
SPINE
SIS
INTERVENTION SOCIETY
25TH ANNUAL MEETING
SAN FRANCISCO MARRIOTT MARQUIS
JULY 19-22, 2017
25th Annual Meeting Slides
LOOKING FORWARD TO THE FUTURE

Stem Cell for Spine Care
- From dish to disc

Wenchun Qu, MD, PhD Mayo Clinic Rochester

LOOKING FORWARD TO THE FUTURE

Disclosures

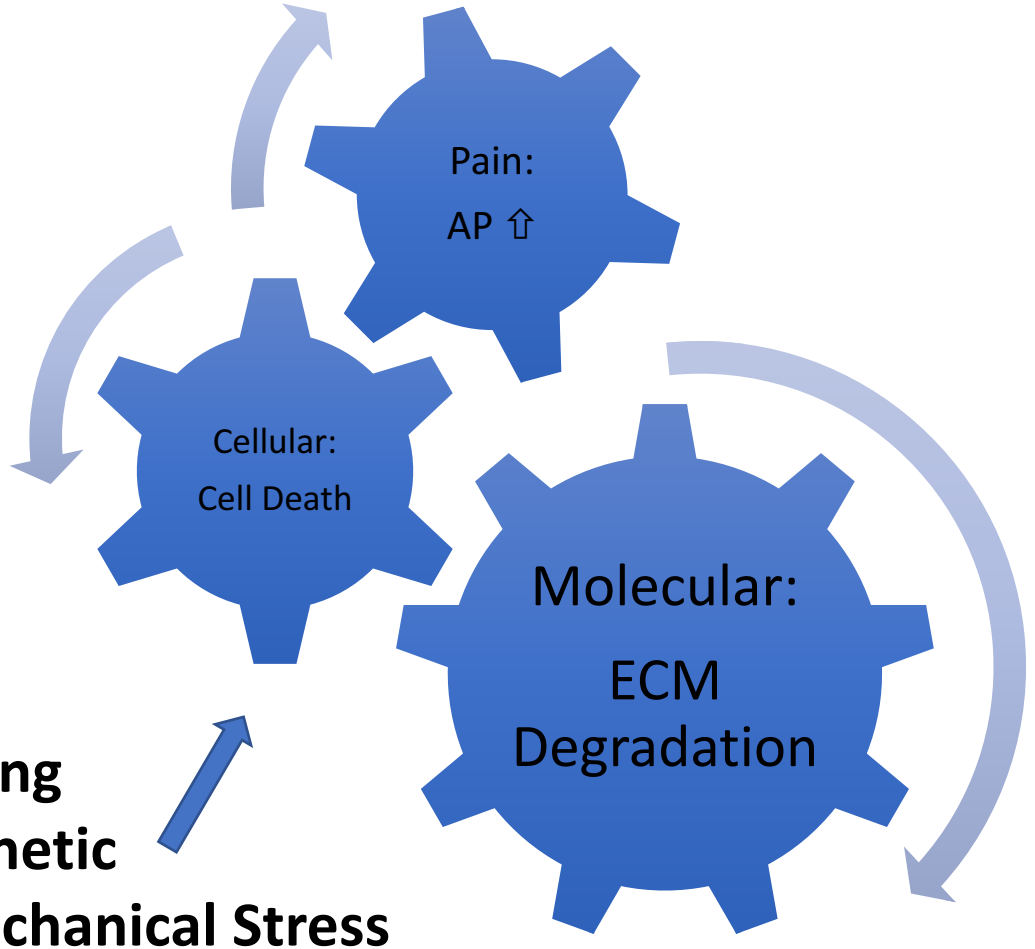
- Consultant, DePuy Synthes
- Board of Directors, American Academy of Regenerative Medicine
- Board of Directors, Society of Chinese American Physician Entrepreneurs

Goals for Discussion

1. To recognize the activities of stem cells
2. To review stem cells based on strategy of preparation
3. To familiarize with current regen spine service and translational research

Processes of Disc & Cartilage Degeneration

- Three processes
  - Cellular process
    - Apoptosis
  - Molecular process
    - Cytokine profile
    - Matrix degradation
  - Painful experience
    - AP frequency ⇧



- Aging
- Genetic
- Mechanical Stress
- Obesity

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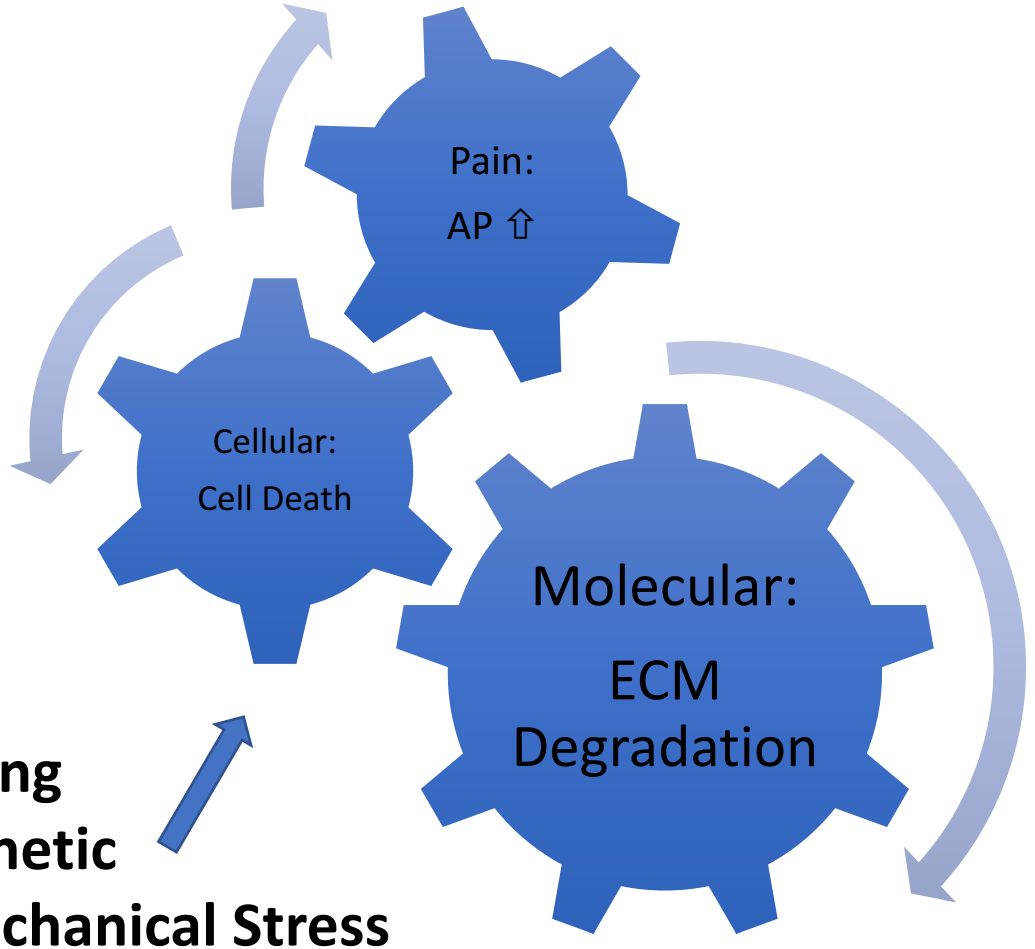
Trophic Effects



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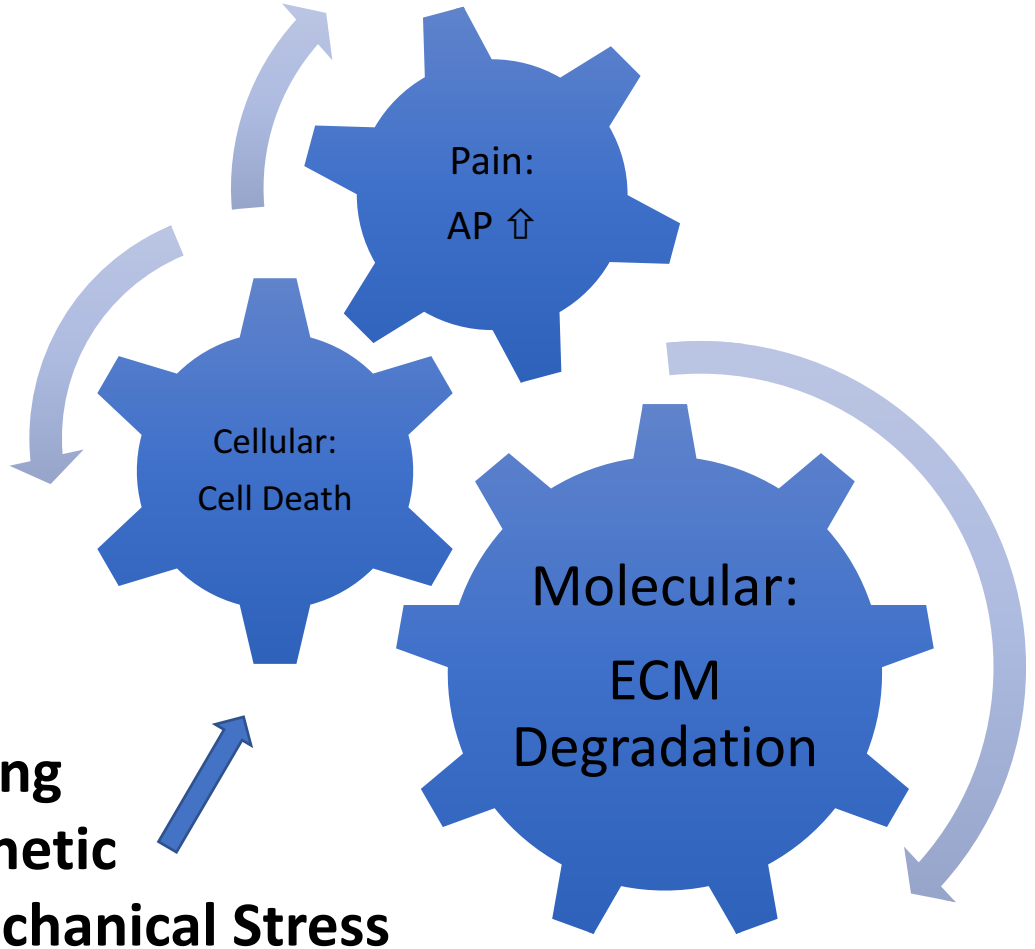
Trophic Effects

Immunomodulation



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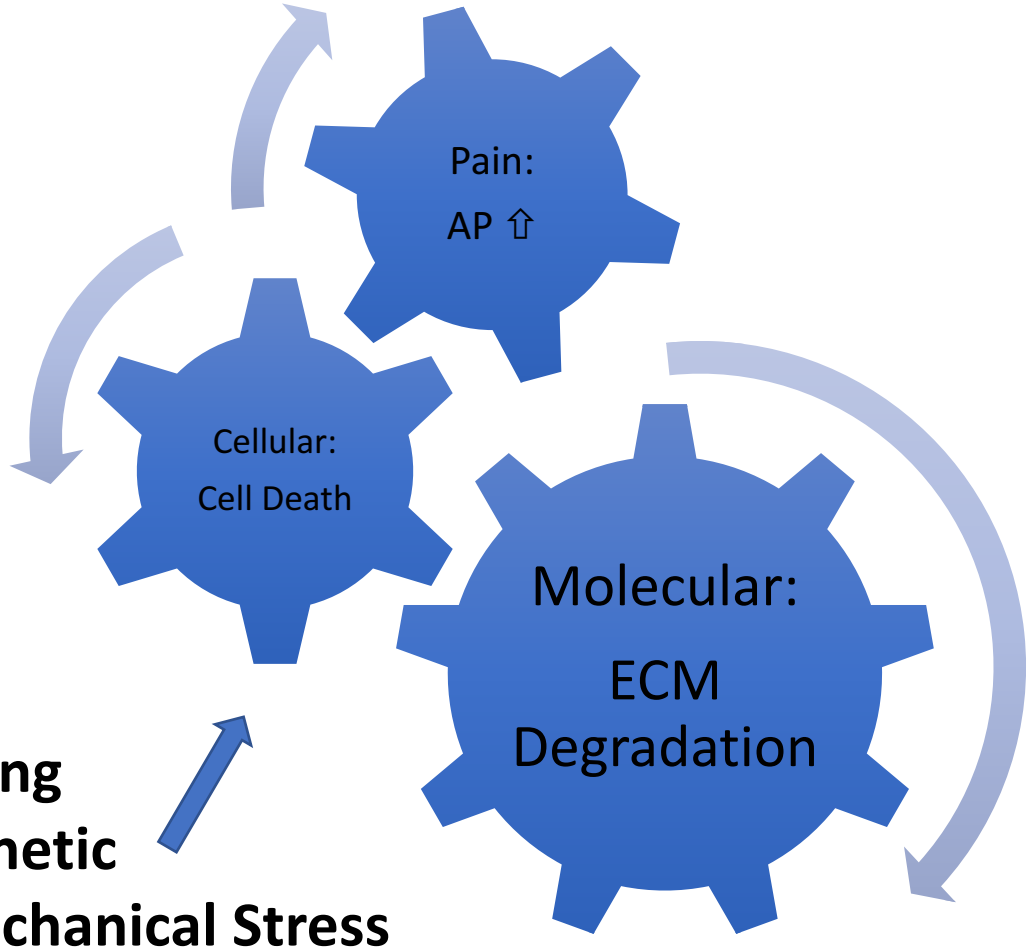
Trophic Effects

Immunomodulation

Pain & Function



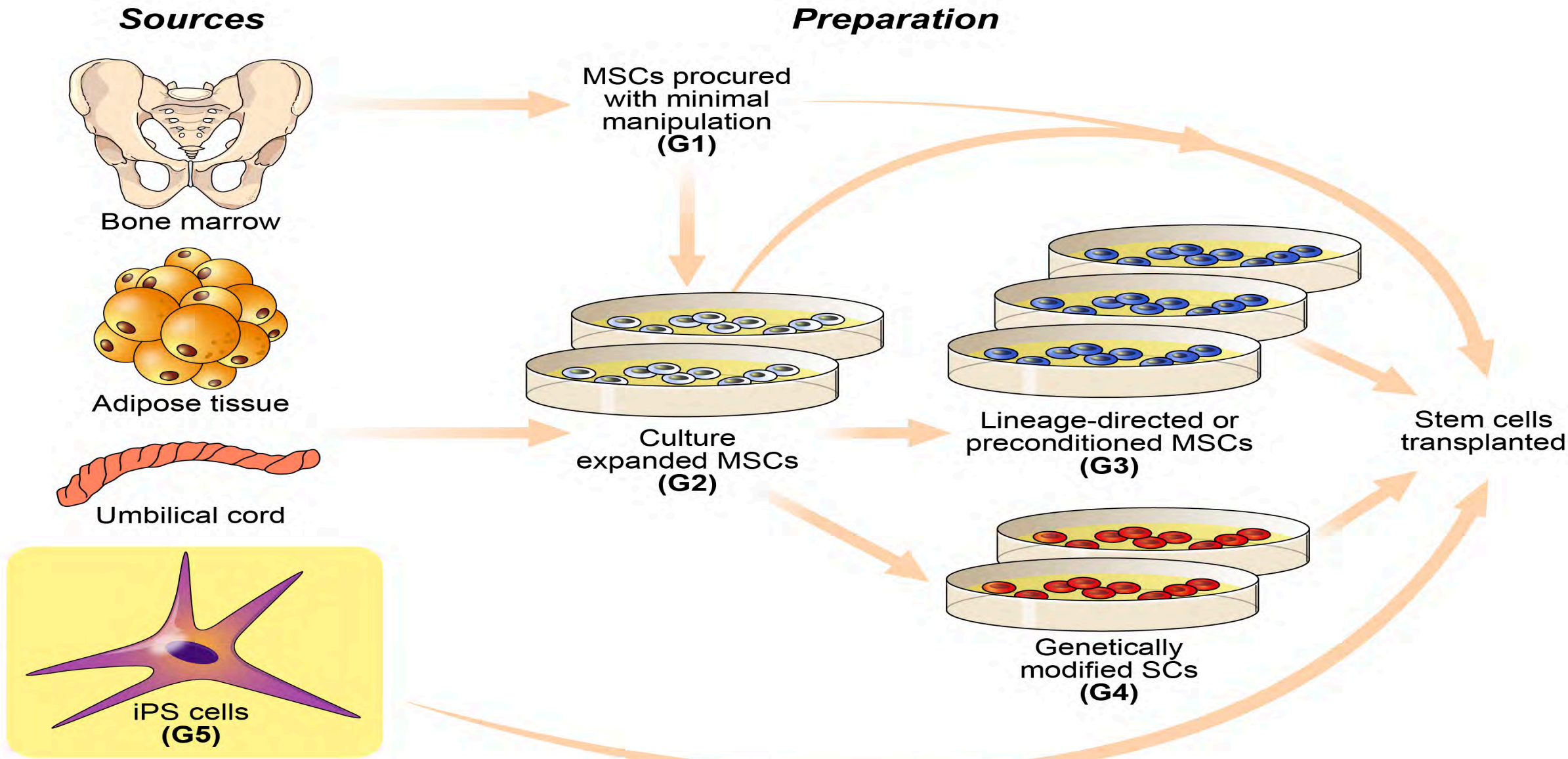
- **Aging**
- **Genetic**
- **Mechanical Stress**
- **Obesity**

Source of MSCs

Human tissue source	CFU-F yield (per cc of tissue)	MSC frequency range (CFU-F/10^6 nucleated cells)
Bone marrow aspirate	109–664	10–83
Adipose/lipoaspirate	2058–9650	205–51000
Umbilical cord blood	0.06	0–0.02
Synovial fluid	4–14	2–250
Amniotic fluid	3	9.2
Peripheral blood	0	0-2
Dermis	Not reported	74 000– 157000

Murphy, *Experimental & molecular medicine*, *45*(11), e54.

Five Generations of Stem Cells Based on Preparation Strategy

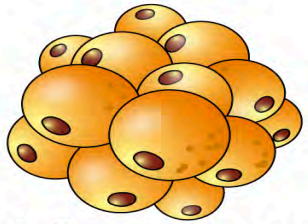


Hunt, 2017

Five Generations of Stem Cells Based on Preparation Strategy

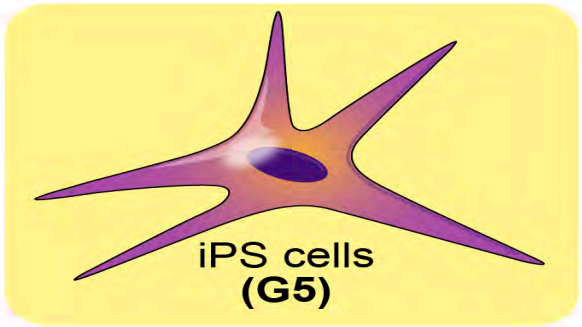
Sources

Bone marrow



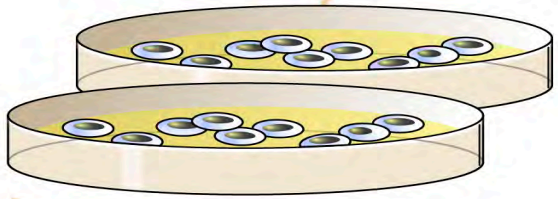
Adipose tissue

Umbilical cord

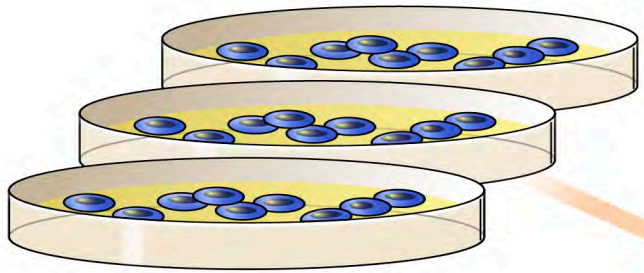


Preparation

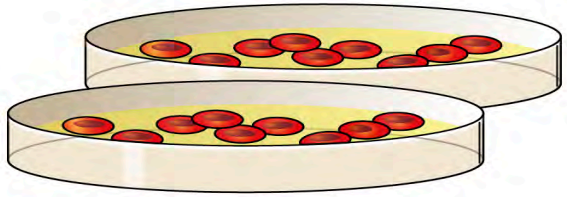
MSCs procured with minimal manipulation **(G1)**



Culture expanded MSCs **(G2)**



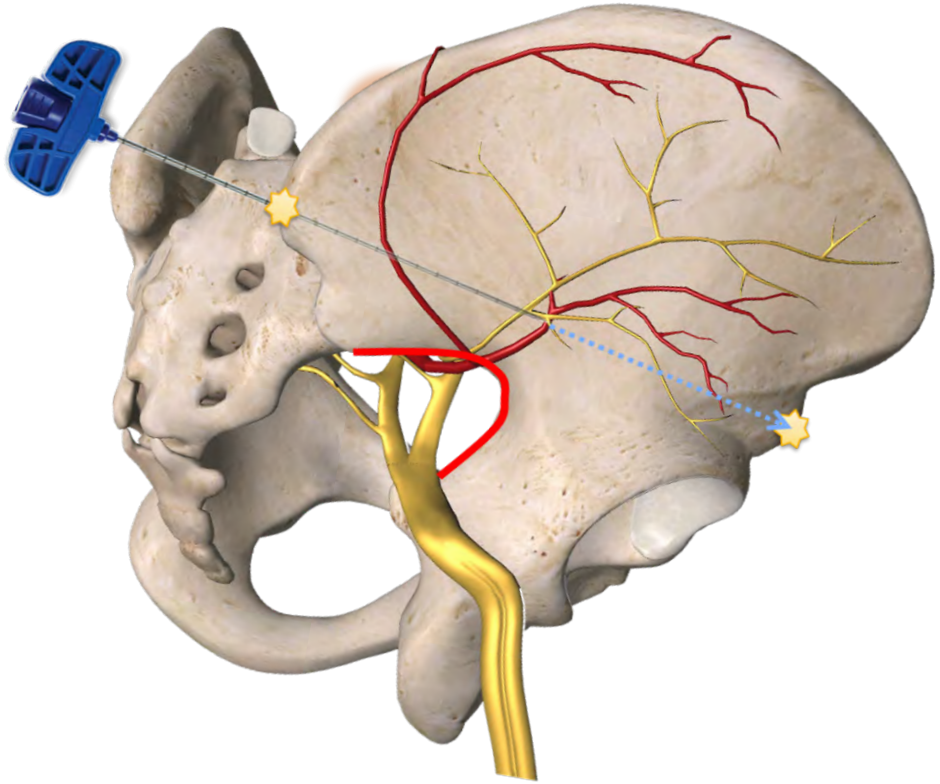
Lineage-directed or preconditioned MSCs **(G3)**

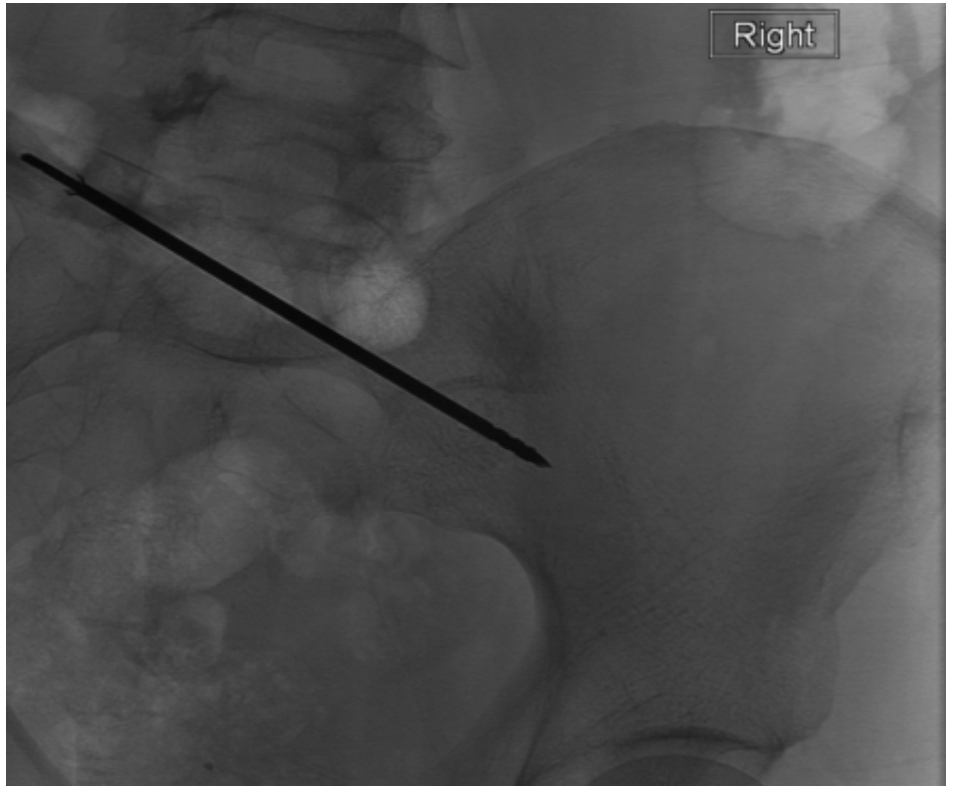


Genetically modified SCs **(G4)**

Stem cells transplanted

Technique of Bone Marrow Aspiration





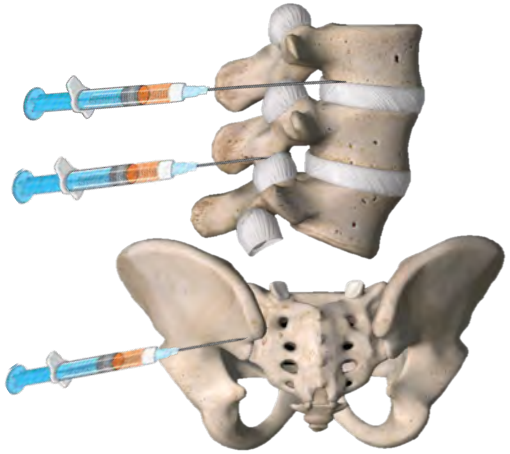
Current Regen Pain Services

- Bone Marrow Aspirate Concentrate Injection

Bone Marrow Aspiration

Bone Marrow Mesenchymal Stem Cell (BMSC)

Bone Marrow Aspirate Concentration (BMAC)



BMAC Injection
- **Disc**
- **Facet**
- **SIJ**

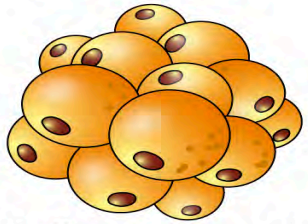
G1:Bone Marrow Aspirate Concentrate

Author, Year	Design	N	Indication	Outcomes	AEs
Pettine et al 2015	Prospective Open label	26	IVD	ODI 57->24** VAS 79->33** MRI	None
Pascual-Garrido et al 2012	Prospective Open label	8	Chronic patellar tendinopathy	Lysholm Tegner2->8* Cincinnati, IKDC 36->69* KOOS 44->71* diagnostic US	None reported
Yan et al, 2015	Retrospective Decomp vs Decomp+ BMAC	86 (42 vs 44)	Femoral head AVN	VAS both* w/ trend	None
Shapiro et al, 2016	RCT BMAC vs Saline	25	Knee OA	VAS both* No grp diff	None

Five Generations of Stem Cells Based on Preparation Strategy

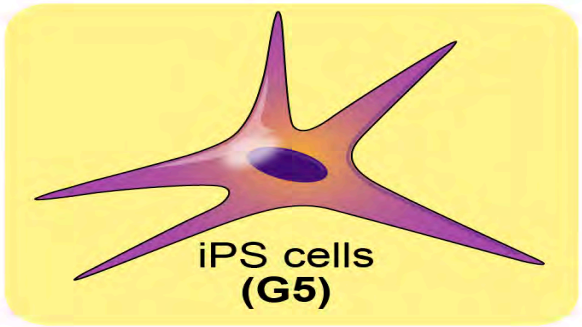
Sources

Bone marrow



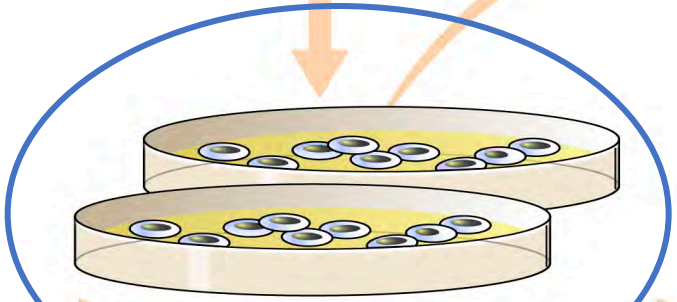
Adipose tissue

Umbilical cord

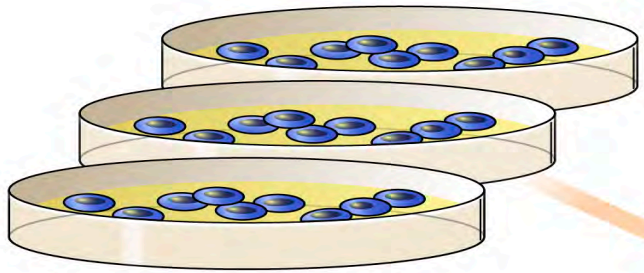


Preparation

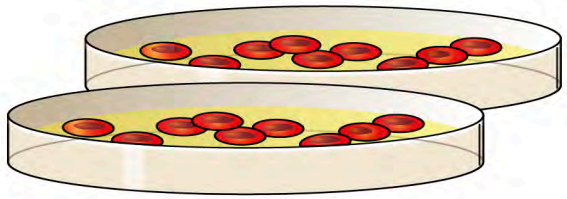
MSCs procured with minimal manipulation **(G1)**



Culture expanded MSCs **(G2)**



Lineage-directed or preconditioned MSCs **(G3)**

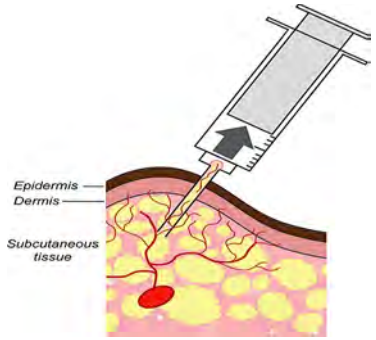


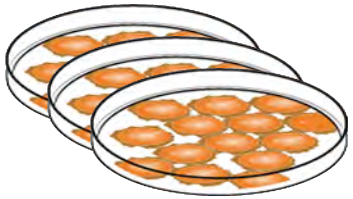
Genetically modified SCs **(G4)**

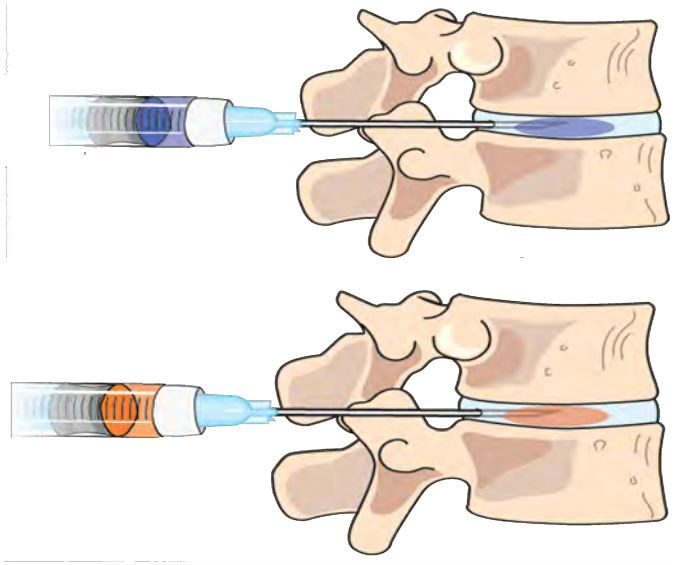
Stem cells transplanted

Transform the Practice Initiative Trial - AMSCs for discogenic pain

- Culture Expanded AMSC Injection







Adipose Biopsy

Adipose Derived Mesenchymal Stem Cell (BMSC)

Culture Expansion of AMSC

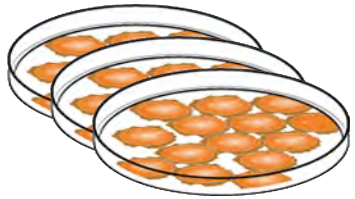
AMAC Injection
- Intradiscal
- Therapy Arm

Industry Trial for Discogenic Pain

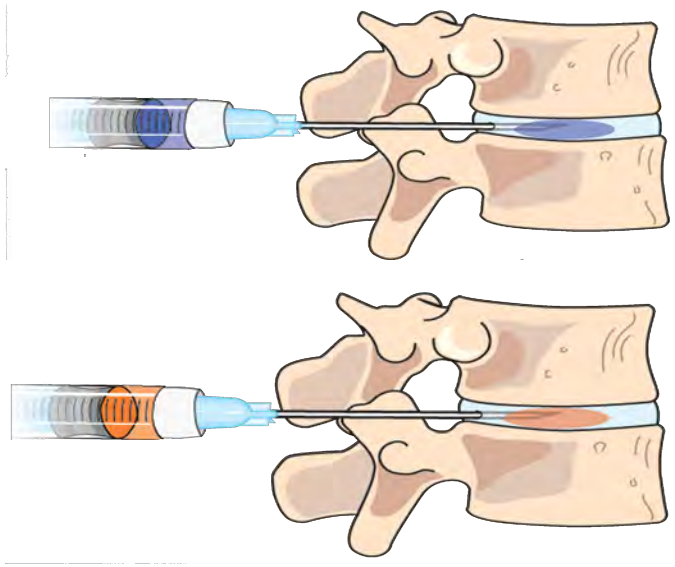
- Culture Expanded BMSC Injection

Bone Marrow Aspiration

Bone Marrow Mesenchymal Stem Cell (BMSC)



Culture Expansion of BMSC



BMAC Injection
- Intradiscal
  - Therapy Arm
  - Control Arm

G2: Completed Trials on Discogenic Pain

Author	N	Design	Cell type	Dosage	Outcomes
Bae et al. 2014	100	RCT, 3 arms	Allogeneic MPC, immunoselected	6M 18M + HA carrier	VAS, ODI, SF-36, WPAI
Coric et al. 2013	15	Open label, single arm	Allogeneic chondrocytes, cultured	100-200M with fibrin carrier	NRS, ODI, SF-36, MRI
Orozco et al. 2011	10	Open label, single arm	Autologous BMSC, cultured	18-28M	VAS, ODI, SF-36, MRI
Pang et al. 2014	2	Case study	Allogeneic HUC-MSCs, cultured	100M	VAS, ODI, MRI
Pettine et al. 2016	26	Open label, 2 arms	Autologous BMSC	2-3 ml	VAS, ODI, MRI
Pettine 2012	14	Open label, single arm	Allogeneic chondrocytes	10M with fibrinogen and thrombin carrier	NRS, ODI, SF-36, MRI

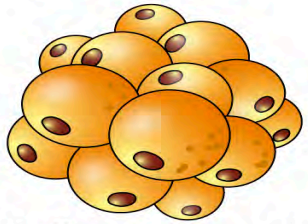
G2: On-going Trials for Discogenic Pain

Sponsor	N	Phase	Design	Cell type	Dosage	Outcomes
Red de Terapia Celular	24	I-II	RCT, 2 arms	Allogeneic BMSC, cultured	25M	VAS, ODI, SF-12, MRI, AEs
Mesoblast	330	III	RCT, 3 arms	Allogeneic MPC	6M 6M + HA	VAS, ODI
Bioheart	100	II	Open label, single arm	Autologous AMSC + PRP	Will vary	VAS, ODI
Biostar	8	I-II	Open label, single arm	Autologous AMSC	40M	VAS, MRI, AEs
Inbo Han, CHA University	10	I	Open label, single arm	Autologous AMSC	20-40M + HA	VAS, ODI, SF-36, MRI, DHI, AEs

Five Generations of Stem Cells Based on Preparation Strategy

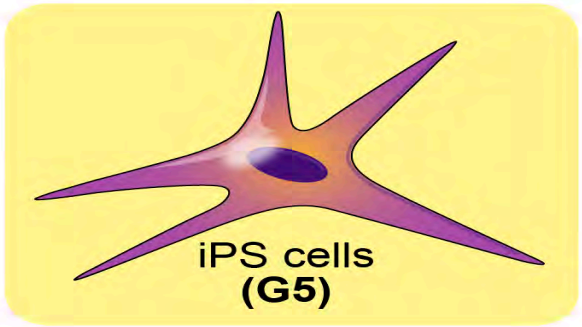
Sources

Bone marrow



Adipose tissue

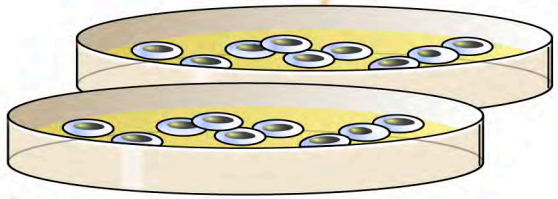
Umbilical cord



iPS cells
(G5)

Preparation

MSCs procured with minimal manipulation
(G1)



Culture expanded MSCs
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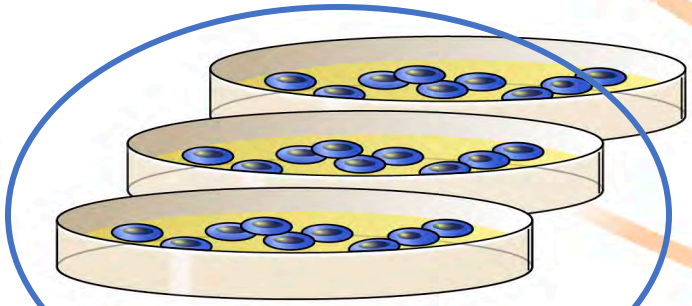
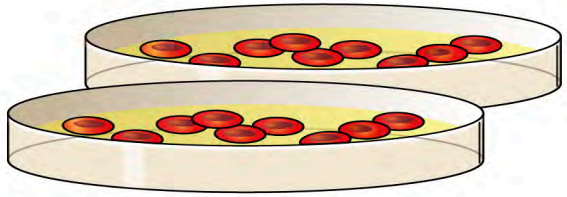


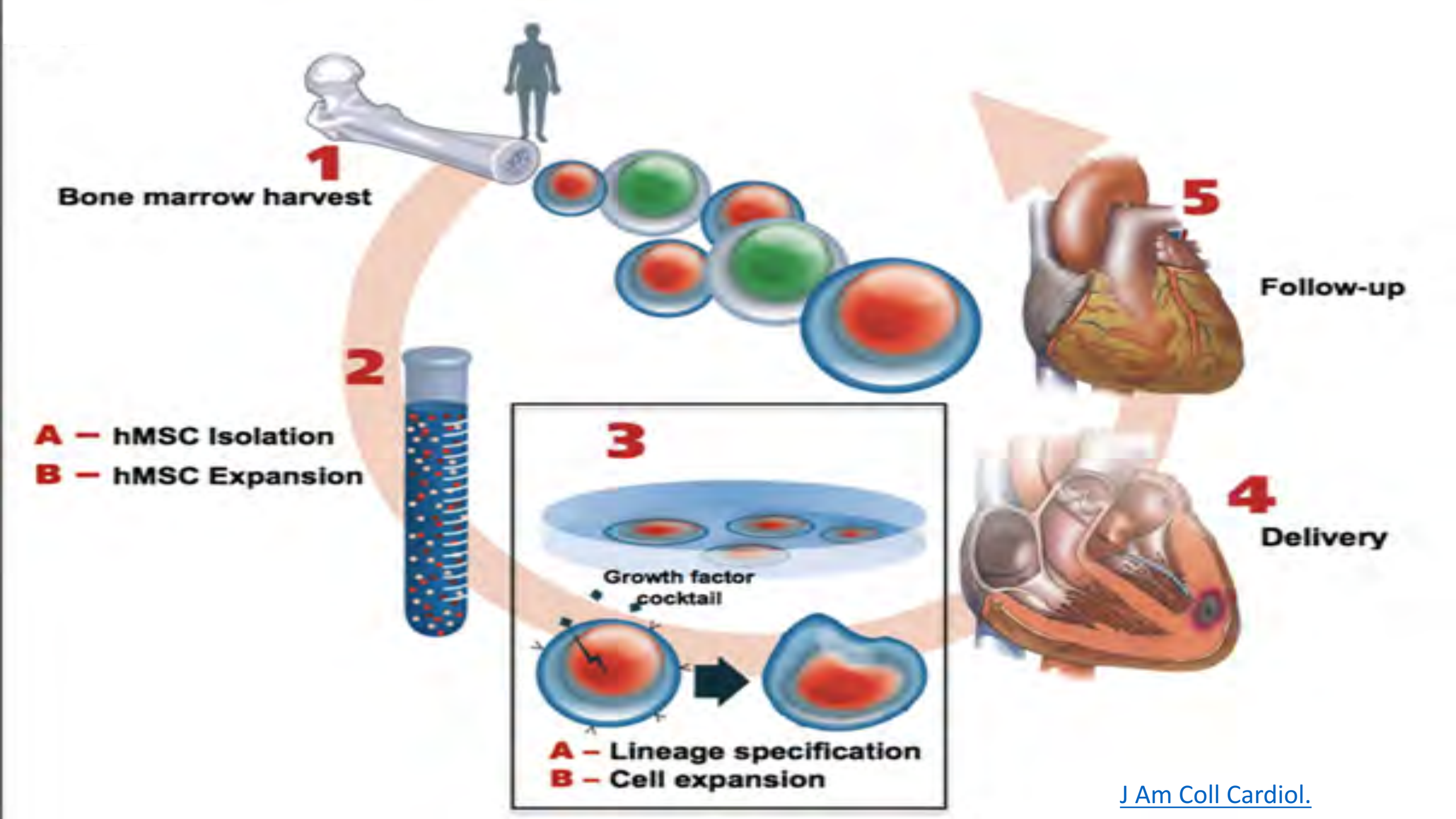
Lineage-directed or preconditioned MSCs
(G3)



Genetically modified SCs
(G4)

Stem cells transplanted

3579607-3(V5)



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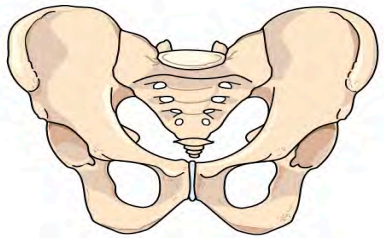
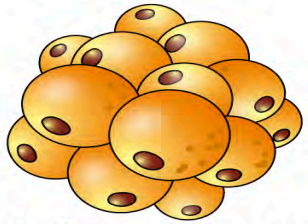
Five Generations of Stem Cells Based on Preparation Strategy

Sources

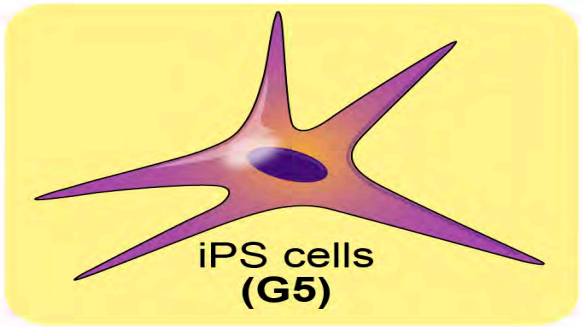


Bone marrow



Adipose tissue

Umbilical cord



iPS cells
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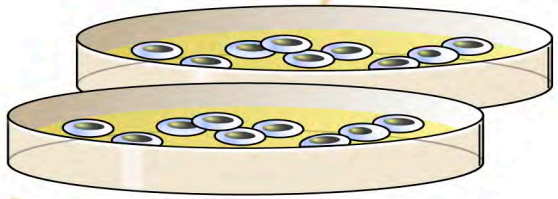
Preparation

MSCs procured with minimal manipulation
(G1)



Culture expanded MSCs
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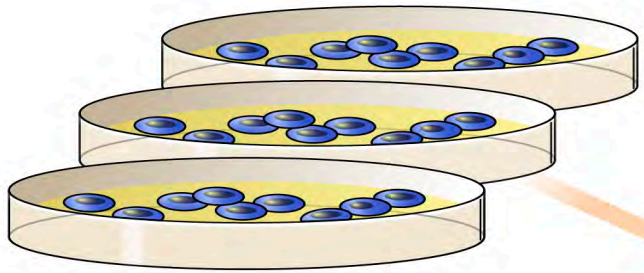

Lineage-directed or preconditioned MSCs
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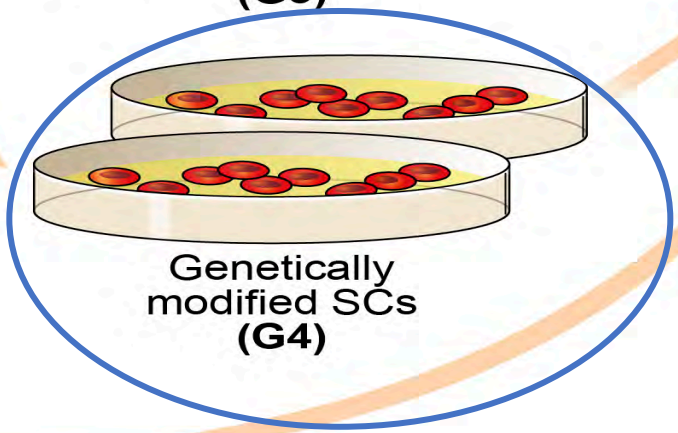


Genetically modified SCs
(G4)

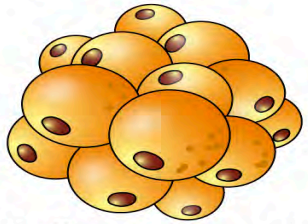
Stem cells transplanted

3579607-3(V5)

Five Generations of Stem Cells Based on Preparation Strategy

Sources

Bone marrow



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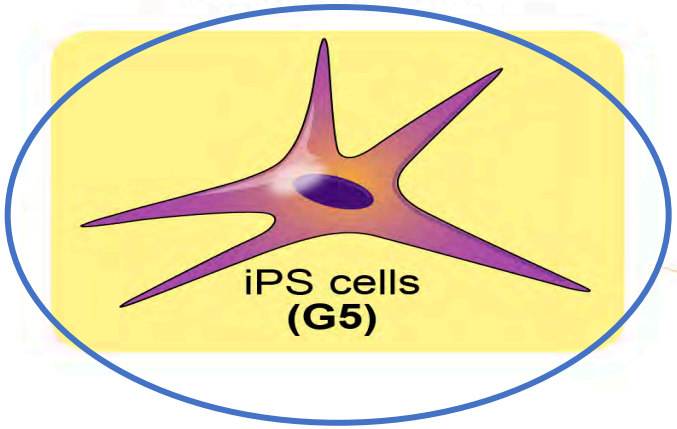
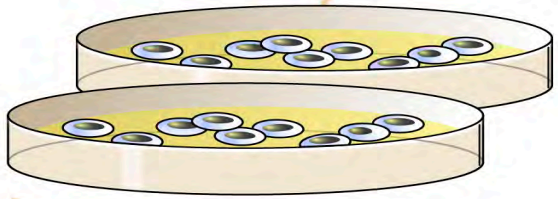
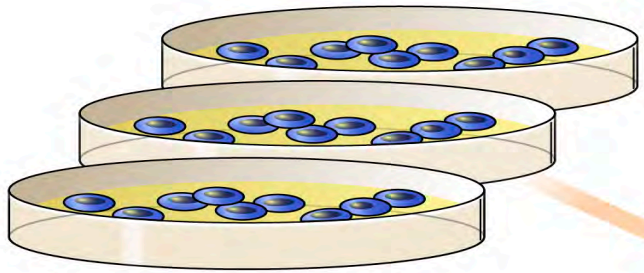


Preparation

MSCs procured with minimal manipulation **(G1)**



Culture expanded MSCs **(G2)**



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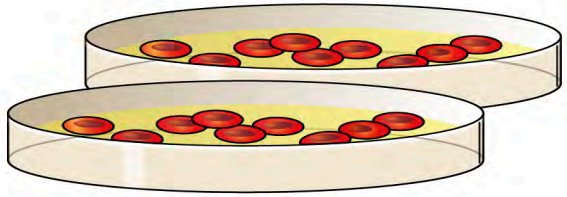

Genetically modified SCs **(G4)**

Stem cells transplanted

State of Stem Cell in Spine Care

					MSC			
Generation	**Source**	**Human**	**Animal**	**Bench**	**Concentrate**	**Culture - Expand**	**TF Induced**	**Gene modified**
1st Gen	Auto	√			√			
2nd Gen	Auto	√			√	√		
	Allo	√			√	√		
3rd Gen	Auto			√	√	√	√	
	Allo				√	√	√	
4th Gen	Auto		√		√	√	+/-	√
	Allo				√	√	+/-	√
5th Gen	iPSC				-	-	+/-	+/-

Thank you!

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