Intradiscal Injections

Annu Navani, MD

Founder, Comprehensive Spine & Sports Ctr
Advisor, Le Reve Regenerative Wellness

www.annunavani.com

www.cssctr.com

Disclosure

- Founder and CEO, Comprehensive Spine and Sports Center
- Advisor/KOL: Le Reve Regenerative Wellness, iHealthFrontier, TOBI Networks, WorCflo
- Board of Directors: American Society of Interventional Pain Physicians, California Society of Interventional Pain Physicians, California Society of Industrial Medicine and Surgery
- Angel and Serial Investor: multiple
- Investor/Research: Scilex Pharmaceuticals, Emcyte, Cornerloc, iHealthFrontier, WorCflo
- Consultant: Emcyte, iHealthFrontier, Cornerloc

Global Chronic Pain Treatment Market

MARKET SIZE

2020 — $80,766.6 Million

2030 — $162,175.2 Million

Market Growth Rate (2020–2030)

7.2%

U.S.

Largest Market By Country (2020)

China

Fastest-Growing Market By Country (2020–2030)

PRESCIENT & STRATEGIC INTELLIGENCE

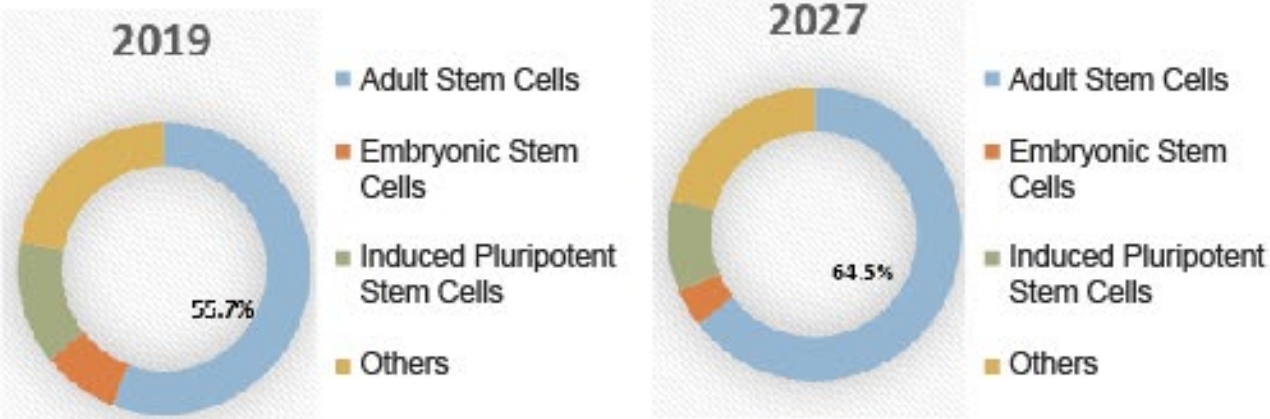
Where knowledge inspires strategy

CAGR 21.1%

STEM CELL THERAPY MARKET ANALYSIS

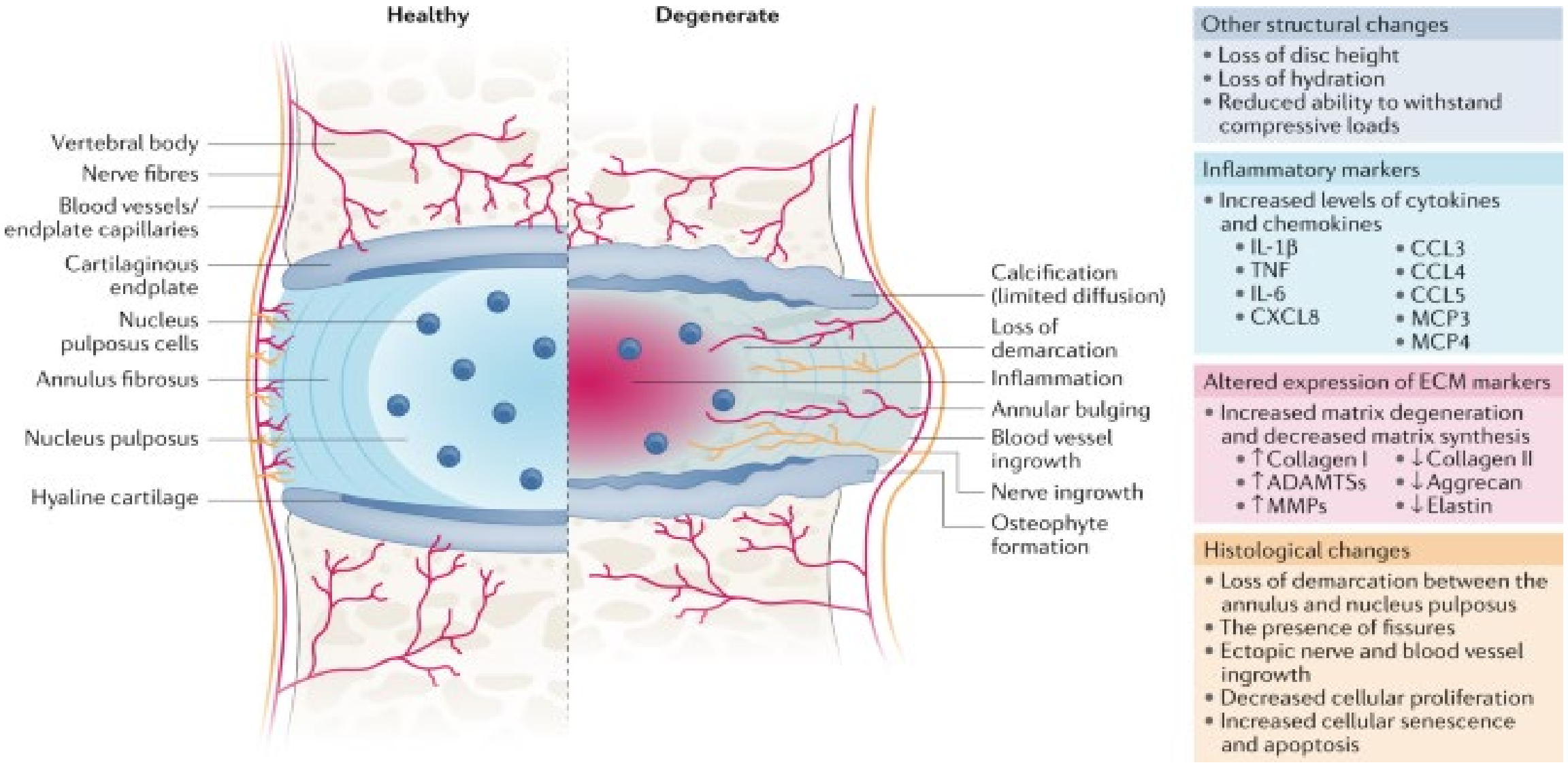
Market Size 2021	Market Size 2027
US$ 7,313.6 Mn	US$ 40.3 Bn

Global Stem Cell Therapy Market Share (%), by Cell Source,2019 and 2027



By Region, 2018

POINT OF VIEW TO POINT OF CARE



Abbie L. A. Binch, Joan C. Fitzgerald, Emily A. Growney, Frank Barry
http://feeds.nature.com/~r/nrrheum/rss/current/~3/7LZPQTcvV3c/s41584-020-00568-w
DOI: 10.1038/s41584-020-00568-w

Intradiscal Injections: Historical view

- Intradiscal steroid injections
  - 1954: Feffer HL: Hydrocortisone
  - 1960: Leao et al: Hydrocortisone vs Prednisolone
  - 1975: Graham: Chymopapain vs Hydrocortisone
  - 1992: Simmons et al: Depomedrol vs Bupivacaine
  - 2004: Derby et al: 0.5% Chondroitin sulfate, 20% Glucosamine hydrochloride, 12% DMSO and 2% Bupivacaine vs. IDET

Muzin S, Isaac Z, Walker J 3rd. The role of intradiscal steroids in the treatment of discogenic low back pain. Curr Rev Musculoskelet Med. 2008;1(2):103-107.

Richard Derby, MD, Björn Eek, MD, Sang-Heon Lee, MD, PhD, Kwan Sik Seo, MD, and Byung-Jo Kim, MD, PhD. Comparison of Intradiscal Restorative Injections and Intradiscal Electrothermal Treatment (IDET) in the Treatment of Low Back Pain. Pain Physician. 2004;7:63-66.

- Intradiscal electrothermal therapy (IDET),
- Intradiscal radiofrequency (RF) thermocoagulation
- Intradiscal decompression: decompressor, nucleoplasty, biacuplasty…..

Table 7. *Characteristics and outcomes of studies of PRP in intervertebral disc degeneration.*

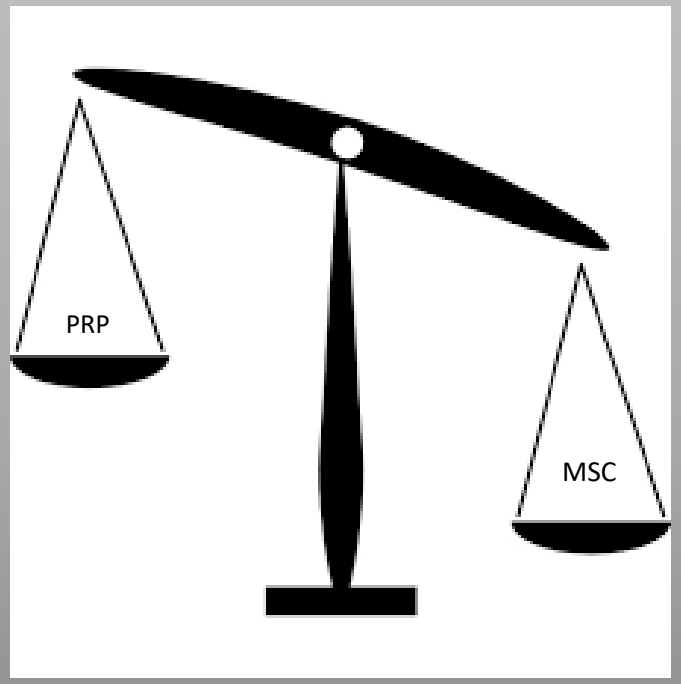
Study Details	Chronicity of Injury and Biologic Used	Follow-up Period	Conclusions
Tuakli-Wosornu et al, 2016 (277) Lumbar discogenic pain Prospective, double-blind, randomized controlled study, n=47	Chronic PRP injections	One year	Intradiscal injections of PRP x1 showed significant improvement at 8-week follow-up, with maintained improvement compared to controls at 1-year follow-up.
Monfett et al, 2016 (276) Lumbar discogenic pain, lumbar disc degeneration Prospective trial, n=29	Chronic PRP injections	2 years	Intradiscal PRP injections show continued safety and improvements in pain and function at 2 years post-procedure
Navani et al, 2018 (274) Lumbar discogenic pain Prospective case series n=20	Chronic PRP, single injection, 2mL injected up to 3 disc levels	18 months	At 18 months, 15 patients remained for survey compared to 18 patients surveyed at 6 months: >50% relief in VAS in 93% of patients at 18 months (n=14/15) and in 94% of patients (n=17/18) at 6 months (2). Improvement in SF-36 scores in 93% of patients at 18 months (n=14/15) compared to 100% (n=18/18) at 6 months.
Akeda et al, 2017 (279) Lumbar discogenic pain Preliminary clinical trial, n=14	Chronic PRP injections	12 months	Intradiscal injection of autologous PRP releasate in patients with low back pain was safe with no adverse events observed during follow-up The results showed reduction in mean pain scores at one month, sustained throughout the observation periods of 6 months and 12 months.
Levi et al, 2016 (275) Lumbar discogenic pain Prospective trial, n=8	Chronic PRP, single injection	6 months	Single or multiple levels (up to 5) of discogenic pain injected with PRP showed encouraging improvement, with more patients developing improvement over time. Cohort up to 6 months.
Kirchner and Anitua, 2016 (278) Lumbar disc degeneration Observational retrospective pilot study, n=86	Chronic PRGF-Endoret	6 months	Fluoroscopy-guided infiltrations of intervertebral discs and facet joints with PRGF in patients with chronic low back pain resulted in significant pain reduction assessed by VAS. The results showed reduction of the VAS over time. The study ended at 6 months with 91% of the patients showing an excellent score, 8.1% showing moderate improvement, and 1.2% showing lack of response.

PRP=platelet-rich plasma; PRGF = plasma rich in growth factors; VAS = Visual Analog Scale; SF-36= 36-item Short Form Survey

Responsible, Safe, and Effective Use of Biologics in the Management of Low Back Pain: American Society of Interventional Pain Physicians (ASIPP) Guidelines.

Pain Physician 2019; 22:S1-S74 •

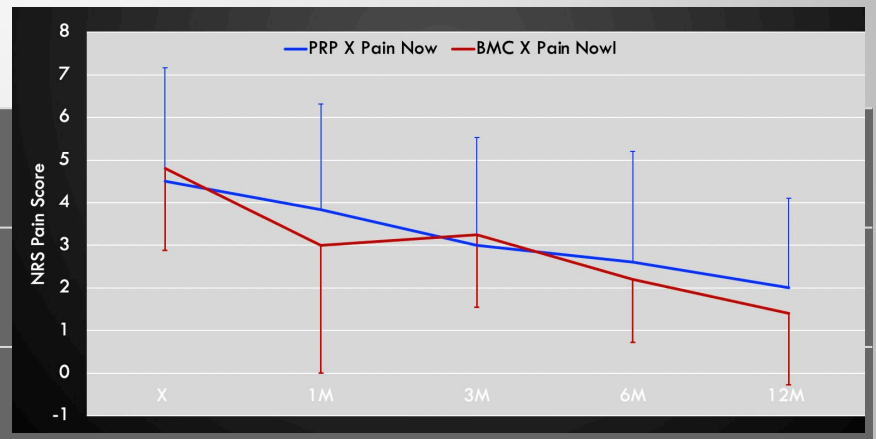
1st EVER HEAD-TO-HEAD
PRP VS. BMC, PROSPECTIVE, MULTI-CTR, RANDOMIZED, PLACEBO-CONTROLLED



Are biologics better than Placebo?

- 4 centers, 40 patients
- Low back or Leg pain with disc pathology
- Randomized into Placebo, PRP or BMC
- Cross over design from Placebo 3 months and from PRP or BMC 6 months
- Autologous PRP or BMC
- Follow up 3, 6 and up to 12 months from last injection
- SAS/STAT software (SAS/STAT version 9.4. Cary, NC: SAS Institute Inc, 2014)
- Primary outcome: Safety and Efficacy
- Secondary outcome:
  - Patient satisfaction: modified NASS
  - Change in medication use, interim hospitalization, spine surgery

Pain Now after Crossing to PRP (N=7) & BMC (N=5)



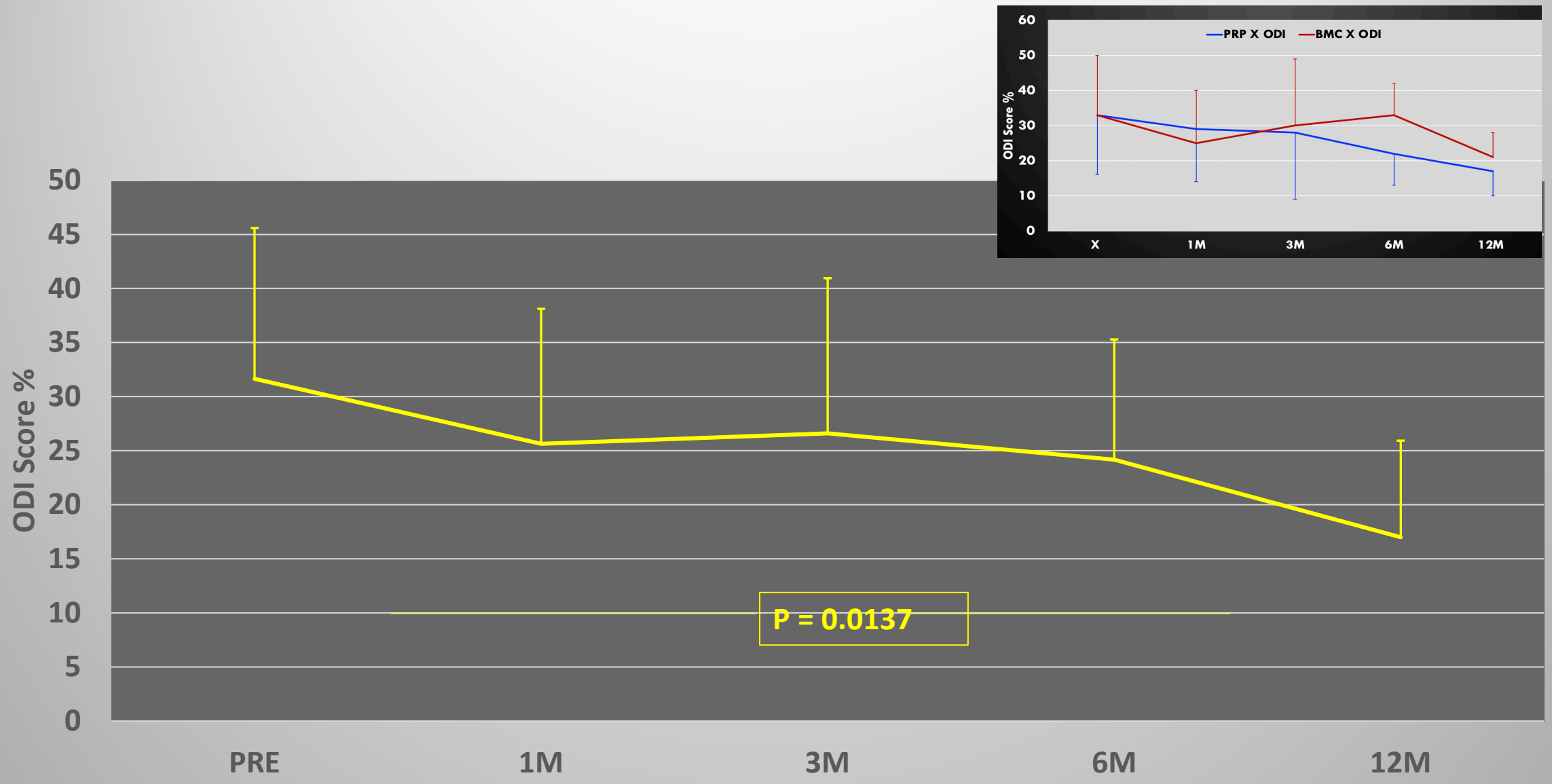
NRS Pain Score

8
7
6
5
4
3
2
1
0

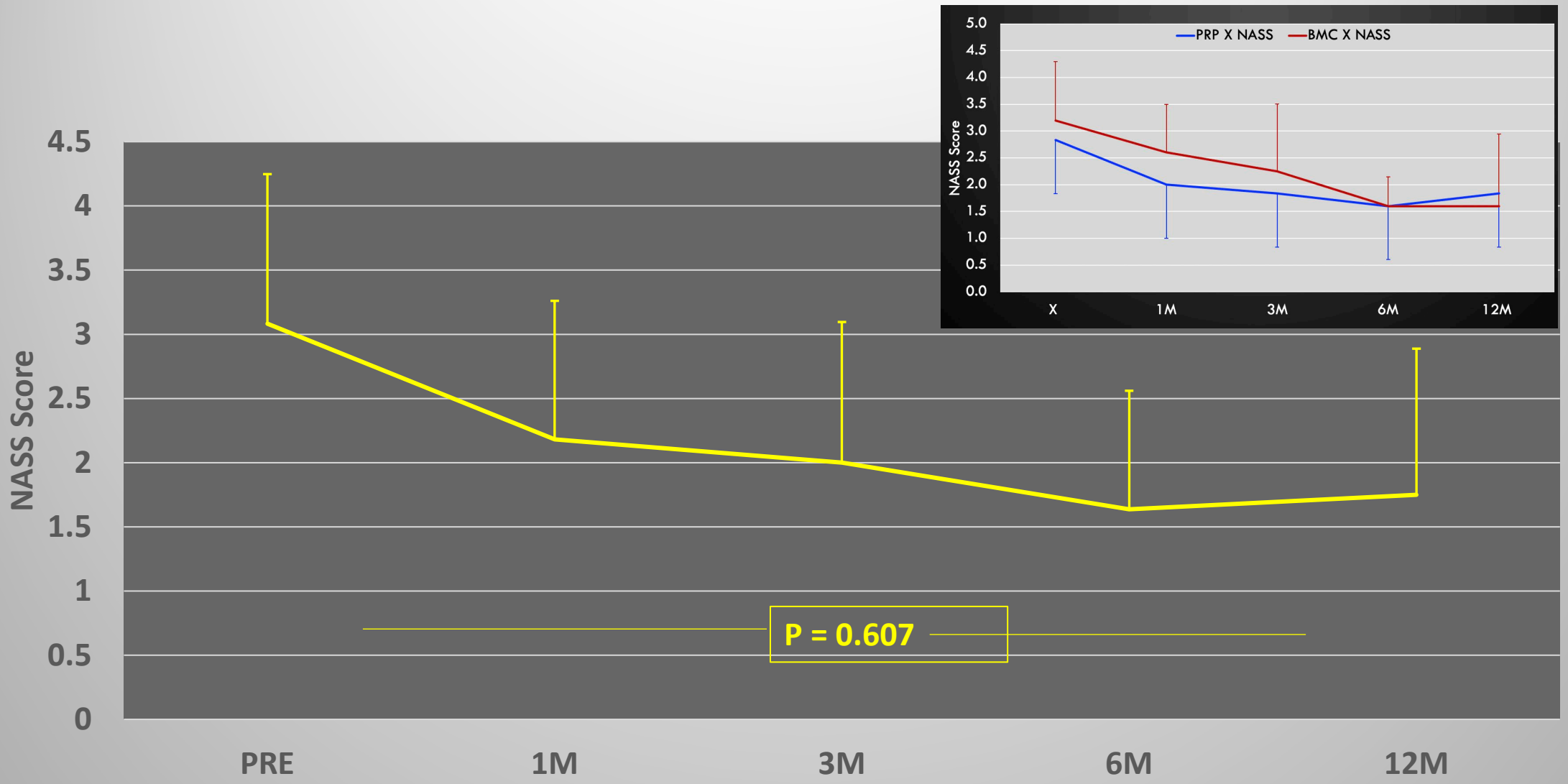
P = 0.0043

PRE
1M
3M
6M
12M

ODI Score after Crossing to PRP(N=7) & BMC (N=5)



NASS Score after Crossing to PRP (N=7) & BMC (N=5)



Navani et al:

Intradiscal PRP vs. BMC vs. Placebo:

prospective, randomized, placebo controlled, multi-center pilot study.

PRP and BMC were equally effective in treating discogenic low back and/or leg pain after 12 months of a single injection.

All placebo patients crossed to a biological interventional procedure after 3 months.

All crossed patients showed significant improvements of NRS pain score, ODI functional score and NASS score up to 12 months.

In none of the patients a secondary biological intervention was indicated.

None of the patients underwent a surgical procedure for back pain or hospitalization due to the biological interventional procedure.

No complications in any subjects.

There was no statistical difference after 12 months between the 3 group with regards to age and gender.

No difference between BMC vs. PRP in the pilot.

International Journal of
Molecular Sciences

MDPI

Article

The safety and effectiveness of orthobiological injections for discogenic chronic low back pain: a prospective randomized controlled study.

Annu Navani [1], Mary Ambach [2], Aaron Calodney[3], Richard Rosenthal [4], Christine Brown Mahoney [5], and Peter Everts [6,] *

[1] Comprehensive Sports and Spine Center, Campbell CA, USA; anavani@csscstr.com
[2] The Ortho Healing Center, Los Angeles CA, USA; ambach@sdomg.com
[3] Texas Spine and Joint Hospital. Tyler TX, USA; aaroncalodney@me.com
[4] Nexus Pain Care, Provo UT, USA; rmrdunbar@icloud.com
[5] Minnesota State University, Mankato MN, USA; christine.mahoney@mnsu.com
[6] Gulf Coast Biologics, Fort Myers FL, USA; peter@gulfcoastbiologics.com
* Correspondence: peter@gulfcoastbiologics.com; Tel.: +1 239 478 2284, PE

Pain Physician 2022; 25:193-207 • ISSN 1533-3159

Prospective Study

Evaluation of the Effectiveness of Autologous Bone Marrow Mesenchymal Stem Cells in the Treatment of Chronic Low Back Pain Due to Severe Lumbar Spinal Degeneration: A 12-Month, Open-Label, Prospective Controlled Trial

Sairam Atluri, MD[1], Matthew B. Murphy, PhD[2], Ryan Dragella, PhD[3], Jessica Herrera, BS[3], Kwadwo Boachie-Adjei, BS, CPH[4], Sachi Bhati[1], Vivek Manocha, MD[5], Navneet Boddu, MD[6], Pavan Yerramsetty, MD[7], Zaid Syed[1], Meghana Ganjam[1], Divit Jain[1], Zaynab Syed[1], Nikhil Grandhi[8], and Laxmaiah Manchikanti, MD[9]

- Prospective, open-label, nonrandomized, parallel-controlled, 2-arm exploratory study.
- The treatment group patients received a one-time bone marrow concentrate injection into spinal structures (i.e., discs, facets, spinal nerves, and sacroiliac joints), along with conventional treatment, the control group received conventional treatment.
- The results showed significant improvements at 12-month follow-up with 67% of the patients in the study group achieving MCID utilizing ODI when compared to 8% in the control group.
- Greater than 2-point pain reduction was seen in 74% of the patients at 3 months, 66% of the patients at 6 months, and 56% of the patients at 12 months.
- Both MCID and pain relief of 2 points were significantly different compared to the control group.
- Opioid use decreased in the investigational group, there was a slight increase in the control group.
- Age, gender, opioid use, and body mass index did not affect the outcomes in the stem cell group.

Hindawi
Pain Research and Management
Volume 2022, Article ID 6181478, 9 pages
https://doi.org/10.1155/2022/6181478

Research Article

Transforaminal Endoscopic Lumbar Discectomy with versus without Platelet-Rich Plasma Injection for Lumbar Disc Herniation: A Prospective Cohort Study

Yi Jiang,[1,2] Rujun Zuo,[2] Shuai Yuan,[2] Jian Li,[2] Chang Liu,[2] Jiexun Zhang,[2] Ming Ma,[2] Dasheng Li,[3] and Yong Hai[2]

- Clinical improvement was noted in both groups.
- There were statistical differences in the VAS scores of back and leg pain and ODI between the two groups at 3 months, 6 months, and 1 year follow-up ($P < 0.05$); the improvement in the PRP group was significant.
- The disc protrusion and SCSA on MRI in the PRP group showed better improvement, with lower recurrence rate, than that in the control group at the final follow-up ($P < 0.05$).
- No adverse events were reported in our study following PRP injection

> Stem Cells Dev. 2019 Sep 1;28(17):1203-1211. doi: 10.1089/scd.2019.0074. Epub 2019 Jul 23.

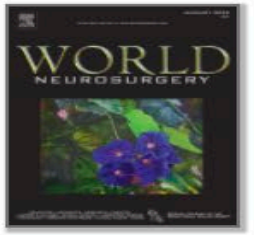
The Traceability of Mesenchymal Stromal Cells After Injection Into Degenerated Discs in Patients with Low Back Pain

Helena Barreto Henriksson [1 2 3], Nikolaos Papadimitriou [1 4], Daphne Hingert [1], Adad Baranto [1 4], Anders Lindahl [3], Helena Brisby [1 4]

- MSCs, labeled with iron sucrose, transplanted into degenerated IVDs were detectable 8 months post-transplantation.

- The detected cellular activity indicates that MSCs have differentiated into chondrocyte-like cells and that the injected MSCs and/or their progeny have survived since the cells were found in large cluster and as solitary cells which were distributed at different parts of the IVD.

World Neurosurgery
Volume 157, January 2022, Pages 282-299



From the Annals of Weill Cornell Neurological Surgery

Innovative Biological Treatment Methods for Degenerative Disc Disease

Sertac Kirnaz [1], Sunidhi Singh [1], Charisse Capadona [1], Marianne Lintz [1], Jacob L. Goldberg [1], Lynn B. McGrath Jr. [1], Branden Medary [1], Fabian Sommer [1], Lawrence J. Bonassar [2, 3], Roger Härtl [1]

Pain Physician 2020; 23:477-484 • ISSN 1533-3159

Randomized Trial

Efficacy of Intradiscal Ozone Therapy with or without Periforaminal Steroid Injection on Lumbar Disc Herniation: A Double-Blinded Controlled Study

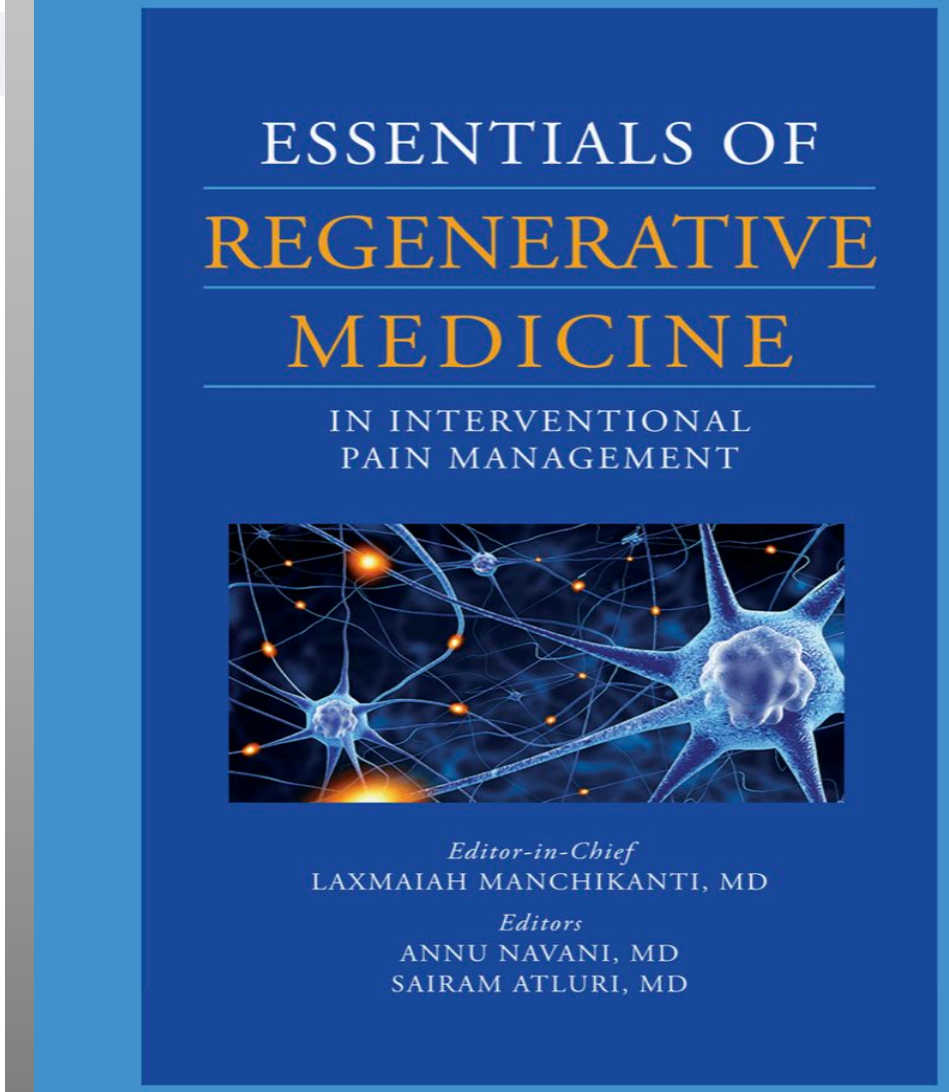
Tulay Ercalik, MD, and Mustafa Kilic, MD

Pain Physician 2019; 22:S1-S74 • ISSN 1533-3159

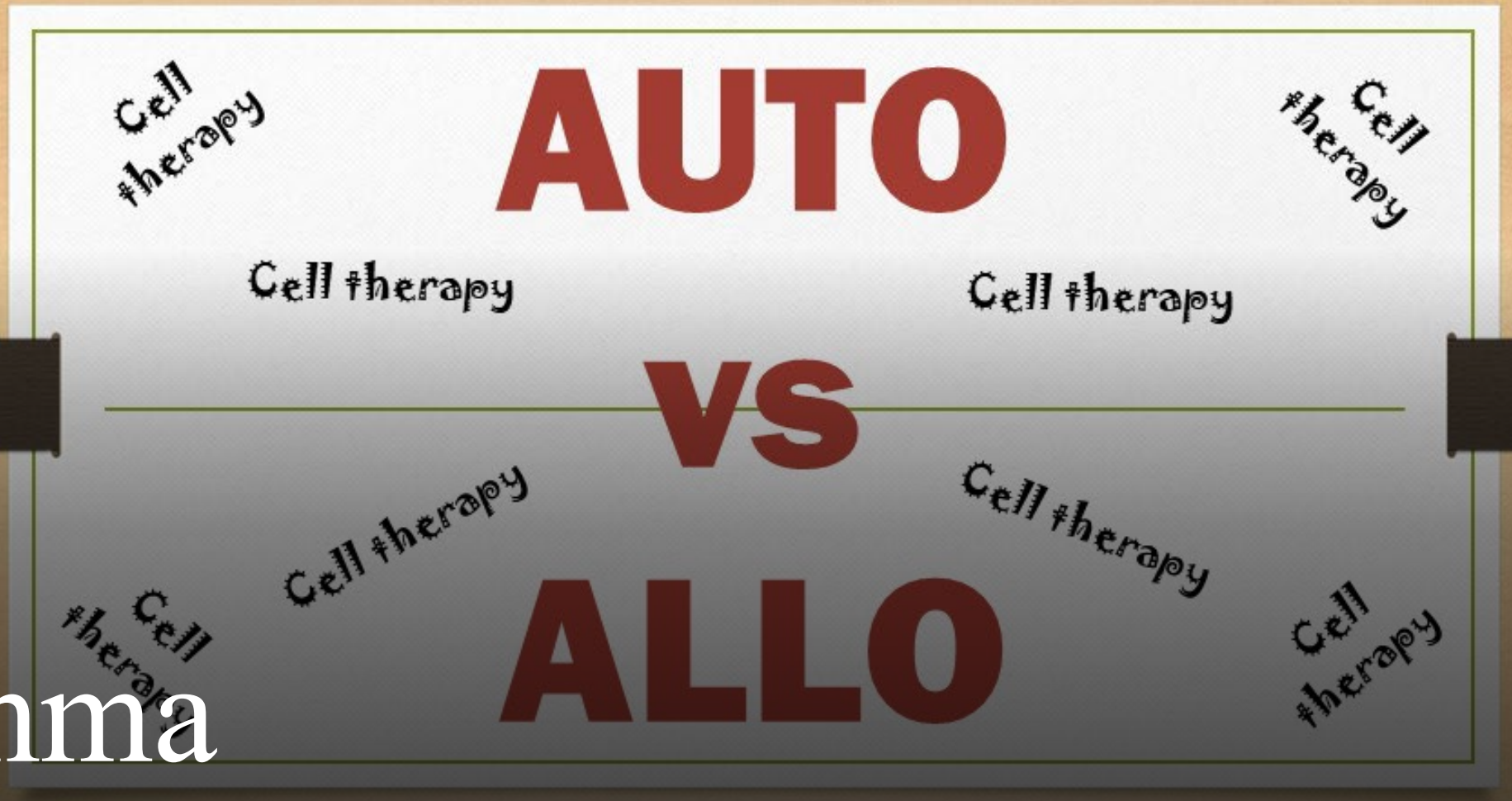
Guidelines

Responsible, Safe, and Effective Use of Biologics in the Management of Low Back Pain: American Society of Interventional Pain Physicians (ASIPP) Guidelines

Annu Navani, MD[1], Laxmaiah Manchikanti, MD[2], Sheri L. Albers, DO[3], Richard E. Latchaw, MD[4], Jaya Sanapati, MD[5], Alan D. Kaye, MD, PhD[6], Sairam Atluri, MD[7],Sheldon Jordan, MD[8], Ashim Gupta, PhD, MBA[9], David Cedeno, PhD[10], Alejandro Vallejo, BS[11], Bert Fellows, MA[12], Nebojsa Nick Knezevic, MD, PhD[13], Miguel Pappolla, MD[14], Sudhir Diwan, MD[15], Andrea M. Trescot, MD[16], Amol Soin, MD[17], Adam M. Kaye, PharmD, FASCP, FCPhA[18], Steve M. Aydin, DO[19], Aaron K. Calodney, MD[20], Kenneth D. Candido, MD[21], Sanjay Bakshi, MD[22], Ramsin M. Benyamin, MD[23], Ricardo Vallejo, MD, PhD[24], Art Watanabe, MD[25], Douglas Beall, MD[26], Todd P. Stitik, MD[27], Patrick M. Foye, MD[28], Erik M. Helander, MBBS[29], and Joshua A. Hirsch, MD[30]

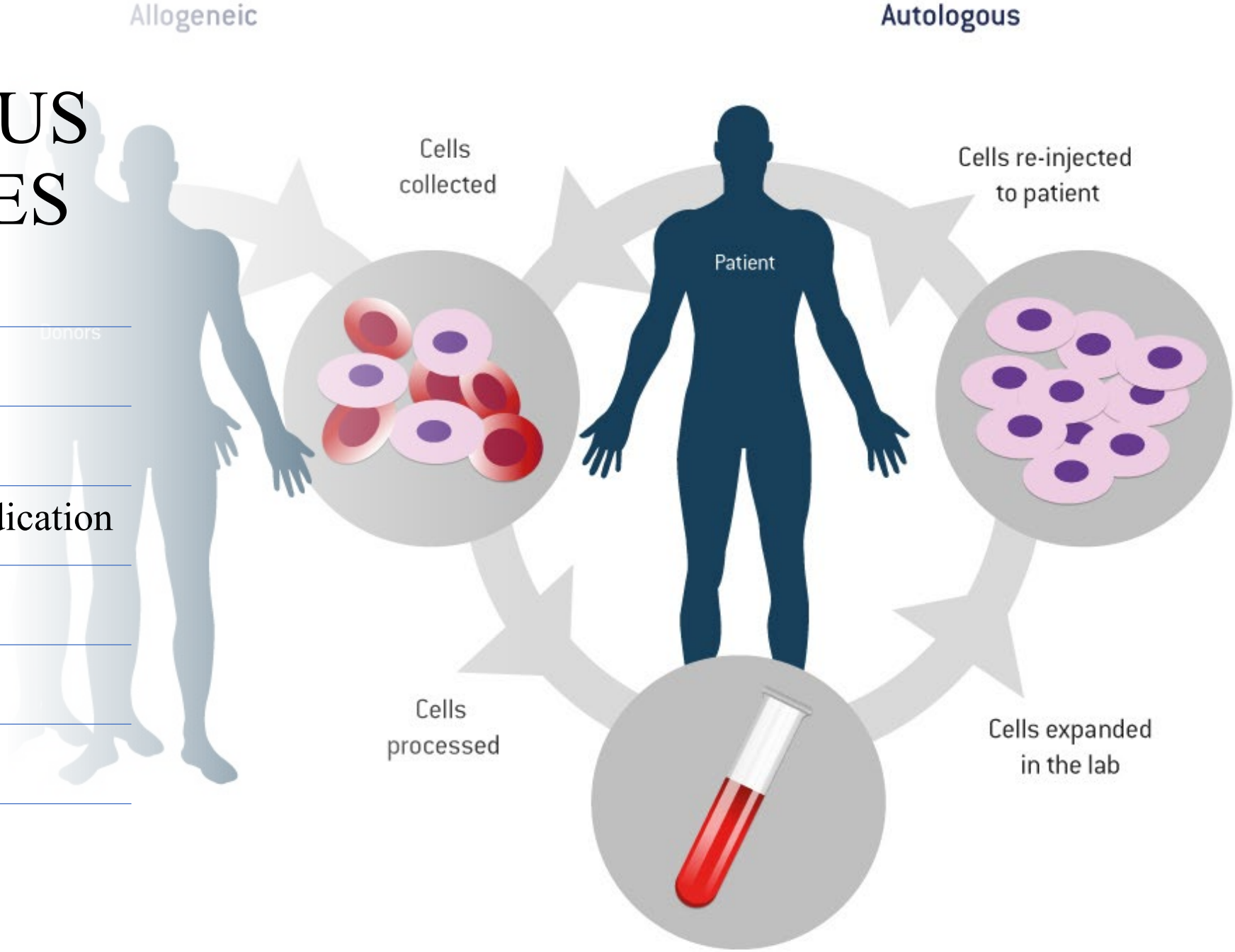


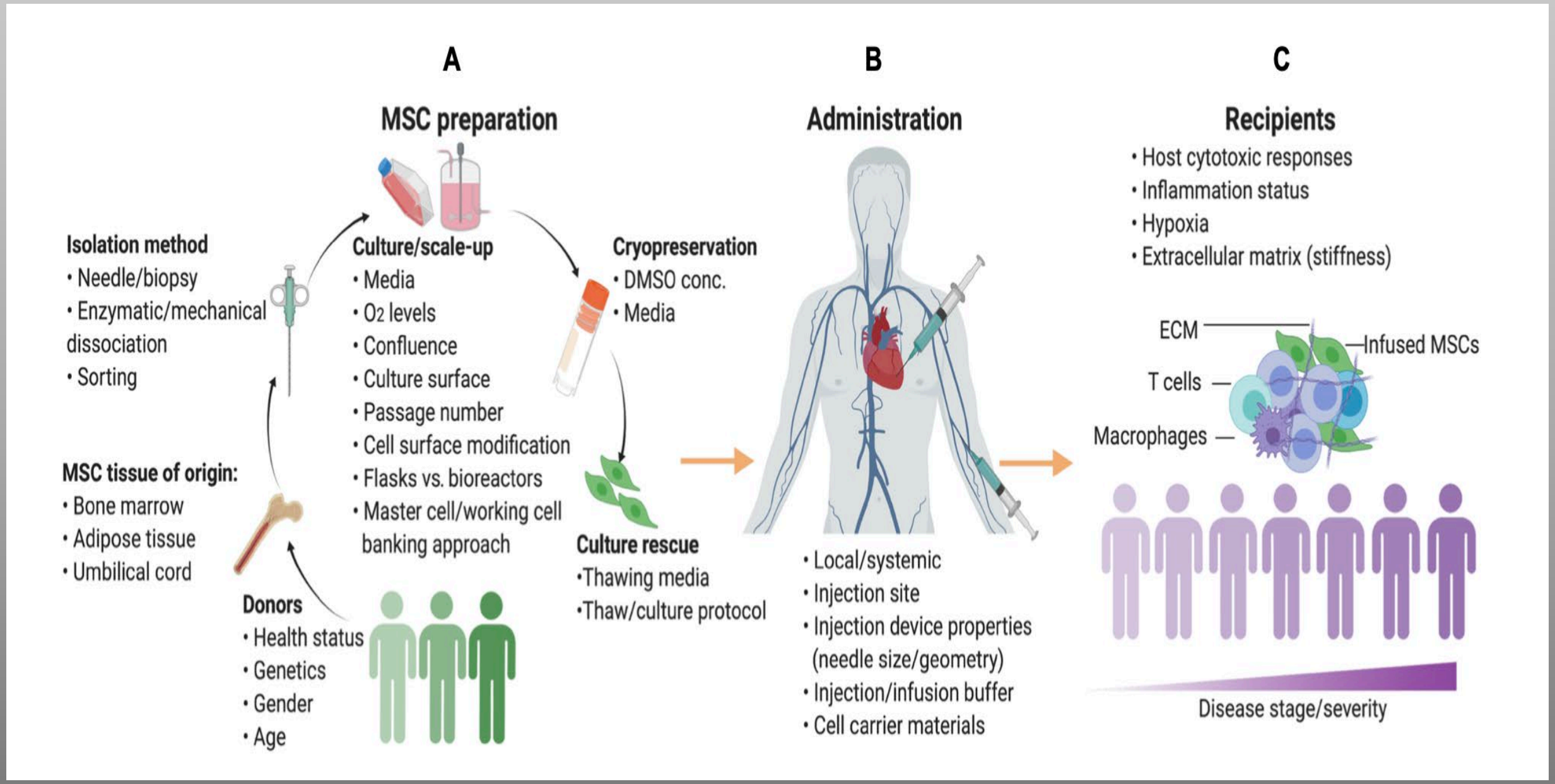
Dilemma


AUTO
Cell therapy
Cell therapy
Cell therapy
Cell therapy
VS
Cell therapy
Cell therapy
Cell therapy
Cell therapy
ALLO

AUTOLOGOUS CHALLENGES

- Volume limitation
- Quality limitation
- Systemic disease contraindication
- Harvesting talent
- Harvesting time
- Cost and Quality
- Consistency

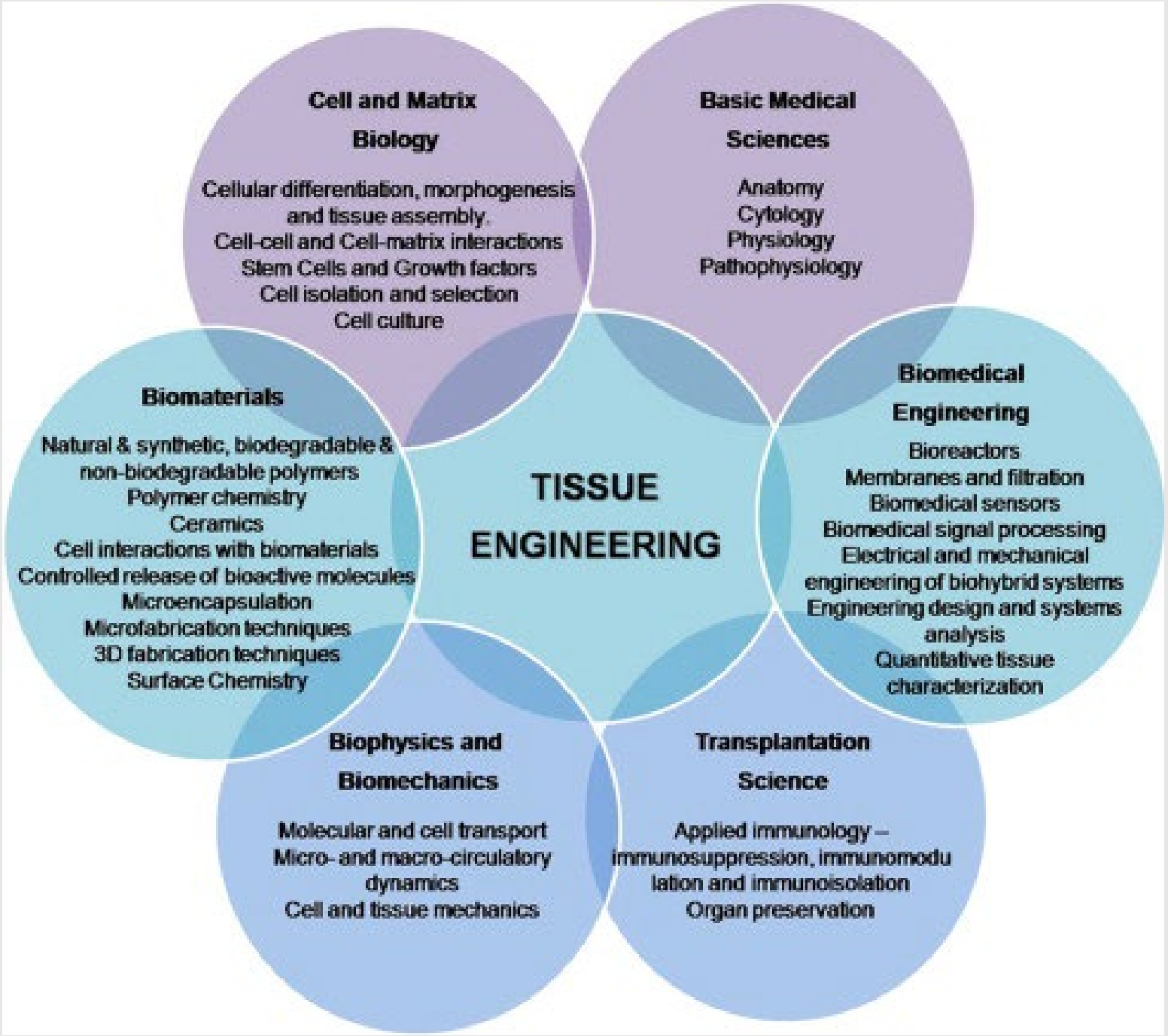




Levy *et al.*, *Sci. Adv.* 2020; **6** : eaba6884 22 July 2020

Host Factors effecting MSCs outcomes

- Disease type and stage
- Differentiation of MSCs
- Administration routes
- Timing of MSC administration
- Dosage of MSC administration
- Comorbidities
- Evaluation time-points
- Primary and Secondary outcomes


Cell and Matrix Biology
Cellular differentiation, morphogenesis and tissue assembly.
Cell-cell and Cell-matrix interactions
Stem Cells and Growth factors
Cell isolation and selection
Cell culture
Basic Medical Sciences
Anatomy
Cytology
Physiology
Pathophysiology
Biomaterials
Natural & synthetic, biodegradable & non-biodegradable polymers
Polymer chemistry
Ceramics
Cell interactions with biomaterials
Controlled release of bioactive molecules
Microencapsulation
Microfabrication techniques
3D fabrication techniques
Surface Chemistry
TISSUE ENGINEERING
Biomedical Engineering
Bioreactors
Membranes and filtration
Biomedical sensors
Biomedical signal processing
Electrical and mechanical engineering of biohybrid systems
Engineering design and systems analysis
Quantitative tissue characterization
Biophysics and Biomechanics
Molecular and cell transport
Micro- and macro-circulatory dynamics
Cell and tissue mechanics
Transplantation Science
Applied immunology – immunosuppression, immunomodulation and immunoisolation
Organ preservation

Journal of Stem Cells Research, Reviews & Reports

Open Access

Austin Publishing Group

Research Article

Biologic Therapies for Intervertebral Degenerative Disc Disease: A Review of Novel Applications

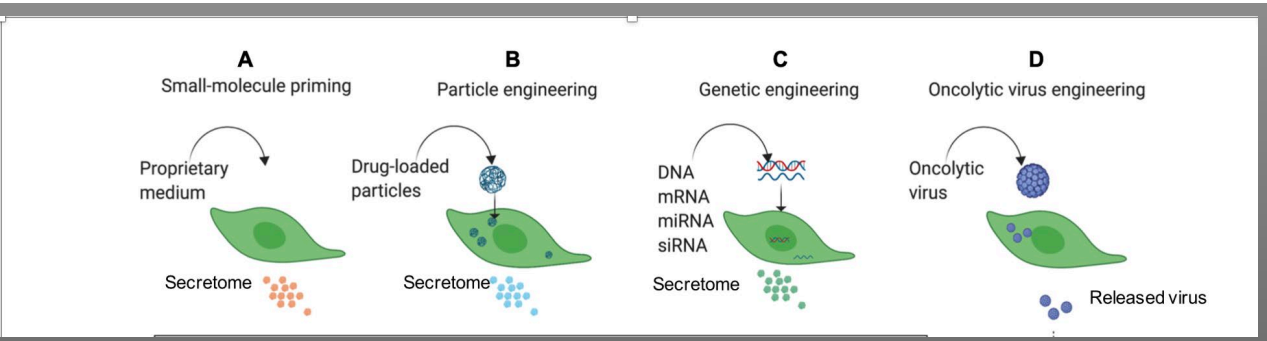
Navani A[1], Ambach MA[2]*, Wei JJ[3] and Gupta D[4]
[1]Comprehensive Spine and Sports Center, USA
[2]Orthohealing Center, USA
[3]Western University of Health Sciences, USA
[4]Rutgers New Jersey Medical School, USA

***Corresponding author:** Mary A Ambach, Orthohealing Center, USA

Received: January 24, 2017; **Accepted:** February 28, 2017; **Published:** March 01, 2017

Abstract

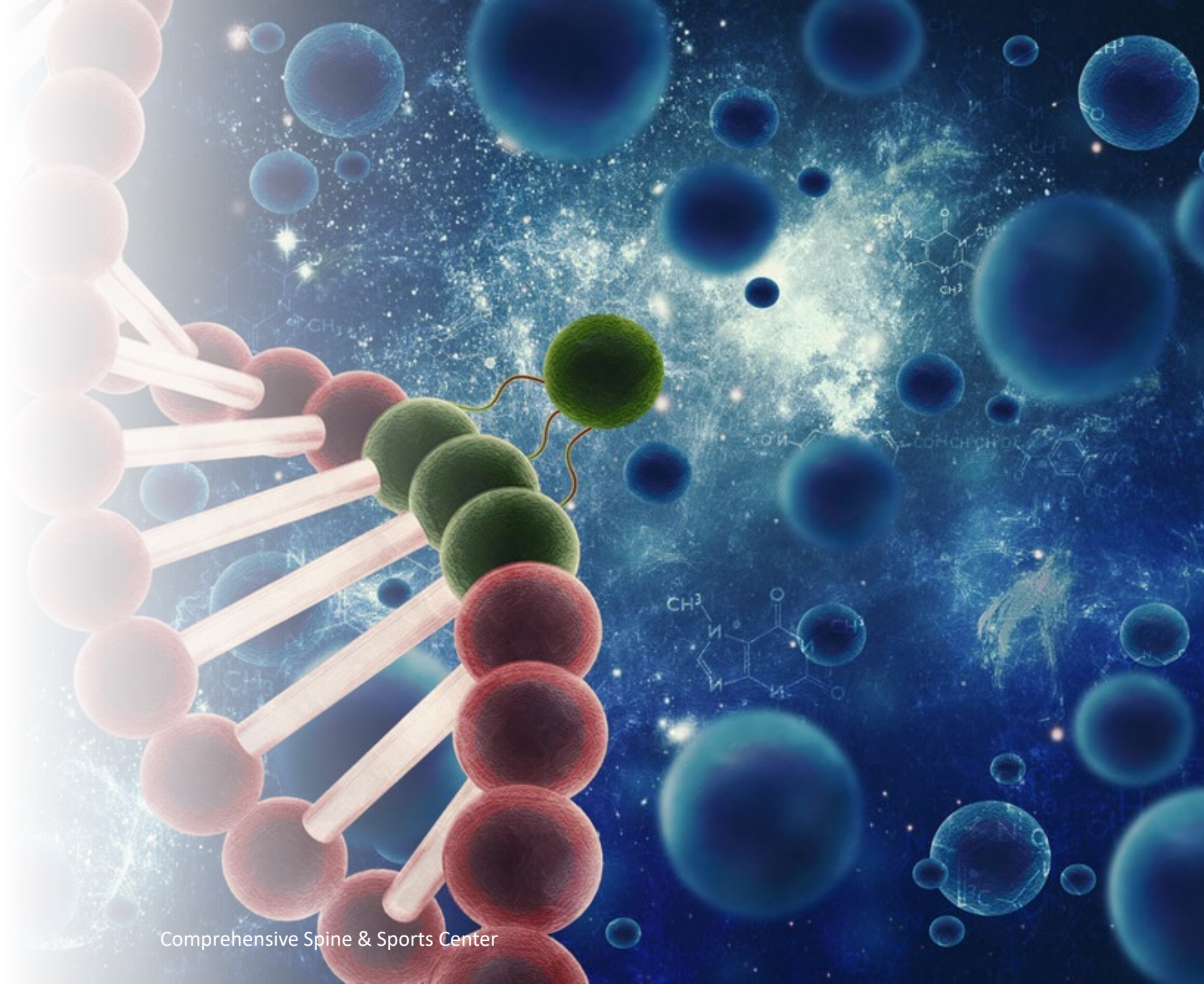
Intervertebral disc disease is a common cause of low back pain affecting both the young and the elderly. Standard treatment options involve conservative treatments such as physical therapy and anti-inflammatory medications but also include more invasive techniques such as injections, thermal ablation, and surgery. Despite these treatments, chronic low back pain in many of these patients continues to persist limiting their function and quality of life. There has been a great interest in using biologic agents, such as Platelet Rich Plasma (PRP) and Mesenchymal Stem Cells (MSCs), to repair the disc degeneration and tears when traditional treatments fail to provide symptomatic relief. This comprehensive report reviews these new approaches including the use of platelet rich plasma injections, bone marrow aspirate injections, lipoaspirate injections, protein based therapy, 3D printing and scaffolds, gene therapy, predictive analytics, and functional imaging. The authors have also shared their vision of anticipated growth and customization of this rapidly growing field as it applies to intervertebral disc degeneration. Regenerative medicine has the potential to revolutionize the way we approach spine care in patients and further collaboration is needed among involved disciplines to advance this very exciting and important field.



Levy *et al.*, *Sci. Adv.* 2020; **6** : eaba6884 22 July 2020

Biologics: 2030

- Biologic-Device combination products
- Microenvironment optimization
- Statistical modeling & Artificial Intelligence
- Genetically programmed cells
- Bioprinting & Nanotechnology
- Novel Disc and Cartilage biologic constructs



Annu Navani, MD
Founder and CEO, Comprehensive Spine & Sports Center
Advisor, Le Reve Regenerative Wellness
www.annunavani.com
anavani@cssctr.com