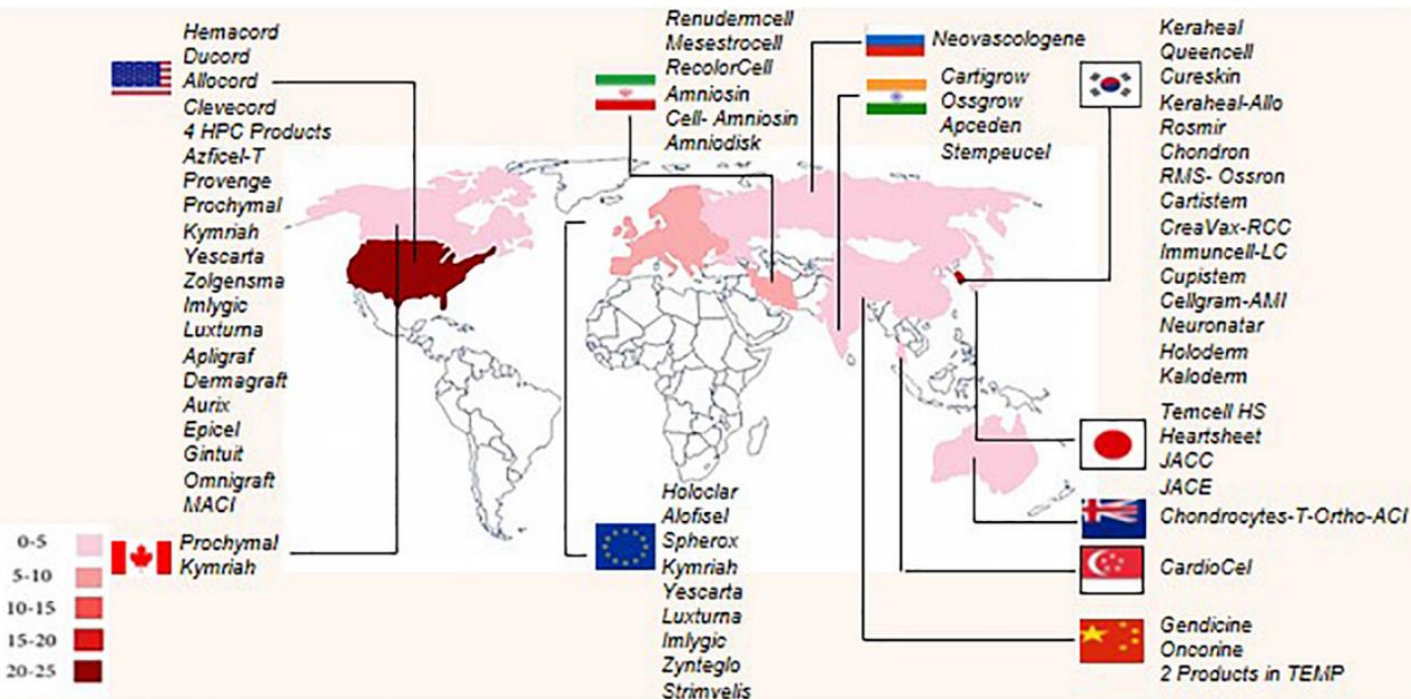


Approval Year of TEPs



Two decades of global progress in authorized Advanced Therapy Medicinal Products: An emerging revolution in therapeutic strategies. *Frontiers in Cell and Developmental Biology*.

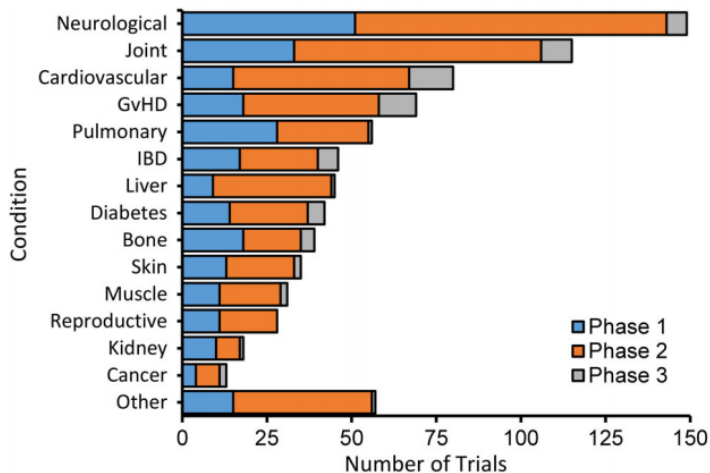
Number of authorized RM products worldwide, according to country



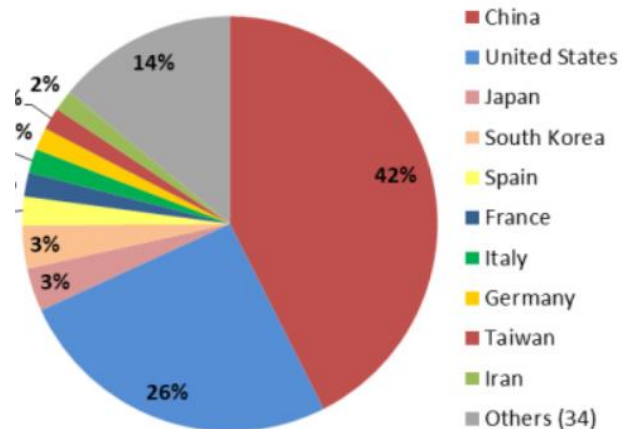
Regenerative Projects around the World



Clinical Trials in Cell Therapy

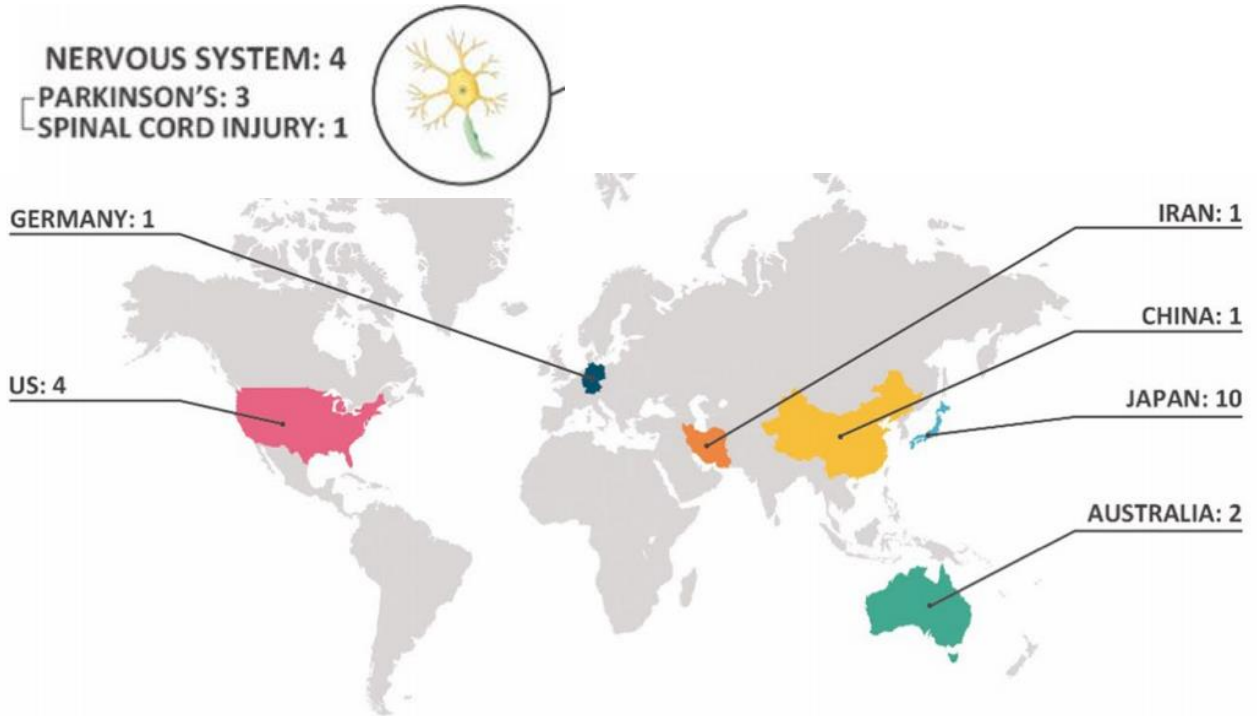


2019 Advanced Cell Therapy Trial Locations



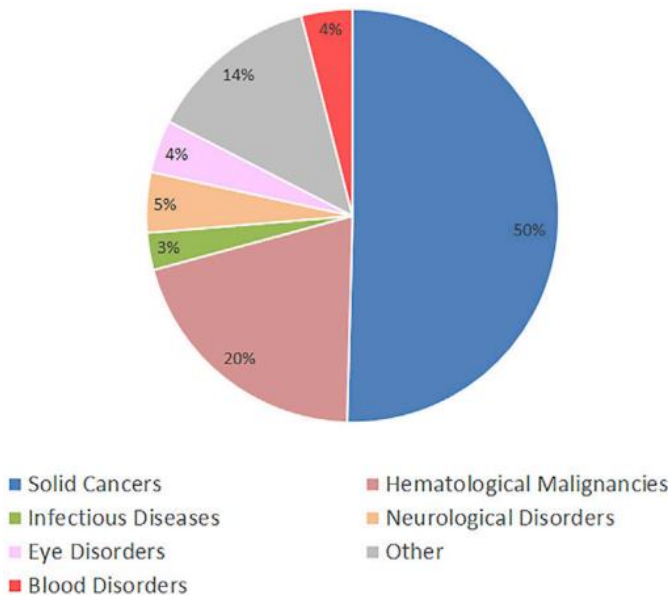
Trends in mesenchymal stem cell clinical trials 2004-2018: Is efficacy optimal in a narrow dose range?

Clinical Trials involving IPSCs



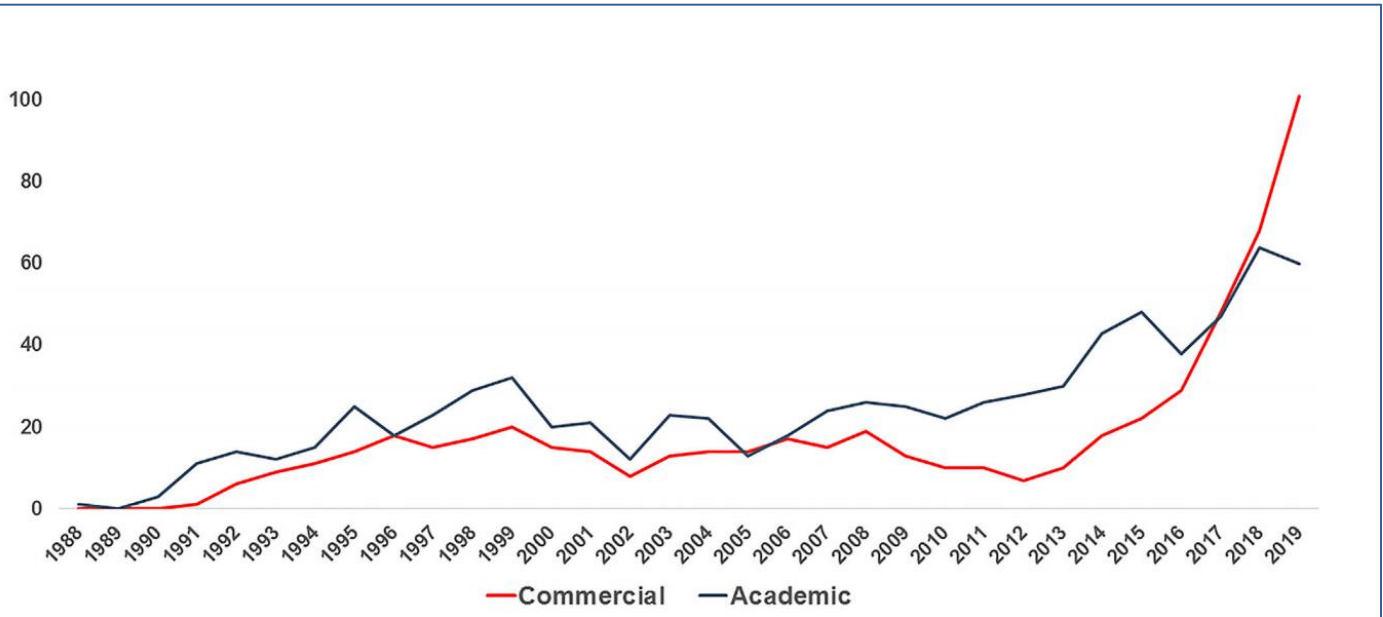
Clinical Trials in Gene Therapy

Among the ongoing programs, 59% include gene therapy products intended to treat rare diseases.

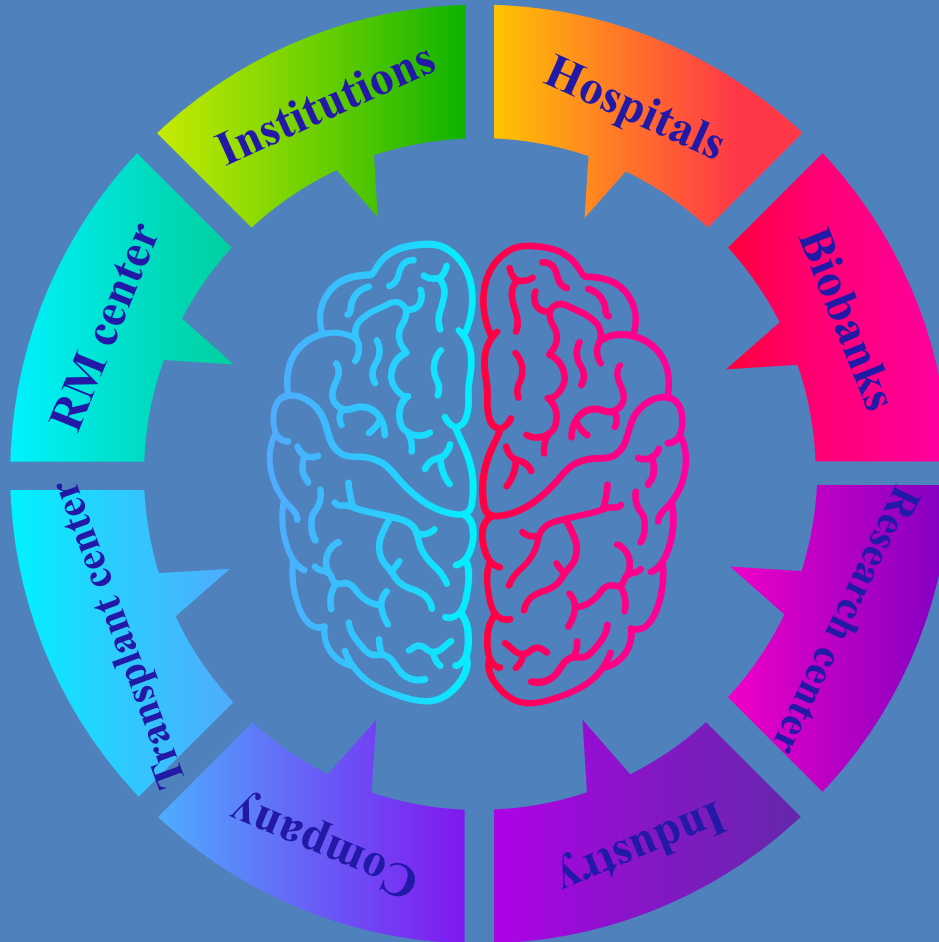


Continue

- ✓ The potential for commercialization of gene therapies is now being realized by the biotechnology and pharmaceutical sectors.

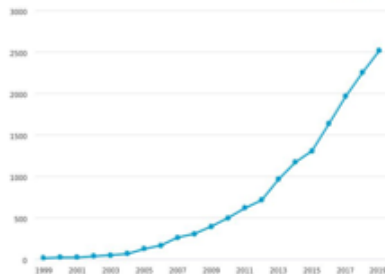


Current Status in Iran



Iran Data

میزان رشد کشور بر اساس تولید علم در جهان



حرکت جمهوری اسلامی ایران در لبه دانش هم راستا با برجسته‌ترین مراکز تحقیقاتی دنیا

U.S. National Library of Medicine

ClinicalTrials.gov

Region Name	Number of Studies
World [map]	110
Middle East	110
Iran, Islamic Republic of	110 [studies]

110

<https://clinicaltrials.gov>

IRCT

Iranian Registry of Clinical Trials - Beta version

Displaying 1-100 of 194 results

- (1) Efficacy assessment of adipose-derived stem cell in cardiovascular fistulae and stem cell research center and sample size is 10 persons. our intention is to evaluate the efficacy of this cell in the arm of this study. Suspension of adipose derived

IRCTID: IRCT20140071943291

194

<https://www.irct.ir>

تعداد کارآزمایی بالینی خاورمیانه



۱۲۹۶ مورد پیوند در سال ۱۳۹۸

۸۶۴۱۵ اهداکننده (۸۱۵۲۵ تایید شده) در ۱۶ مرکز

+160

توسعه و بهبود قوانین، دستورالعمل‌ها و استانداردهای تولید محصولات سلول درمانی

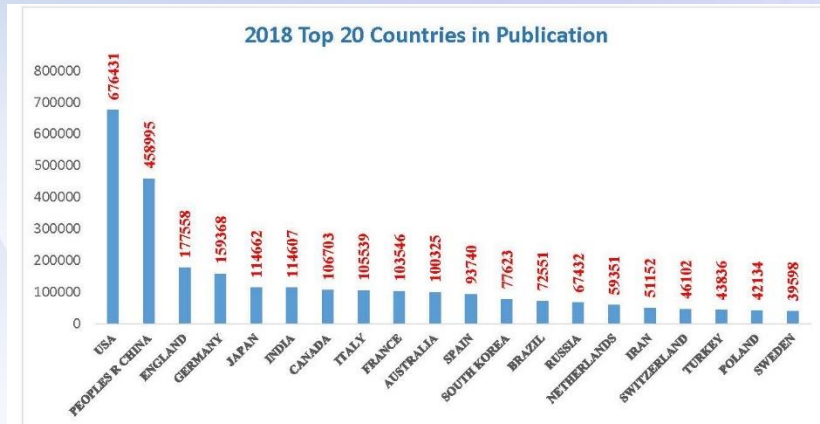
۱۹ مرکز سلول درمانی فعال در زمینه پیوند سلول‌های بنیادی خونساز

۱۳ مرکز پذیرنده نویسی و اهداکنندگان و ۳ بانک بندناف

+600

Current Status in Iran

- Potential therapeutic applications, both basic and translational research are being promoted.
- **Iran in rank of 14 in the world.**
- **Iran 1st in islamic country**
- **Iran is top 20 countries in publication.**



Iran Regenerative Medicine Center

✓ Nine Regenerative Medicine Center



Royan Institute

- **Established in 1991** by the late Dr Saeid Kazemi Ashtiani and his colleague in Iran university of medical sciences.
- **In 2002, the research fields** in Royan Institute extended into **stem cell** studies as well.
- Success rate of **infertility treatment & cell therapy** clinical services.



Royan Renders

- First time use of adult stem cells in the treatment of MI during CABG in Iran, 2004.
- Establishment of the first Private Cord Blood Bank in Iran, 2005.
- Establishment of cell therapy pre-hospital, 2011.
- Establishment of Stem Cell Bank, 2011
- Products that are being developed included Mesenchymal stem cells (ChymiaCell), Keratinocyte sheet, Bilayer skin.



Stem Cell Transplant Center

Today, 80 disease have been treated with hematopoietic stem cell

First Iranian stem cell transplantation center established at 2007

18 stem cell transplant center grafted 1200-1500 stem cell annually, right now.

بیمار	نام بیماری	نوع پیوند	مرکز پیوند
پسر ۹ ساله	اوتیسم	autologous	بیمارستان منتصریه مشهد
دختر ۸ ساله	تالاسمی	autologous	بیمارستان شریعتی
پسر ۲۶ ساله	آسیب مغزی	autologous	بیمارستان منتصریه مشهد
دختر ۲ ساله	CP	autologous	بیمارستان منتصریه مشهد



Stem Cell Transplant Center n Pediatric Hospital

- Pediatric stem cell transplant center established at 2016.
- First stem cell grafted on a 5 years child with LAD disease at 2016.
- Today, stem cell transplant on SMA, Neuroblastoma and Diseases.



Cinna Gen

- ✓ Founded in 1994 with the goal of manufacturing hi-tech products in biotechnology and related fields.
- ✓ Products on cell therapy are **amniosin, cell-amniosin and amniodisk**



Cell Tech Pharmed

- Founded in 2013 with the goal of manufacturing cell therapy products
- **Renudermcell, mesestrocell and recolorcell**
- **Vartocell for cerebral palsy**



International Stem Cell Tourism

- **The cost per stem cell treatment is between us\$10000 and us\$60000, excluding travel expenses**

Table 2. Leading clinical indications for stem cell therapy (after Connolly et al.¹⁵)

Descending rank	Clinical indication
1	Multiple sclerosis
2	Anti-ageing
3	Parkinson's disease
4	Stroke
5	Spinal cord injury
6	Cerebral palsy
7	Autism
8	Amyotrophic lateral sclerosis
9	Alzheimer's disease
10	Arthritis

Example of RM Clinic

California cities with for-profit stem cell clinics

California has more consumer stem cell clinics than any other state. Clusters are in the Bay Area, greater Los Angeles and San Diego. With 18 businesses, Beverly Hills has the highest concentration of clinics. The numbers are based on a 2016 survey of clinics marketing stem cell therapies online.

NORTHERN CALIFORNIA



CENTRAL AND SOUTHERN CALIFORNIA



Image: Kyoto University



Best Neural Stem Cell Therapy Hospitals in South Korea

Continue



CBC Health AG

Stem cell clinic, Germany

CBC Health offers umbilical cord blood treatments for ischemic stroke survivors (among others) around the world. Our parent company, Cord Blood Center Group, has + 20 years of experience providing therapeutic components with above-average quantities of nucleated cells

[View profile](#)[Request Info](#)

Hospital Quirónsalud Barcelona

Private Hospital, Spain

Quirónsalud Hospital Barcelona is the benchmark for private healthcare in southern Europe, providing world-class service for the past seventy years.

[View profile](#)[Request Info](#)

Listed stem cell specialist:



Dr. Nils H. Thoennissen MD
Head Physician

Conditions treated with stem cells:

Procedure	Prices
Multiple Sclerosis	upon request
Stroke	upon request
Cerebral Palsy	upon request
Umbilical Cord Blood Treatment	upon request

Conditions treated with stem cells: [view all >](#)

Procedure	Prices
Leukaemia	upon request
Myeloma	upon request
Lymphoma (Stem Cell Therapy)	upon request
Arthritis	upon request
Hemiplegia	upon request
Cartilage Regeneration	upon request

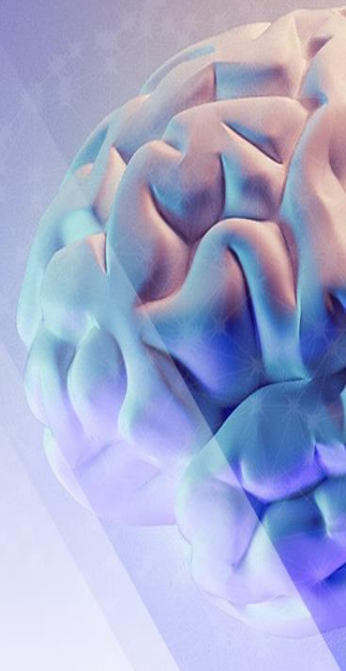
Conclusion

- Regenerative medicine show great promise for incurable disease.
- There is enormous potential in human stem cell research Both adult and embryonic stem cells should be studied.
- Much research needed before therapies are realized.



References

- ✓ Two decades of global progress in authorized Advanced Therapy Medicinal Products: An emerging revolution in therapeutic strategies. *Frontiers in Cell and Developmental Biology*.
- ✓ The translation of cell-based therapies: clinical landscape and manufacturing challenges. *Regenerative medicine*. 2015.
- ✓ Update review on five top clinical applications of human amniotic membrane in regenerative medicine. *Placenta*. 2021
- ✓ A stem-cell treatment for spinal-cord injuries will soon be available in Japan, 2019 Springer Nature Limited.
- ✓ International stem cell tourism: a critical literature review and evidence-based recommendations. *International health*. 2021
- ✓ Review of the Current Trends in Clinical Trials Involving Induced Pluripotent Stem Cells. *Stem Cell Reviews and Reports*. 2021.
- ✓ Progress in clinical trials of cell transplantation for the treatment of spinal cord injury: how many questions remain unanswered?. *Neural Regeneration Research*. 2021 Mar 1;16(3):405.
- ✓ Clinical Development of Gene Therapies: The First Three Decades and Counting. *Molecular Therapy-Methods & Clinical Development*. 2020.
- ✓ Trends in mesenchymal stem cell clinical trials 2004-2018: Is efficacy optimal in a narrow dose range?. *Stem cells translational medicine*. 2020 Jan;9(1):17-27.
- ✓ Current state of stem cell-based therapies: An overview. *Stem cell investigation*. 2020.
- ✓ Global trends in clinical trials involving pluripotent stem cells: A systematic multi-database analysis. *NPJ Regenerative medicine*. 2020.
- ✓ A scoping review of trials for cell-based therapies in human spinal cord injury. *Spinal cord*. 2020.
- ✓



An underwater photograph showing sunlight rays filtering down through the water surface, creating a serene and ethereal atmosphere. The water is a deep blue, and the light rays are bright and distinct.

Thank You