대학과 병원기반의 줄기세포 치료제개발, K-바이오의 미래

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서울성모병원 내과

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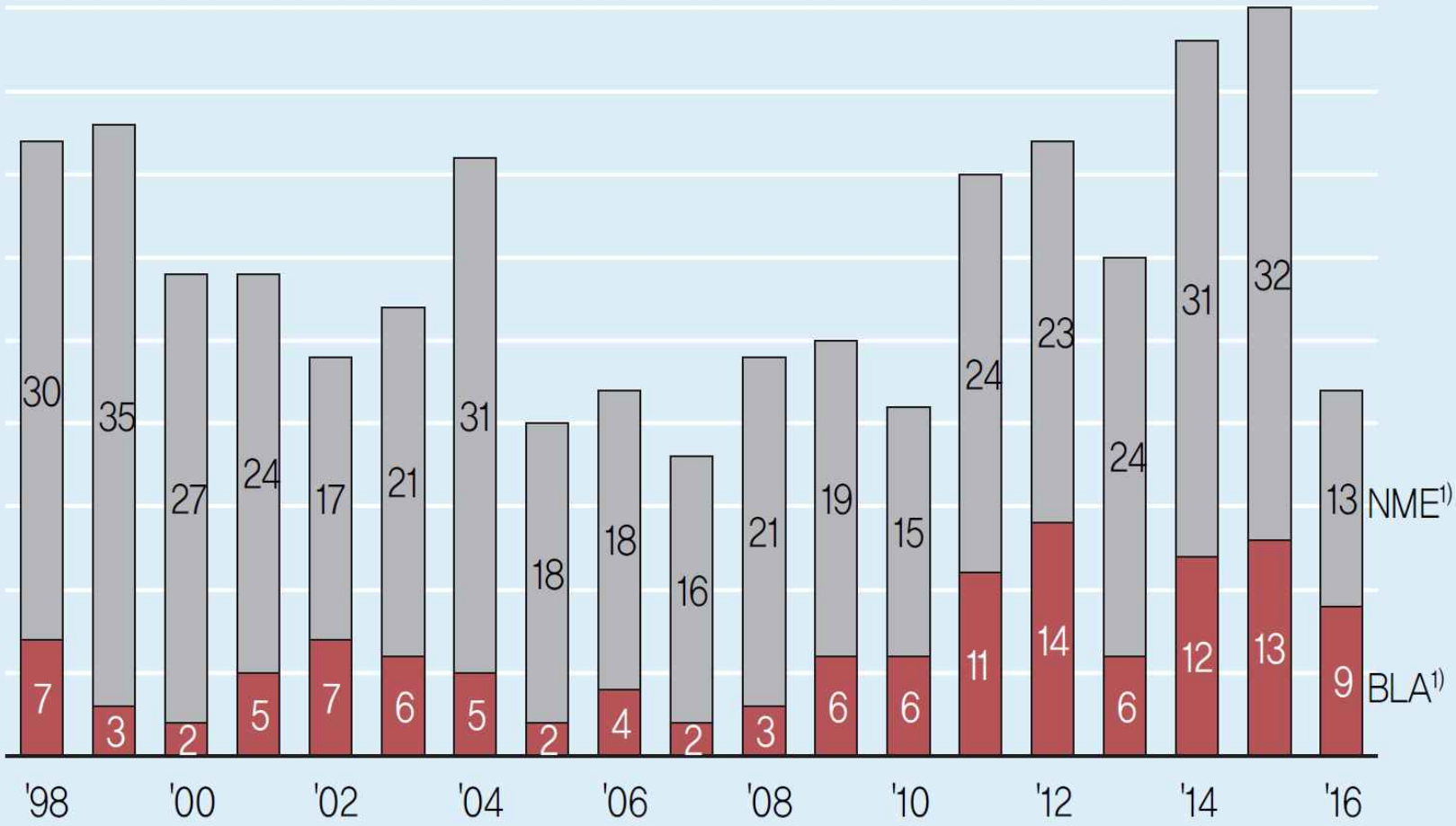
글로벌 매출 Top10 의약품

순위	제품명	판매 기업	2016 매출($B)	구분
1	휴미라(Humira)	애브비(AbbVie)	16.1	단일클론항체
2	하보니(Harvoni)	길리어드(Gilead)	9.1	화학합성의약품
3	엔브렐(Enbrel)	암젠/화이자(Amgen/Pfizer)	8.9	융합단백질
4	리툭산(Rituxan)	로슈/바이오젠(Roche/Biogen)	8.6	단일클론항체
5	레미케이드(Remicade)	존슨앤존슨/머크 (Johnson & Johnson / Merck)	7.8	단일클론항체
6	레블리미드(Revlimid)	셀진(Celgene)	7.0	화학합성의약품
7	아바스틴(Avastin)	로슈(Roche)	6.8	단일클론항체
8	허셉틴(Herceptin)	로슈(Roche)	6.8	단일클론항체
9	란투스(Lantus)	사노피(Sanofi)	6.1	재조합단백질
10	프리베나(Prevenar 13)	화이자(Pfizer)	5.7	백신

자료: GEN(Genetic Engineering & Biotechnology News), 2017.3.
주: ▭ 바이오 의약품

FDA 신약 승인건수



자료: Nature Biotechnology, 2017.2.

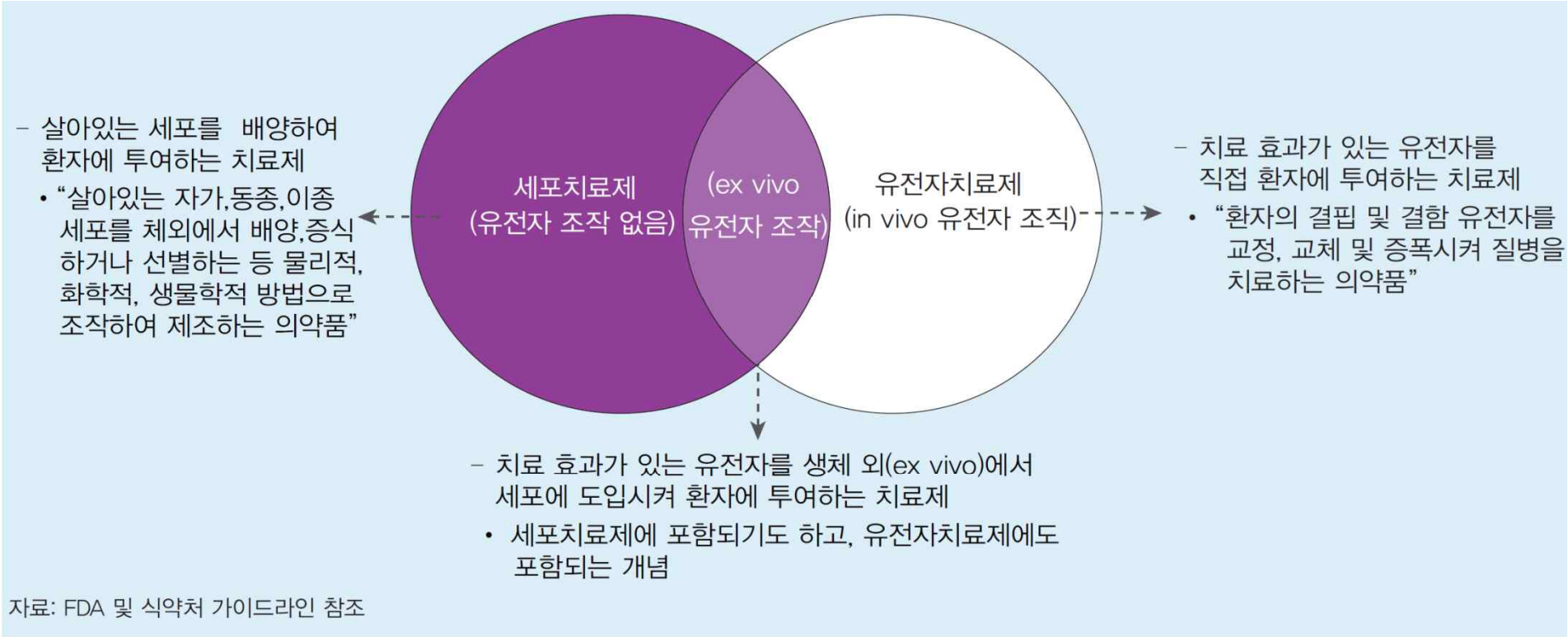
1) NME, New Molecular Entities (신물질 화학합성의약품)
BLA, Biological License Applications (바이오 의약품)

최근 주목받고 있는 바이오의약품

구분		개념	특성
차세대 항체	이중항체 (Bispecific Antibody)	2가지 이상의 항원을 인식할 수 있는 항체	다수 질병 타깃이 가능, 기존 항체 의약품 대비 대상 질환 다양
	ADC (Antibody Drug Conjugate)	항체-약물 결합체	톡신(강한 암세포 사멸)과 항체 (표적 타겟팅)의 장점 융합
RNA 치료제		특정 질병을 일으키는 단백질을 mRNA 단계에서 파괴하여 합성을 억제	항체 대비 작은 크기로 효과적인 타겟팅 가능
유전자치료제		유전 물질(DNA/RNA)을 체내에 직접 주입, 결핍 및 결함 유전자를 교정	가장 근원적인 질병 치료법
세포치료제		줄기세포나 면역세포를 체외에서 배양 후(필요 시 유전자 조작) 체내에 주입	재생의료 관점에서 난치 퇴행성 질환 치료 가능

1) 차세대 항체, 유전자치료제, 시장 규모 및 성장률 수치는 Technavio, RNA 치료제는 Marketandmarkets, 세포치료제는 Frost & Sullivan

세포치료제의 개념



자료: FDA 및 식약처 가이드라인 참조

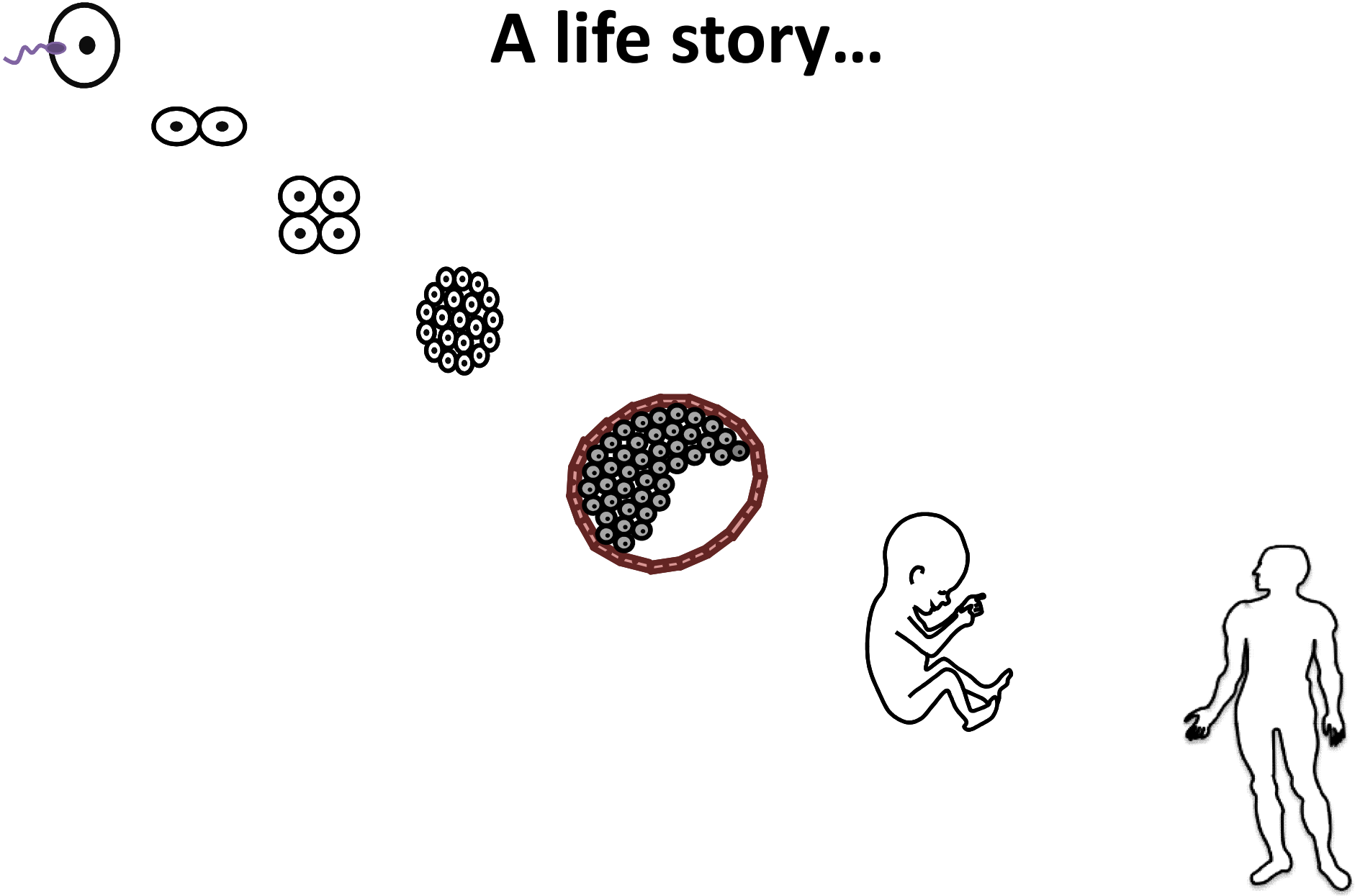
세포치료제의 유형

	종류	세부 유형 예시	적용 질환 예시
줄기세포	배아줄기세포 (Embryonic Stem Cells)	– 조혈모줄기세포(HSC[2]) – 중간엽줄기세포(MSC[3])	– 심혈관질환 – 척수손상 – 관절염, 당뇨
	역분화줄기세포(iPS[1])		
	성체줄기세포(Adult Stem Cells)		
면역세포	T세포(T cells)	– 종양 침윤 T 세포(TIL[4]) – CAR[5]–T 세포 – TCR[6]–T 세포	– 백혈병, 림프종 – 간암, 폐암, 전립선암 – 자가면역질환
	자연살해세포(NK cells[7])	– CAR–NK 세포	
	수지상세포(Dendritic cells)	– 유전자 조작 수지상세포	
체세포	피부세포(Epidermal cells)	– 표피, 진피 세포	– 피부화상, 흉터
	연골세포(Chondrocytes)		– 퇴행성 관절염

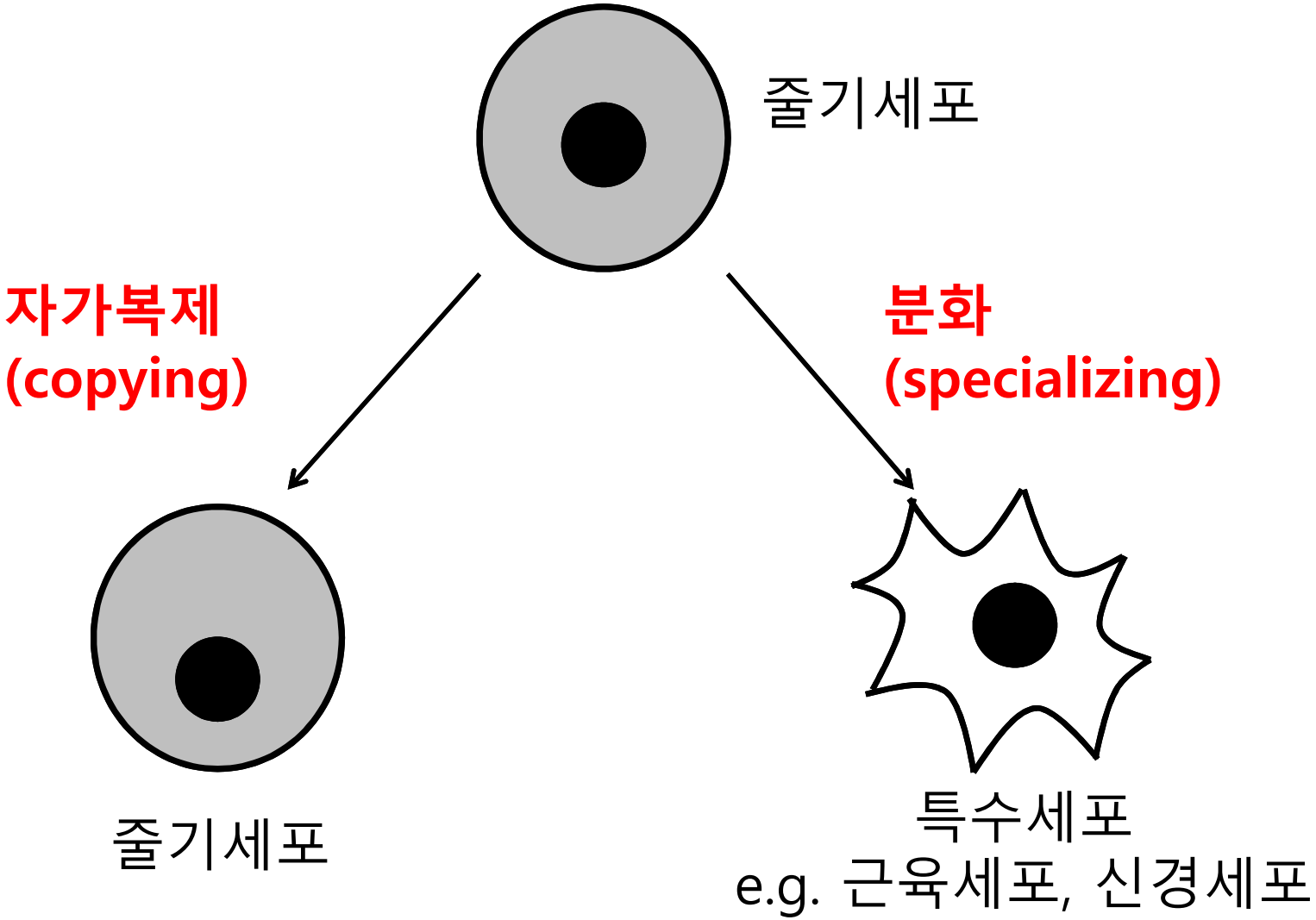
1) induced Pluripotent Stem Cells
2) Hematopoietic Stem Cell, 혈액과 면역세포로 분화되는 줄기세포
3) Mesenchymal Stem Cell, 근육, 뼈, 지방 등의 중간엽 조직으로 분화되는 줄기세포
4) Tumor Infiltrating Lymphocytes, 암세포 주변에 모여 있는 림프구
5) Chimeric Antigen Receptor
6) T Cell Receptor
7) Natural Killer cells, 외부 바이러스나 암세포를 공격하는 면역세포

목 차

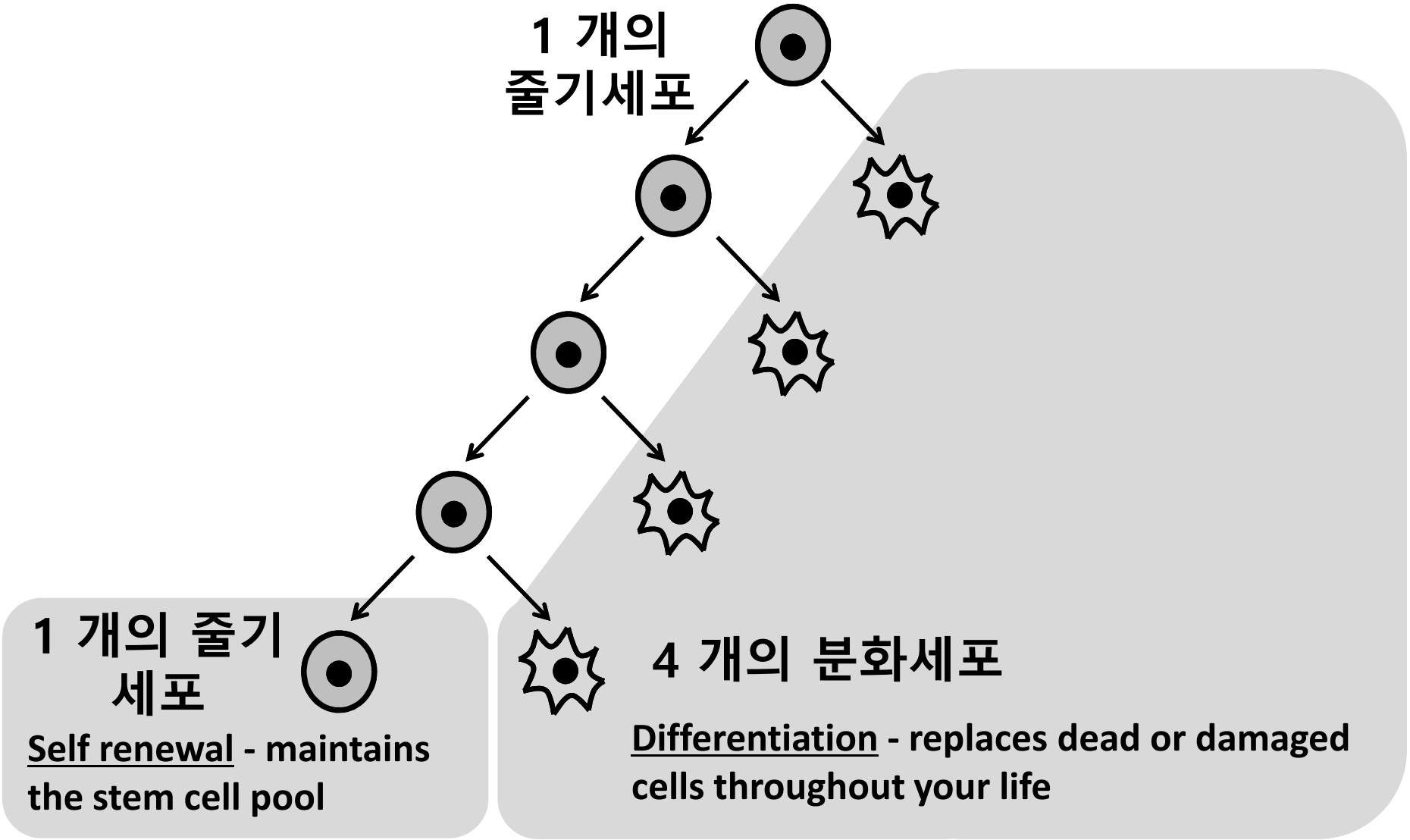
A life story…



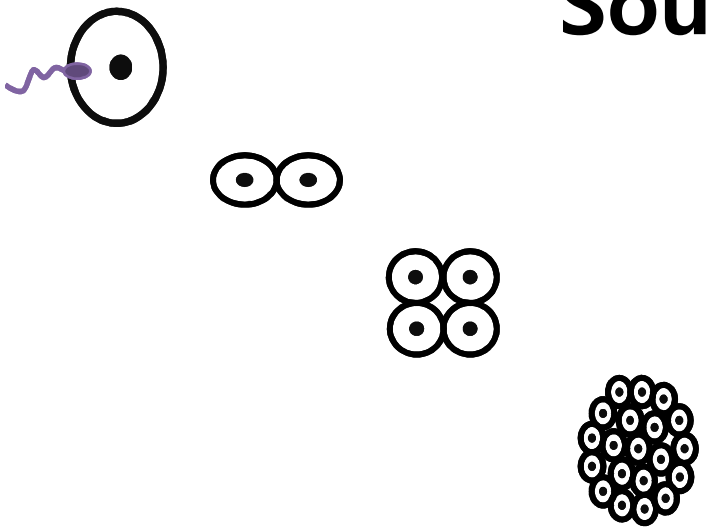
줄기세포란?



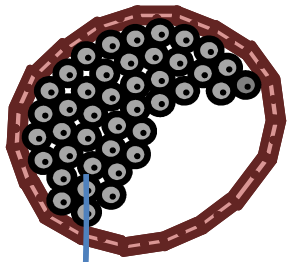
줄기세포는 자가복제와 분화기능이 왜 ?



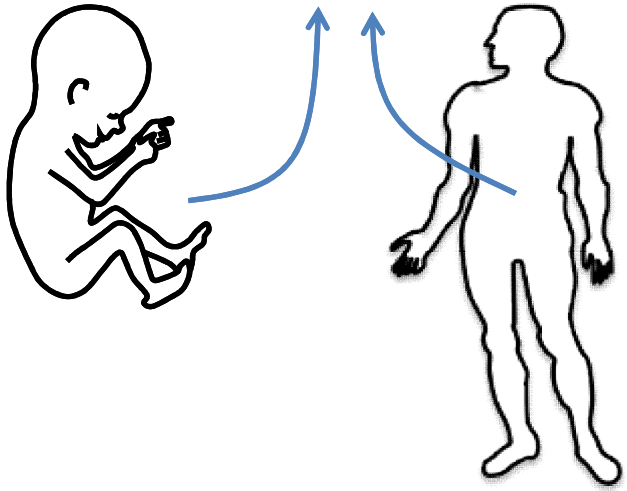
Source of stem cell?

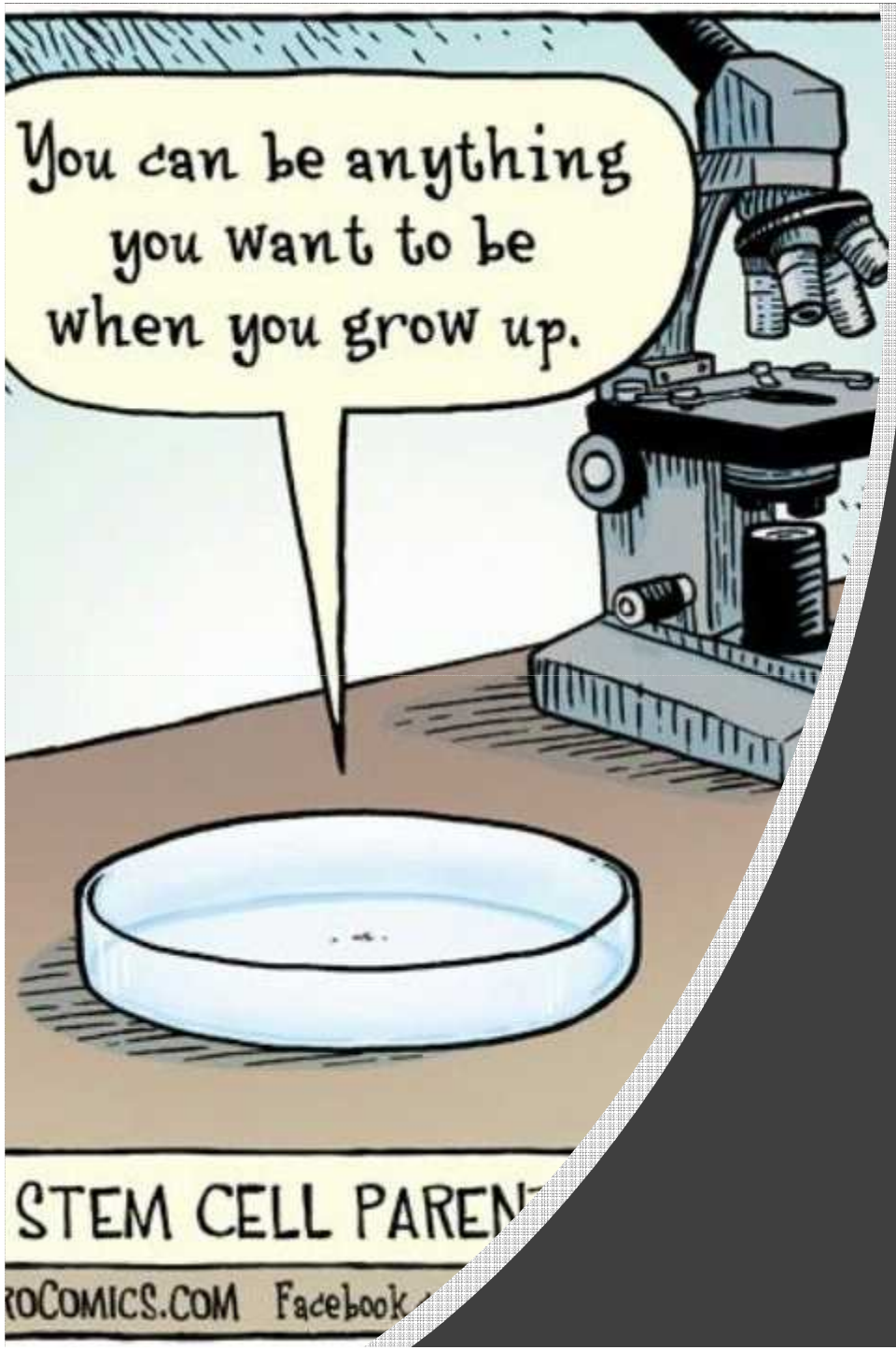


배아줄기세포:
blastocyst - a very early embryo



조직내의 성체줄기세포:
fetus, baby and throughout life

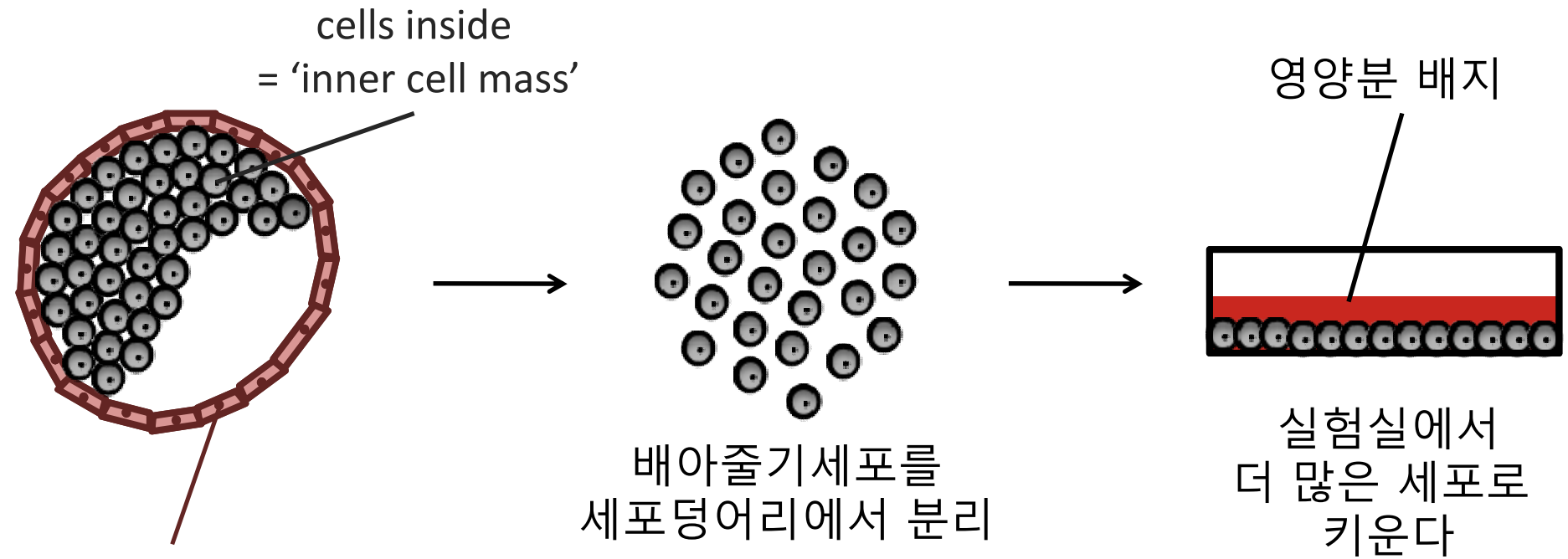




줄기세포의유형
: 배아줄기세포 (1)

배아줄기세포(ESC):

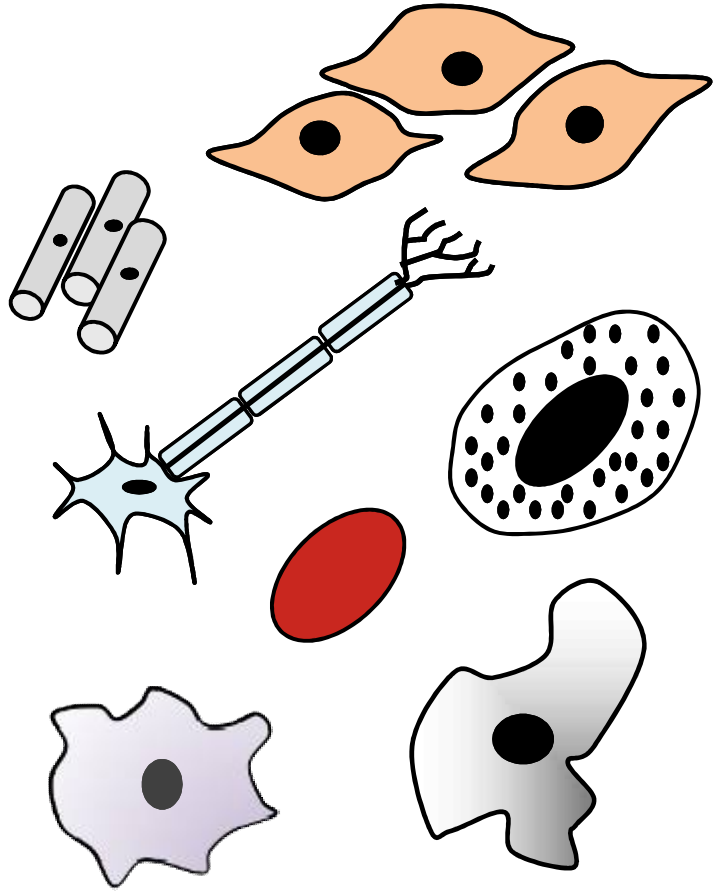
Blastocyst (배반포)



배아줄기세포:

embryonic stem cells

분화



all possible types of specialized cells

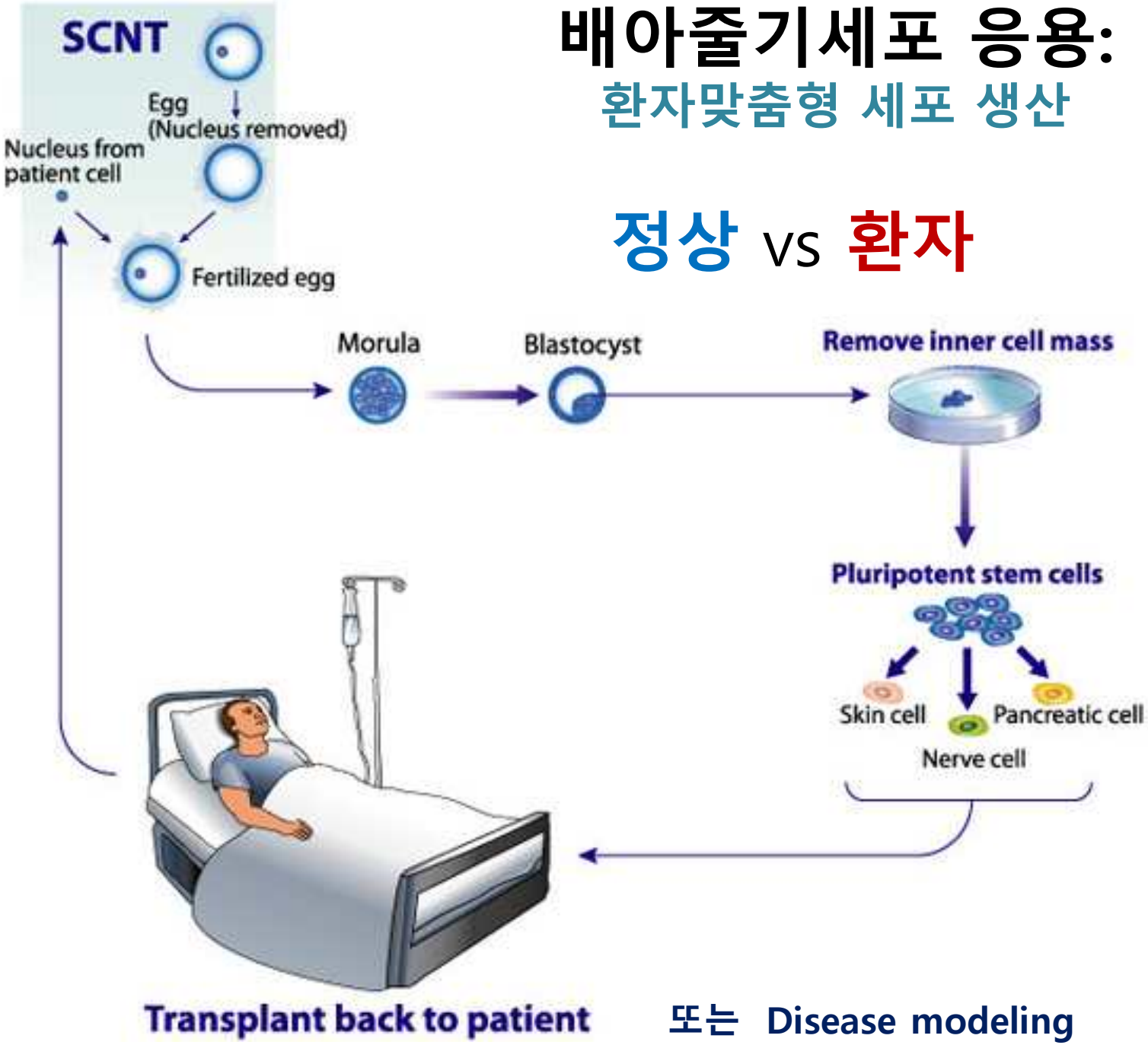
만능성

Source of stem cell?-variant ESC

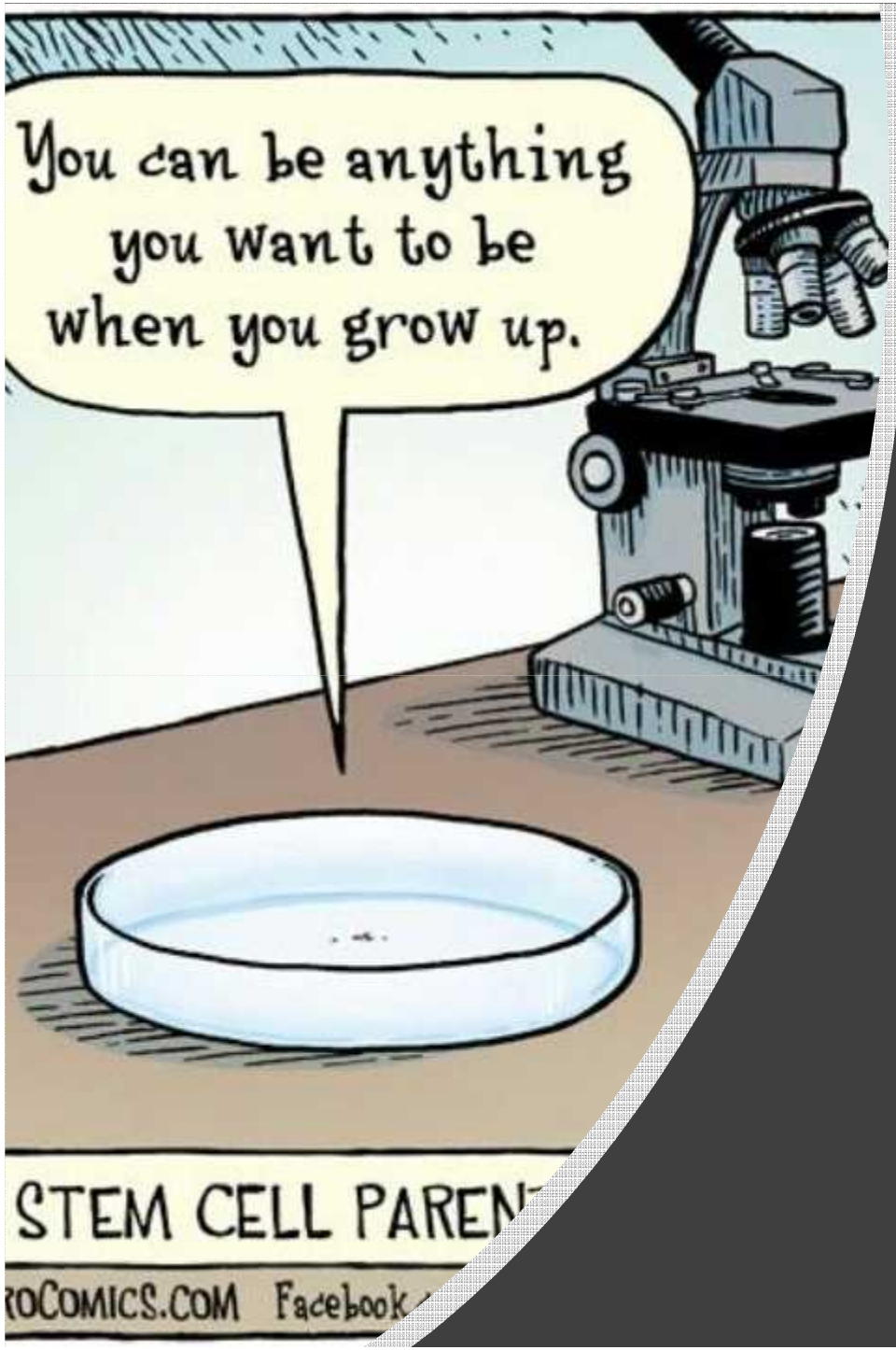
배아줄기세포 응용:

환자맞춤형 세포 생산

정상 vs **환자**



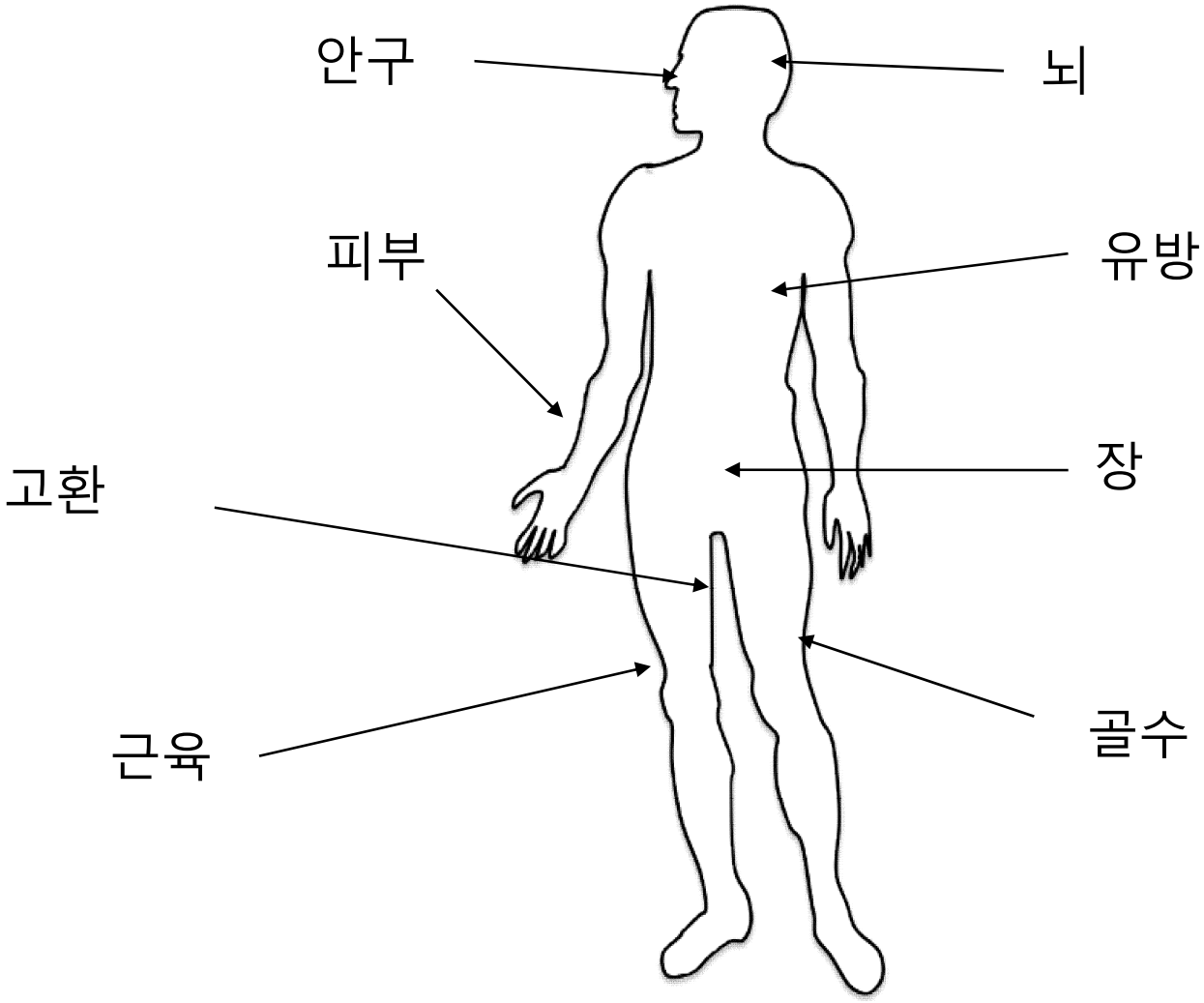
또는 Disease modeling



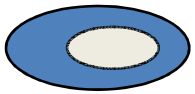
줄기세포의유형
: 성체줄기세포 (2)

성체줄기세포:

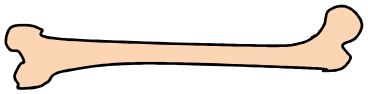
adult stem cell/tissue stem cell



성체줄기세포:



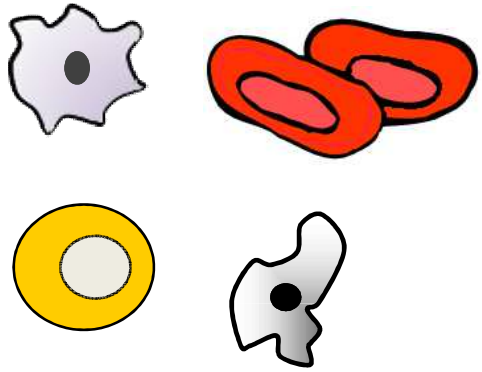
줄기세포



골수에서 존재

다분화능

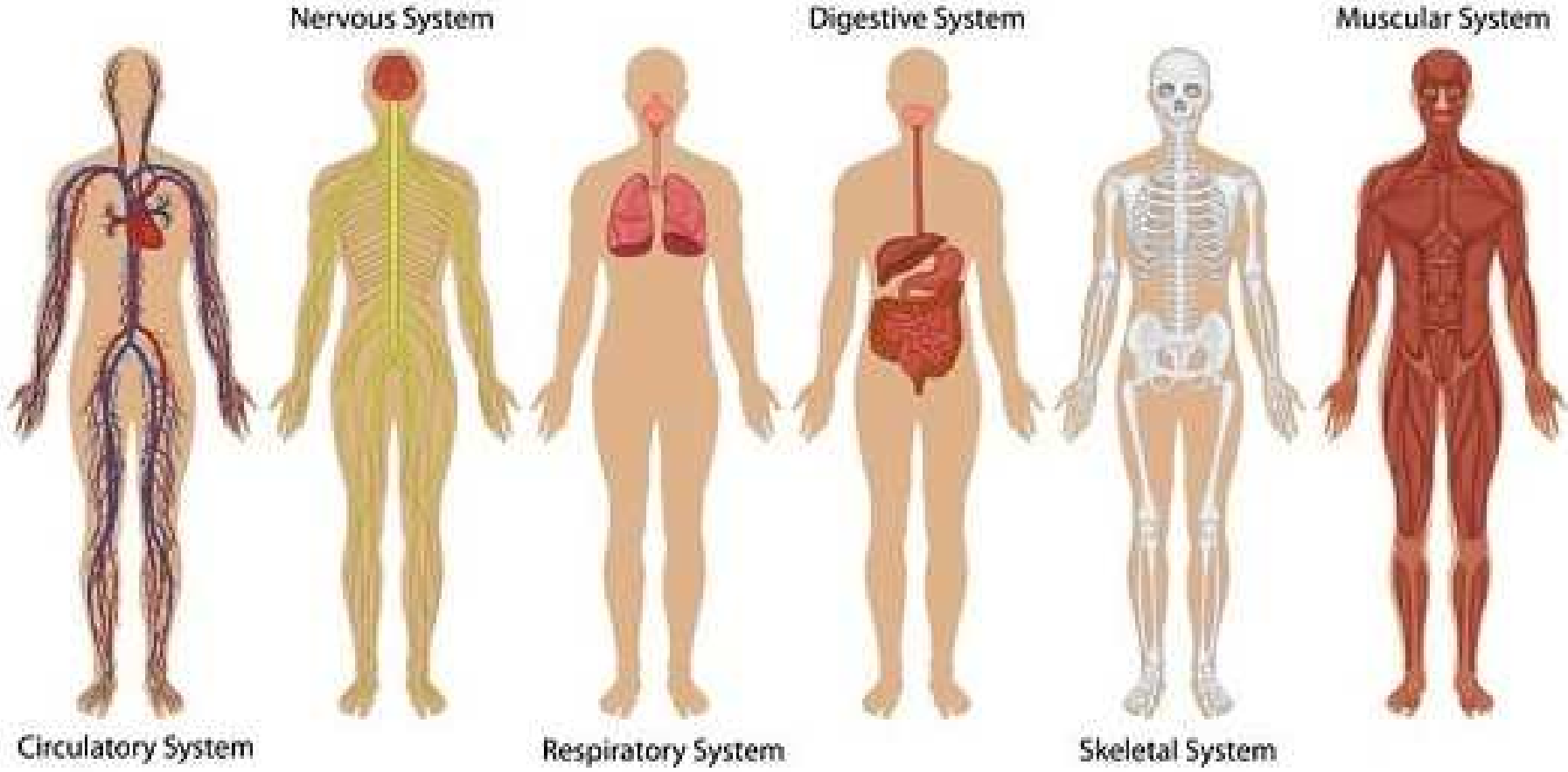
분화

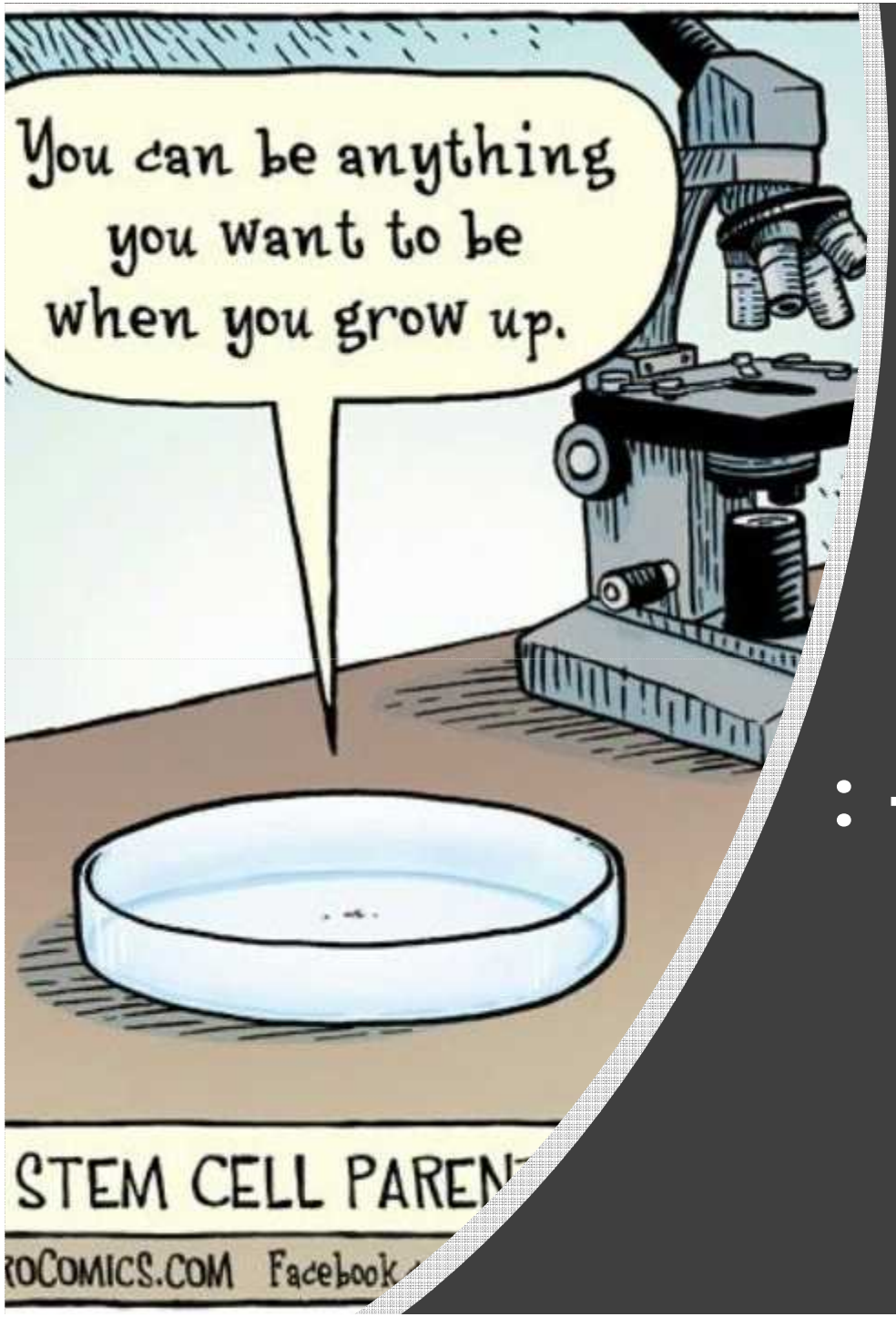


일부특화된 세포로만 분화가능:
적혈구, 백혈구, 혈소판

면역조절능

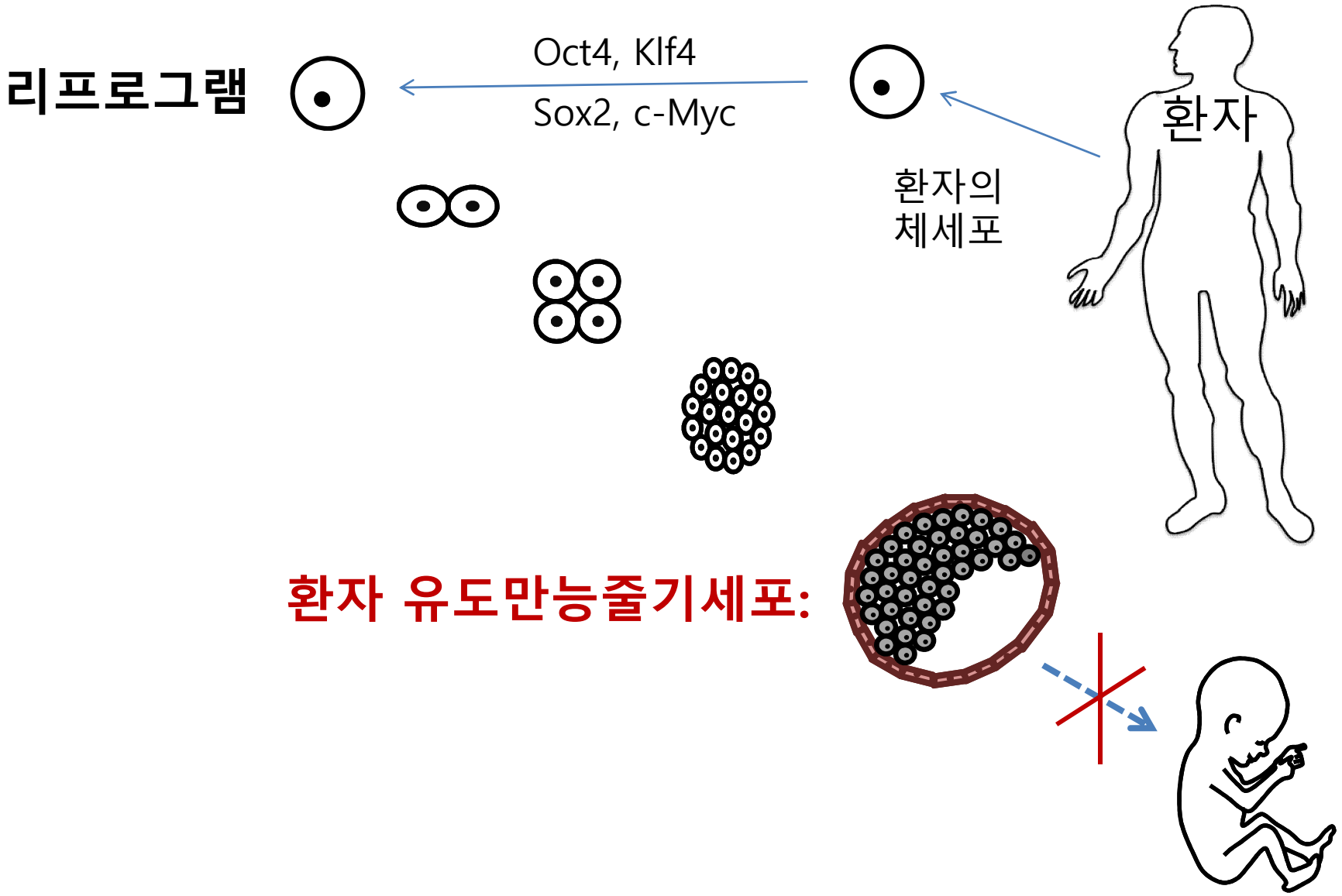
Adult Stem Cells Support These Body Systems



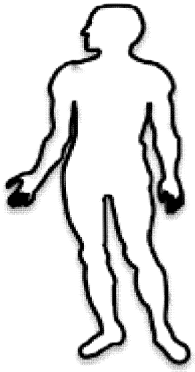


줄기세포의유형
: 유도만능줄기세포 (3)

Source of stem cell?-mimic ESC



역분화줄기세포, 유도만능줄기세포(iPS cells)



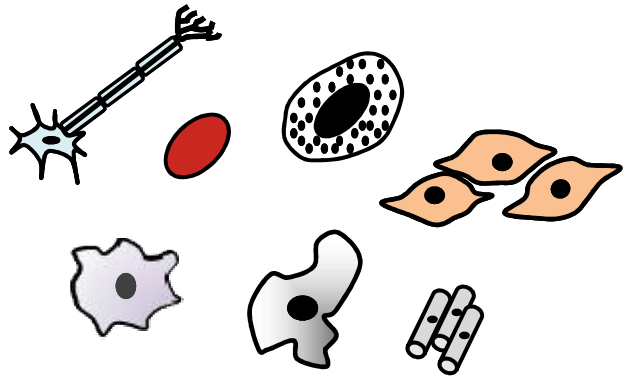
'리프로그램'
= add certain genes to the cell

성체세포

역분화줄기세포 iPS cell
배아줄기세포와 비슷한 만능성

분화

배양된 iPSC



모든 종류의 세포와 조직분화

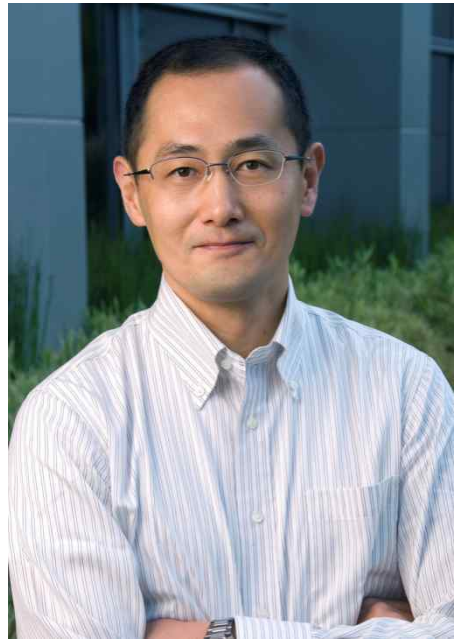
장점: 1) 더 이상 배아가 필요없다!
2) 자기의 ESC수준의 줄기세포를 만들 수 있다!
3) SCNT 개념의 질병줄기세포를 만들 수 있다!

2006 "Cell" -> **2013** Nobel prize

Cell

Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors

Kazutoshi Takahashi[1] and Shinya Yamanaka[1,2,*]
[1]Department of Stem Cell Biology, Institute for Frontier Medical Sciences, Kyoto University, Kyoto 606-8507, Japan
[2]CREST, Japan Science and Technology Agency, Kawaguchi 332-0012, Japan
*Contact: yamanaka@frontier.kyoto-u.ac.jp
DOI 10.1016/j.cell.2006.07.024



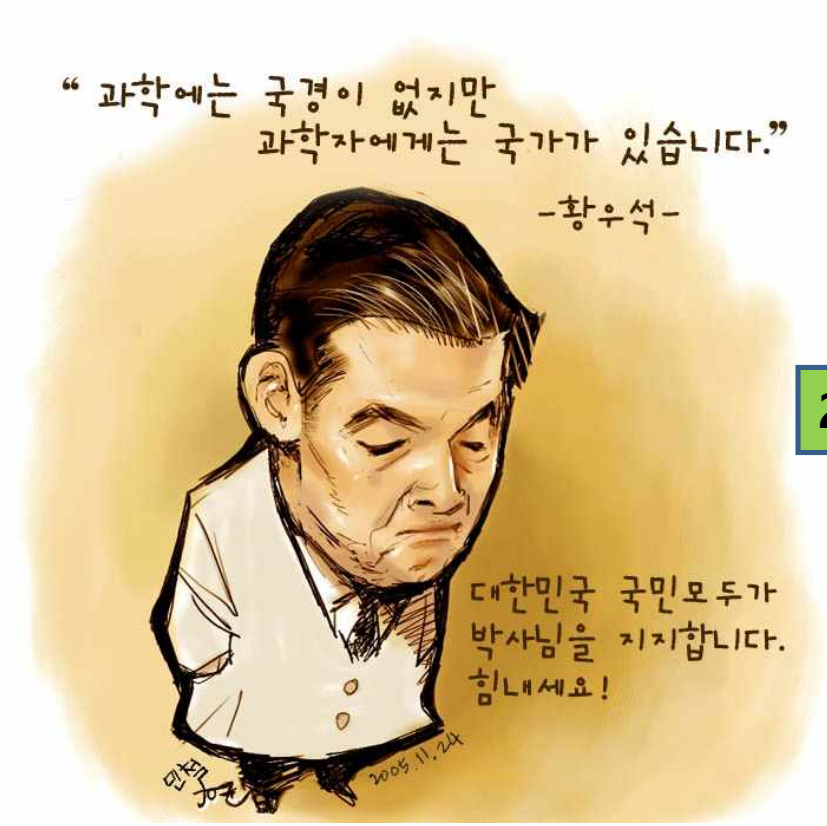
Shinya Yamanaka MD

2018.3 Keystone symposia

National change of world stem cell Initiative

SCNT, 환자맞춤형
배아줄기세포

iPSC, 환자맞춤형
유도만능줄기세포



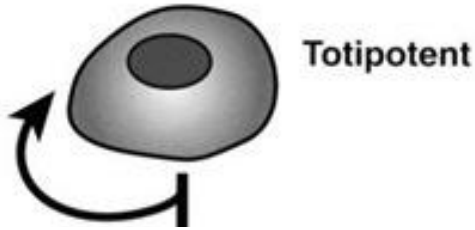
2006년

Hwang YS, Korea

Yamanaka Shinya, Japan

Stem cells hierarchy에 따른 줄기세포분류

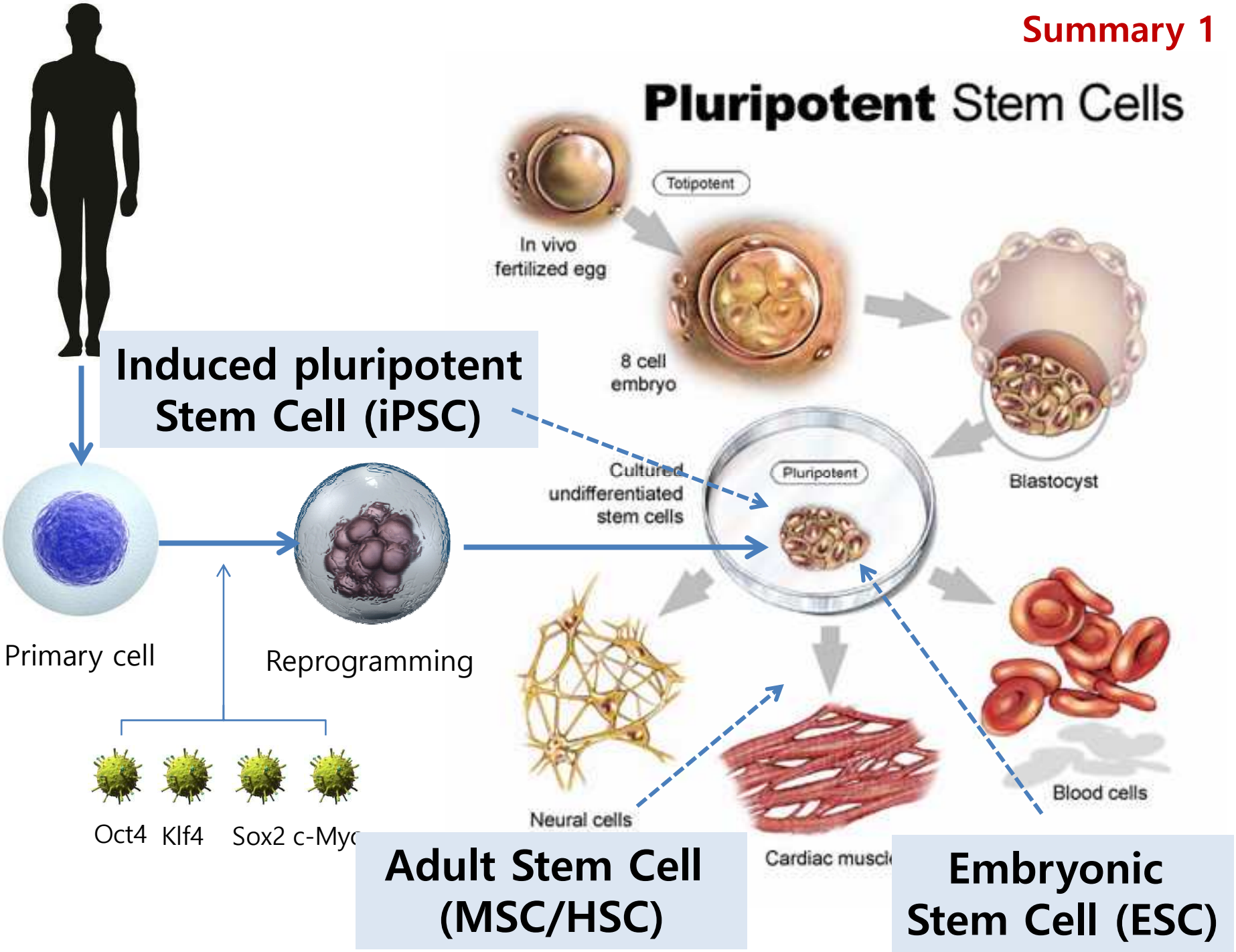
전능성



줄기세포의 분류: 줄기세포의 분화능/기원에 따라

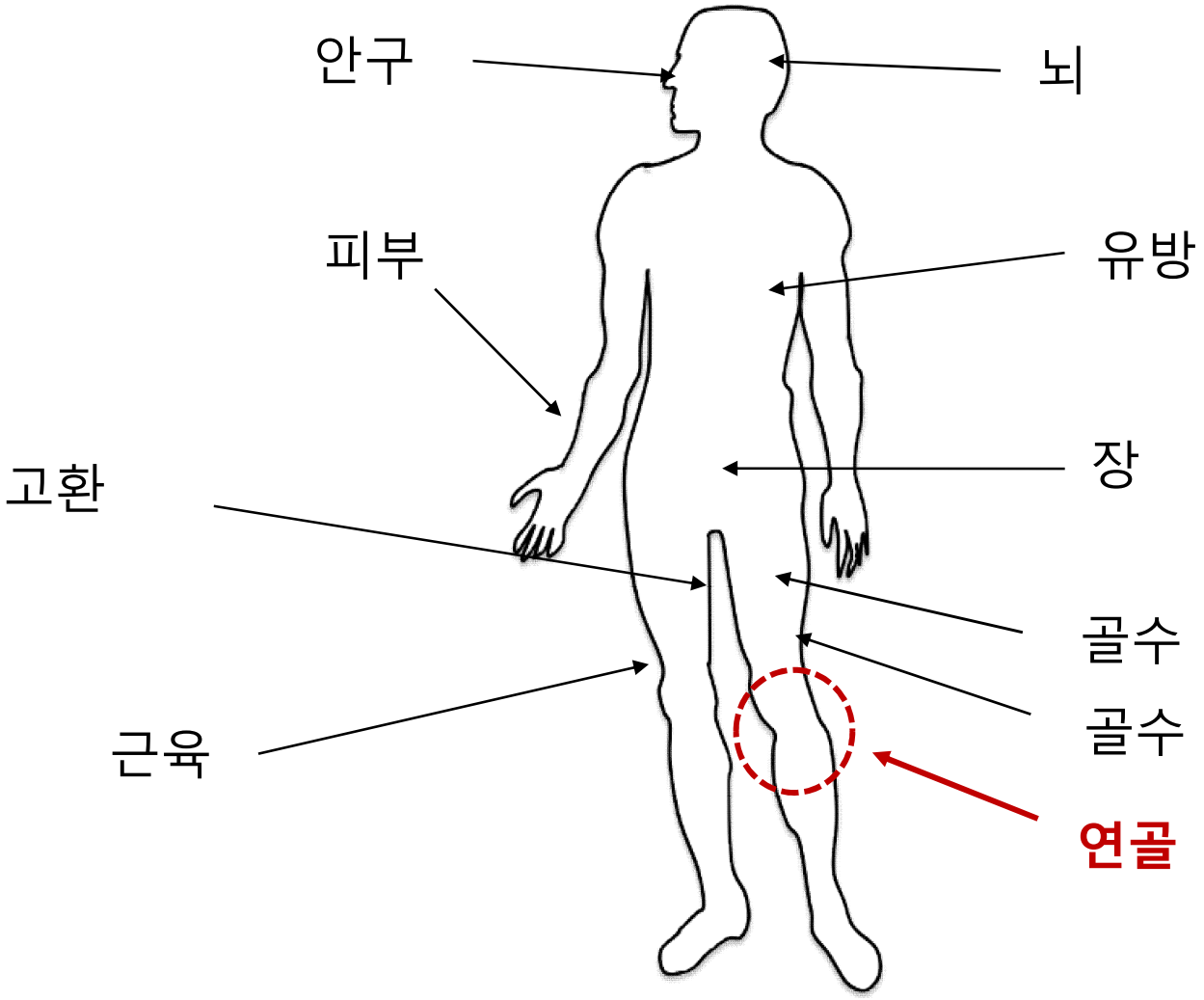
Stem cell type	Potency	Tissue source
Embryonic stem cells	Pluripotent	Blastocyst
Induced pluripotent stem cells	Pluripotent (reprogrammed)	Skin fibroblasts, keratinocytes, T cells, hepatocytes, other somatic cells
Fetal stem cells	Multipotent	Fetal blood, bone marrow, liver, lung, kidney, pancreas
Adult stem cells	Multipotent	Hematopoietic stem cells, mesenchymal stem cells: umbilical cord, adult tissues (peripheral blood, bone marrow, synovial membrane, periosteum, adipose tissue, dental pulp)

Summary 1


Pluripotent Stem Cells
Totipotent
In vivo fertilized egg
8 cell embryo
Blastocyst
Induced pluripotent Stem Cell (iPSC)
Cultured undifferentiated stem cells
Pluripotent
Primary cell
Reprogramming
Oct4
Klf4
Sox2
c-Myc
Neural cells
Cardiac muscle
Blood cells
Adult Stem Cell (MSC/HSC)
Embryonic Stem Cell (ESC)

목 차

성체줄기세포의 감소 = 노화?



고령화: South Korea, spotlighted!

Future life expectancy in 35 industrialised countries: projections with a Bayesian model ensemble

Vasilis Kontis, James E Bennett*, Colin D Mathers, Guangquan Li, Kyle Foreman, Majid Ezzati*

Summary

Background Projections of future mortality and life expectancy are needed to plan for health and social services and pensions. Our aim was to forecast national age-specific mortality and life expectancy using an approach that takes into account the uncertainty related to the choice of forecasting model.

Methods We developed an ensemble of 21 forecasting models, all of which probabilistically contributed towards the final projections. We applied this approach to project age-specific mortality to 2030 in 35 industrialised countries with high-quality vital statistics data. We used age-specific death rates to calculate life expectancy at birth and at age 65 years, and probability of dying before age 70 years, with life table methods.

Findings Life expectancy is projected to increase in all 35 countries with a probability of at least 65% for women and 85% for men. There is a 90% probability that life expectancy at birth among South Korean women in 2030 will be higher than 86·7 years, the same as the highest worldwide life expectancy in 2012, and a 57% probability that it will be higher than 90 years. Projected female life expectancy in South Korea is followed by those in France, Spain, and Japan. There is a greater than 95% probability that life expectancy at birth among men in South Korea, Australia, and Switzerland will surpass 80 years in 2030, and a greater than 27% probability that it will surpass 85 years. Of the countries studied, the USA, Japan, Sweden, Greece, Macedonia, and Serbia have some of the lowest projected life expectancy gains for both men and women. The female life expectancy advantage over men is likely to shrink by 2030 in every country except Mexico, where female life expectancy is predicted to increase more than male life expectancy, and in Chile, France, and Greece where the two sexes will see similar gains. More than half of the projected gains in life expectancy at birth in women will be due to enhanced longevity above age 65 years.

Interpretation There is more than a 50% probability that by 2030, national female life expectancy will break the 90 year barrier, a level that was deemed unattainable by some at the turn of the 21st century. Our projections show continued increases in longevity, and the need for careful planning for health and social services and pensions.

Lancet 2017; 389: 1323–35

Published Online
February 21, 2017
http://dx.doi.org/10.1016/S0140-6736(16)32381-9

See Comment page 1278

*Contributed equally

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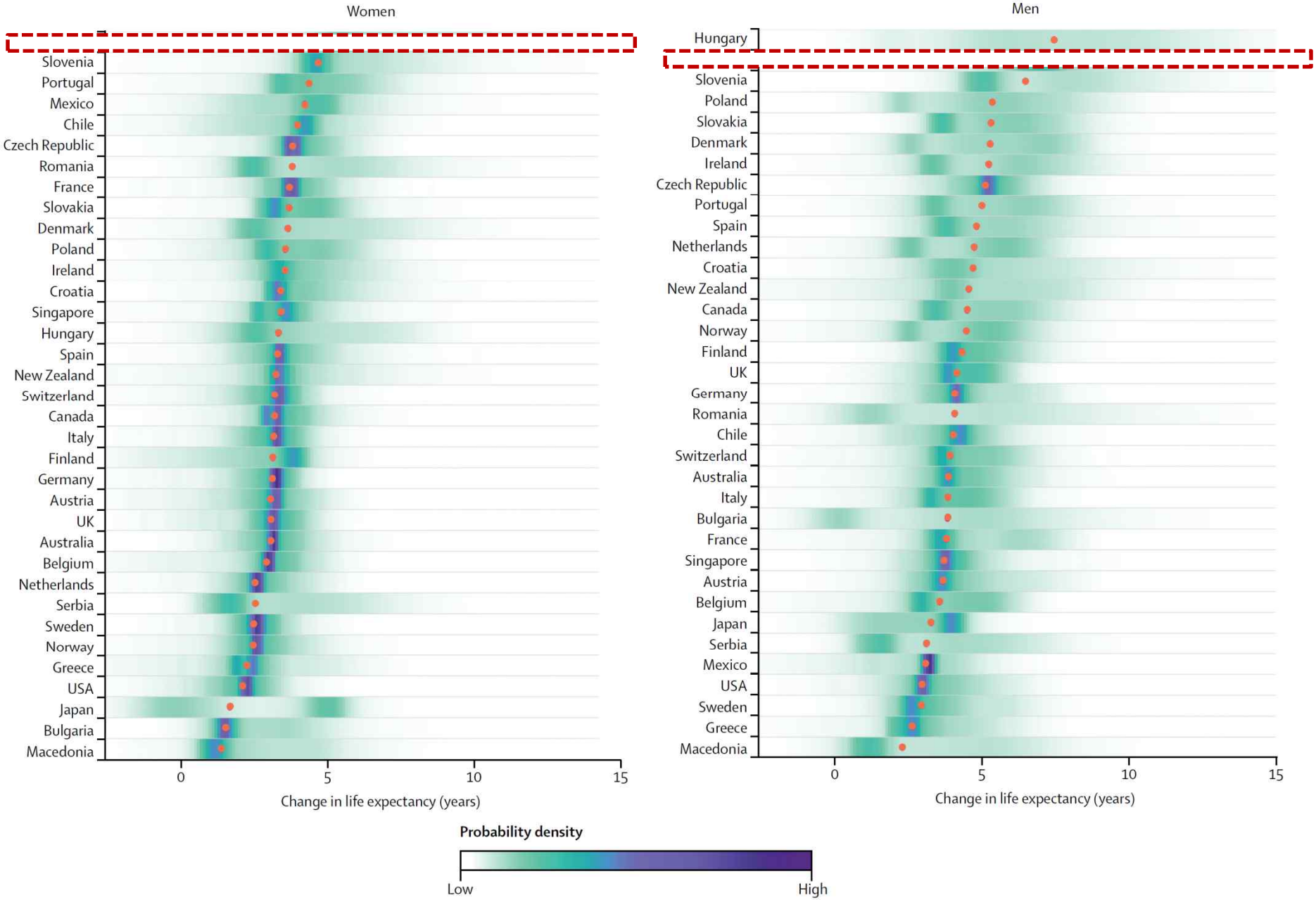
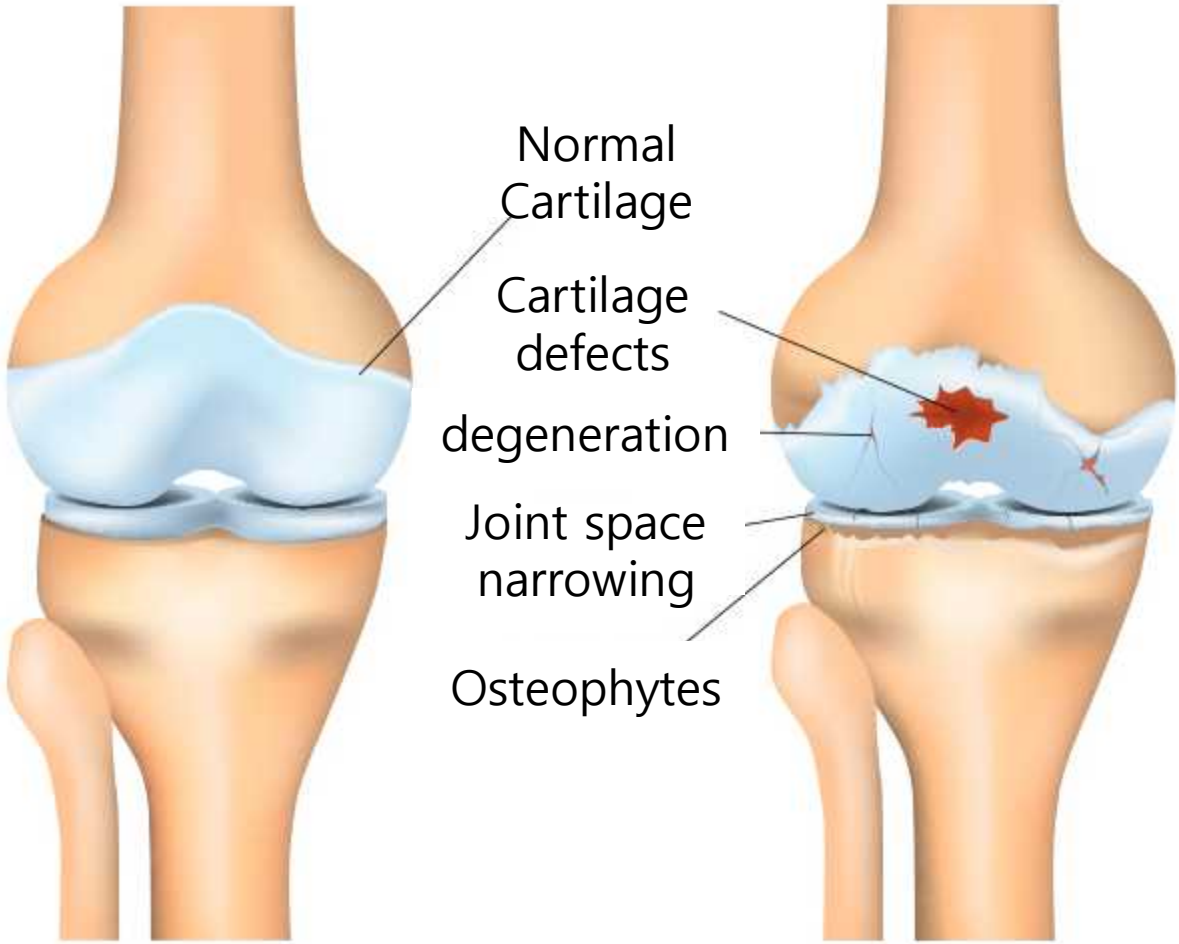
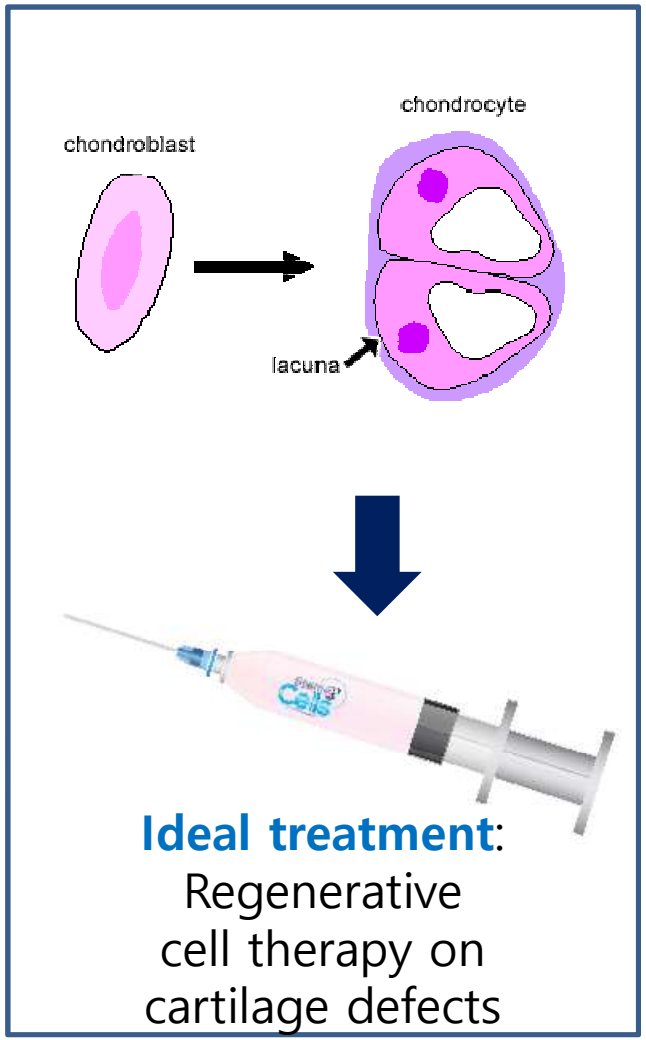
World records, rapidly aging in South Korea



No feasible therapeutic options in osteoarthritis





Ideal treatment: Regenerative cell therapy on cartilage defects

1st MSC clinical trial in 1995

Format: Abstract Send to

Bone Marrow Transplant. 1995 Oct;16(4):557-64.

Ex vivo expansion and subsequent infusion of human bone marrow-derived stromal progenitor cells (mesenchymal progenitor cells): implications for therapeutic use.

Lazarus HM[1], Haynesworth SE, Gerson SL, Rosenthal NS, Caplan AI.

Author information

Abstract

We report a phase I trial to determine the feasibility of collection, ex vivo culture-expansion and intravneous infusion of human bone marrow-derived progenitor stromal cells (mesenchymal progenitor cells (MPCs)). Ten milliliter bone marrow samples were obtained from 23 patients with hematologic malignancies in complete remission. Bone marrow mononuclear cells were separated and adherent cells were culture-expanded in vitro for 4-7 weeks. Autologous MPCs were reinfused intravenously and a bone marrow examination repeated 2 weeks later for histologic assessment and in vitro hematopoietic cultures. Patient age ranged from 18 to 68 years and 12 subjects previously had undergone an autologous or syngeneic bone marrow transplant 4-52 months prior to collection of MPCs. A median of 364 x 10(6) nucleated bone marrow cells (range: 103 to 1004 x 10(6)) were used for ex vivo expansion. Median number of MPCs which were obtained after ex vivo culture expansion was 59.0 (range: 1.1 to 347 x 10(6)) representing a median cell doubling of 16,000-fold (13 doublings). Fifteen of 23 patients completed the ex vivo expansion and underwent MPC infusion. Time to infusion of MPCs after collection ranged from 28 to 49 days. Five patients in each of three groups were given 1, 10 and 50 x 10(6) MPCs. No adverse reactions were observed with the infusion of the MPCs. MPCs obtained from cancer patients can be collected, expanded in vitro and infused intravenously without toxicity.(ABSTRACT TRUNCATED AT 250 WORDS)

PMID: 8528172

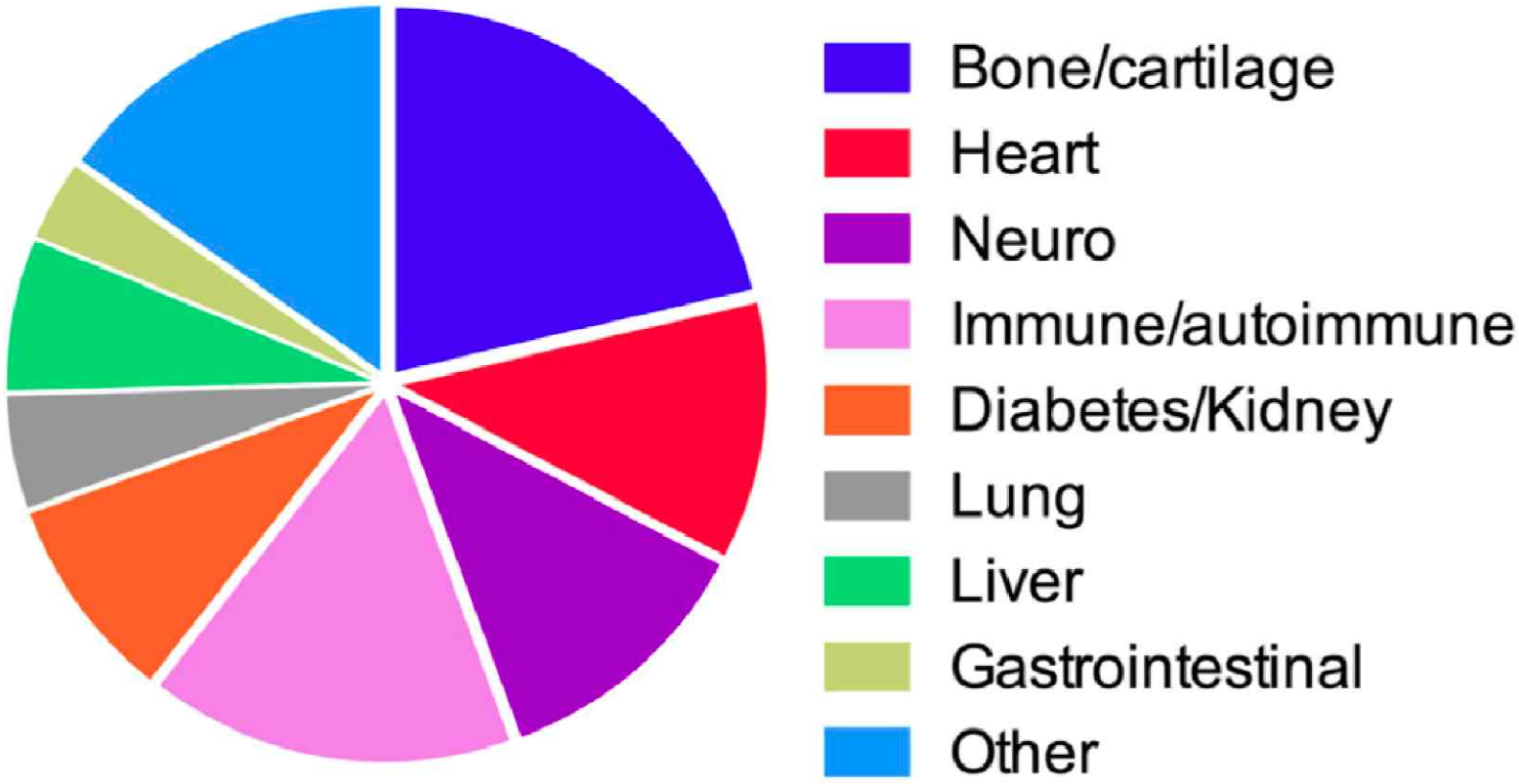
[Indexed for MEDLINE]

Bone Marrow Transplant 1995, 16:557

MSC definition by ISCT in 2006

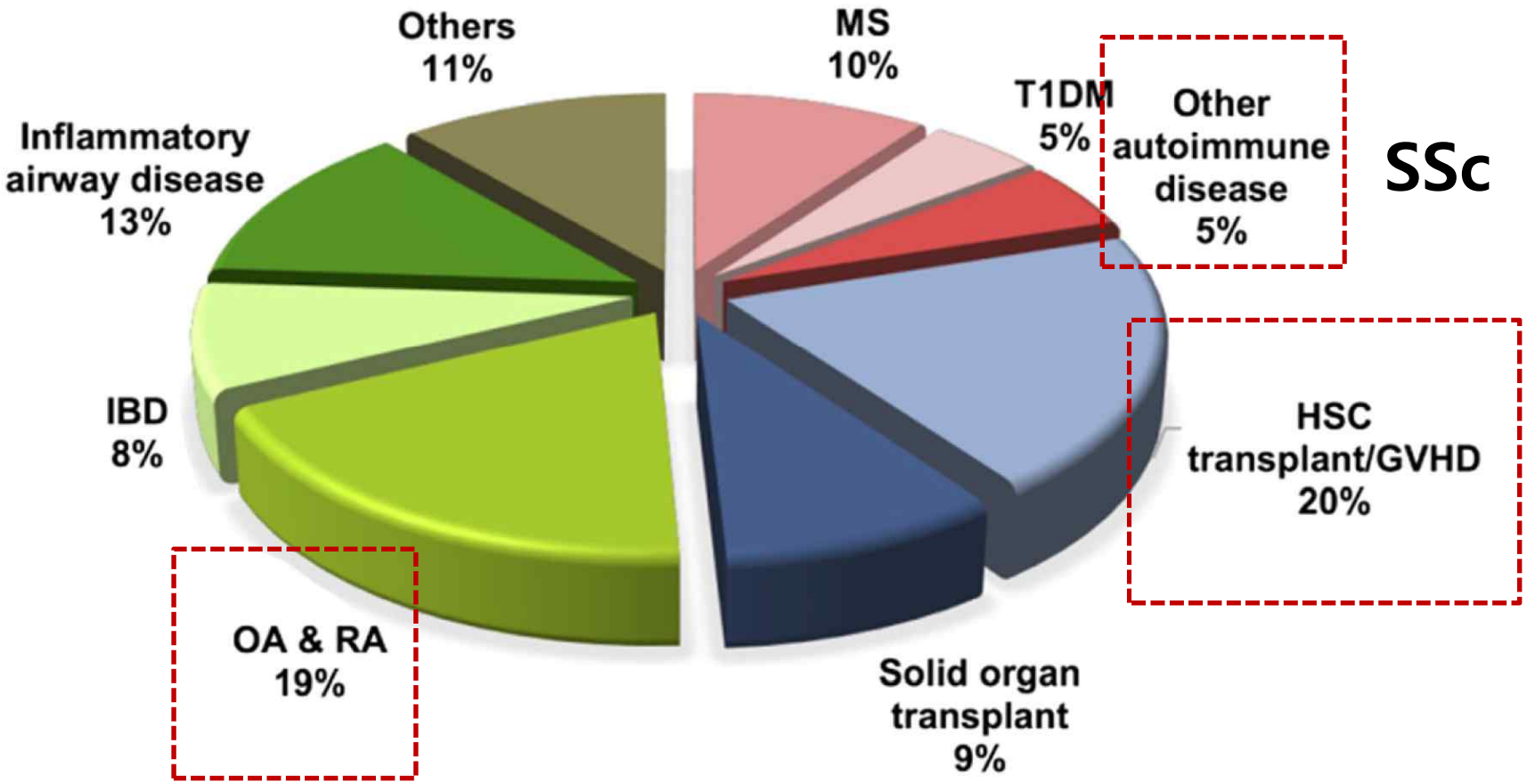
- Plastic-adherant cells
- **Positive markers:** CD73+,CD90+,CD105+
- **Negative markers:** CD45-,CD34-,CD14-,CD11b-, CD19-,CD79a-,HLA DR-
- Trilineage mesenchymal differentiation capacity into osteoblast, adipocyte and chondrocytes

현재 진행중인 MSC의 임상 연구
(NCT 등록된 임상연구 352개)



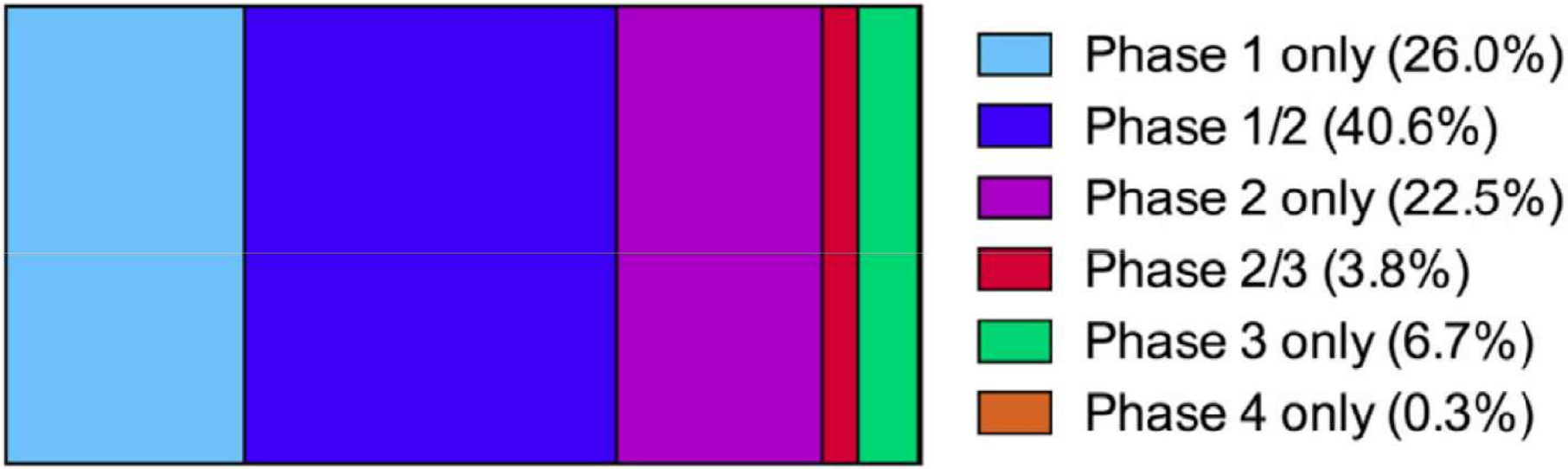
Cell stem cell 2015

hMSC for immune/inflammatory diseases



http://clinicaltrials.gov, April 2016

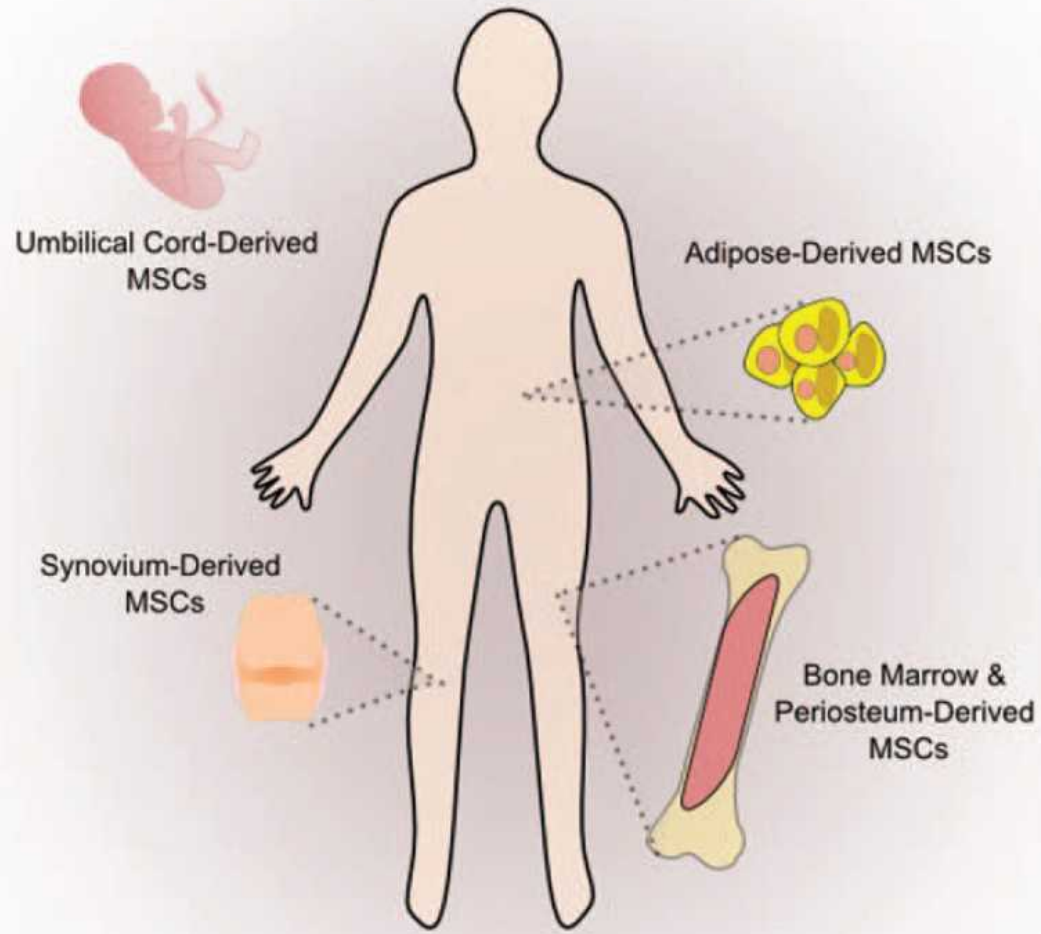
Clinical phase에 따른 MSC 임상연구 현황



Cell stem cell 2015

MSC sources used in clinical trials

14~19%



16%

41%

Curr Opinion Rheumatol 2017, 29:201

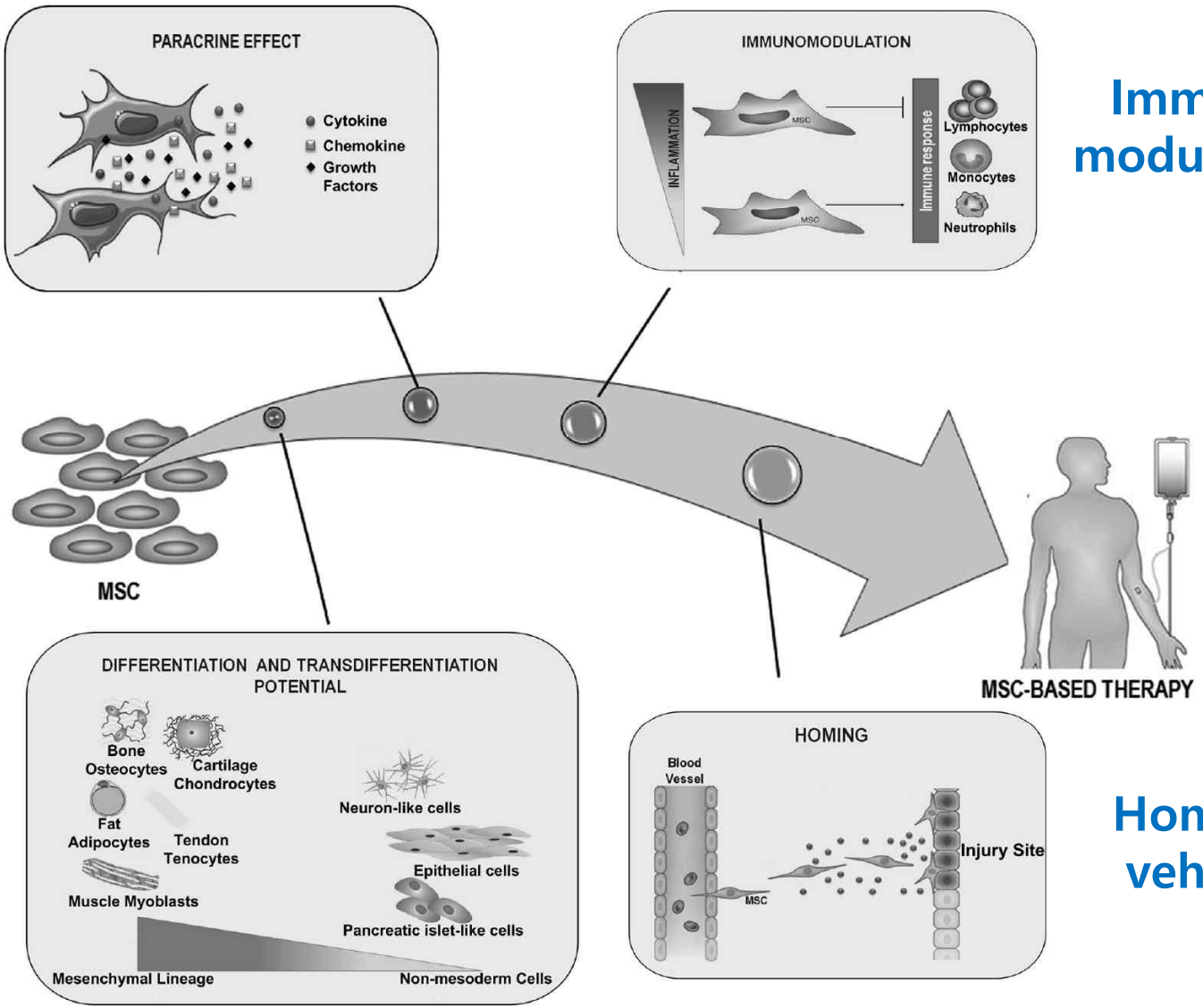
임상에 응용될 수 있는 MSC의 특성

Paracrine effect

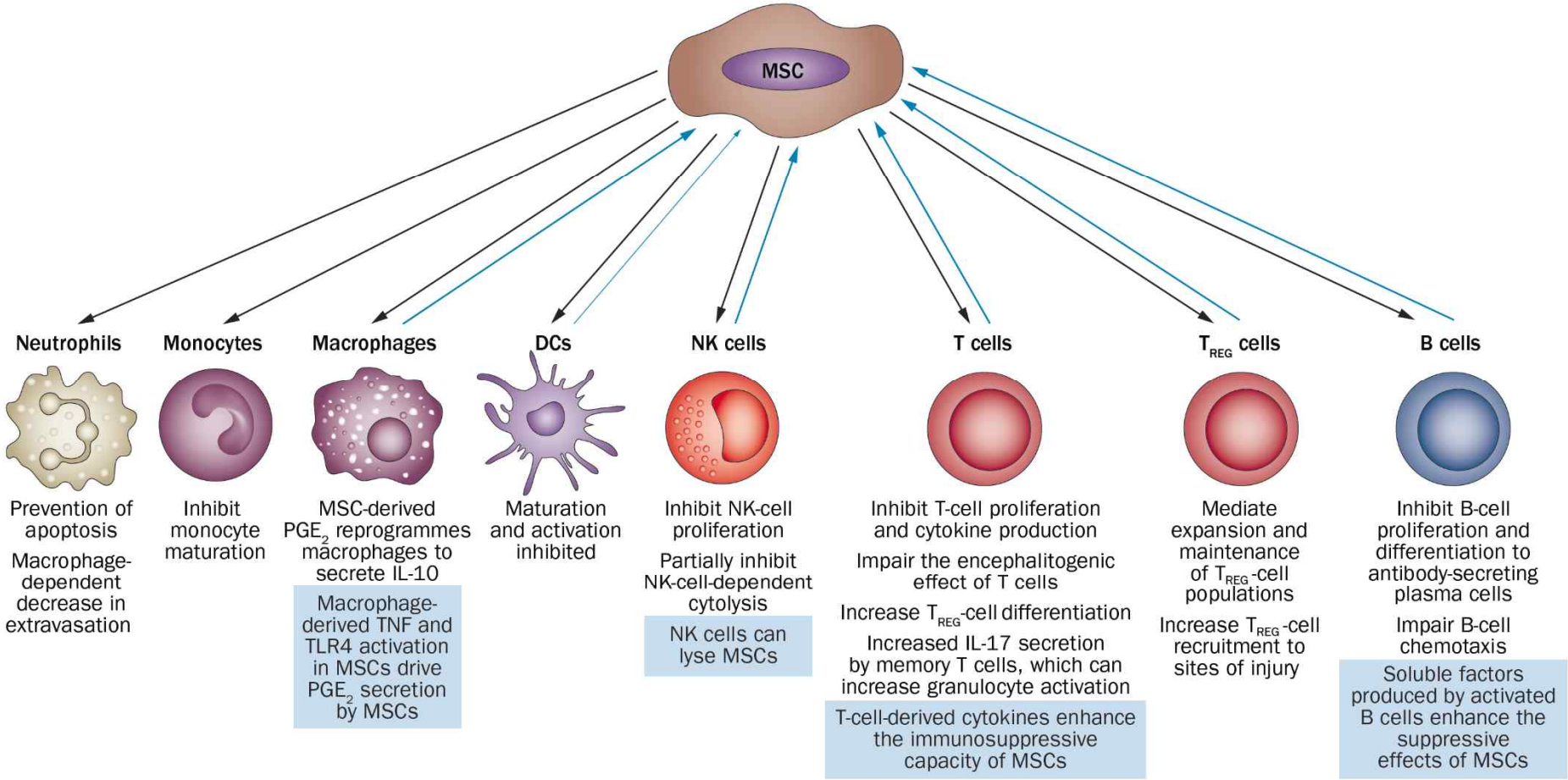
Immune modulation

Regeneration

Homing vehicle



Interaction of MSC with various immune cells



Nature review rheumatology 2014

Preclinical MSC-based study for RA & OA

Table 2. Recent preclinical MSC-based studies for RA and OA treatment.

Rheumatic disease	Experimental model	Source of MSCs	Dose of MSCs	Route and frequency of administration	Control	End-point after MSC injection	Reference
Inflammatory arthritis	CIA (8 w.o. DBA/1 mice)	hAd-MSCs	1×10^6	i.v.	Ringer's Lactate solution	7 days	Lopez-Santalla *et al.*[74]
	CIA (6–8 w.o. DBA/1 mice)	hUC-MSCs	1×10^6	i.v.	Not injected	62 days	Liu *et al.*[75]
	CIA (10 w.o. DBA/1 mice)	hESC-derived MSCs	1×10^6	i.p. (1×, 3×)	PBS	10 days after arthritis onset	Gonzalo-Gil *et al.*[122]
	CIA (8–10 w.o. DBA/1 mice)	Syngeneic mAd-MSCs	2×10^6	i.p.	PBS	14 days	Garimella *et al.*[78]
	CIA (8–12 w.o. DBA/1 mice)	Syngeneic mBM-MSCs and mouse Tr1 cells	5×10^5	i.p. (MSCs), i.v. (Tr1 cells); (2×)	PBS; 5×10^5 mouse Tr1 cells (i.v.)	6.5 weeks	Lim *et al.*[123]
	CIA (8 w.o. DBA/1 mice)	Syngeneic mBM-MSCs with AAV-miR-548e	1×10^6	i.p.	PBS; AAV-antisense-miR-548e	4 weeks	Yan *et al.*[77]
	CIA (8 w.o. DBA/1 mice)	CD146+ or CD146- hUC-MSCs	1×10^6	i.a.	PBS	14 days	Wu *et al.*[124]
	CIA (6–8 w.o. DBA/1 mice)	C57BL/6 mouse gingival MSCs (wt, $FasL^{-/-}$, FasL overexpression)	1×10^6	i.v.	PBS	35 days	Gu and Shi[76]
	CII-immunized IL-1Ra-KO BALB/c mice	hAd-MSCs (wt, sRAGE-overexpressing)	1×10^6	i.v. (3×)	PBS	6 weeks	Park *et al.*[125]
OA – osteochondral defects	MMR (New Zealand rabbits)	Equine UC-MSCs	3.5×10^6	i.a.	PBS	Up to 53 days	Saulnier *et al.*[100]
	ACTL (10–12 w.o. Lewis rats)	hSMSCs	1×10^6	i.a. (single or weekly)	PBS	Up to 12 weeks	Ozeki *et al.*[102]
	MMx (Sprague-Dawley rats)	hAd-MSCs	2.5×10^6	i.a.	PBS	Up to 10 weeks	Li *et al.*[126]
	Bilateral medial anterior hemimeniscectomy (12 m.o. New Zealand rabbits)	hAd-MSCs	2×10^6; 6×10^6	i.a.	Ringer's lactate solution	4 weeks	Riester *et al.*[127]
	Full-thickness cartilage defect (4–6 w.o. C57BL/6 mice)	Sca-1+ mSMSCs from C57BL6 or MRL/MpJ mice	1×10^5	i.a.	PBS	4 weeks	Mak *et al.*[112]

AAV, adeno-associated virus; ACTL, anterior cruciate ligament transection; CIA, collagen-induced arthritis; CII, type II collagen; hAd-MSCs, human adipose tissue mesenchymal stem cells; hESC-MSCs, human embryonic stem cell-derived mesenchymal stem cells; i.a., intra-articular; i.p., intra-peritoneal; i.v., intravenous; mAd-MSCs, mouse adipose tissue mesenchymal stem cells; m.o., months old; MMR, medial meniscal release; MMx, medial meniscectomy; PBS, phosphate buffered saline; sRAGE, soluble receptor for advanced glycation end products; Tr1 cells, IL-10-producing type 1 regulatory T cells; UC-MSCs, umbilical cord mesenchymal stem cells; w.o., weeks old.

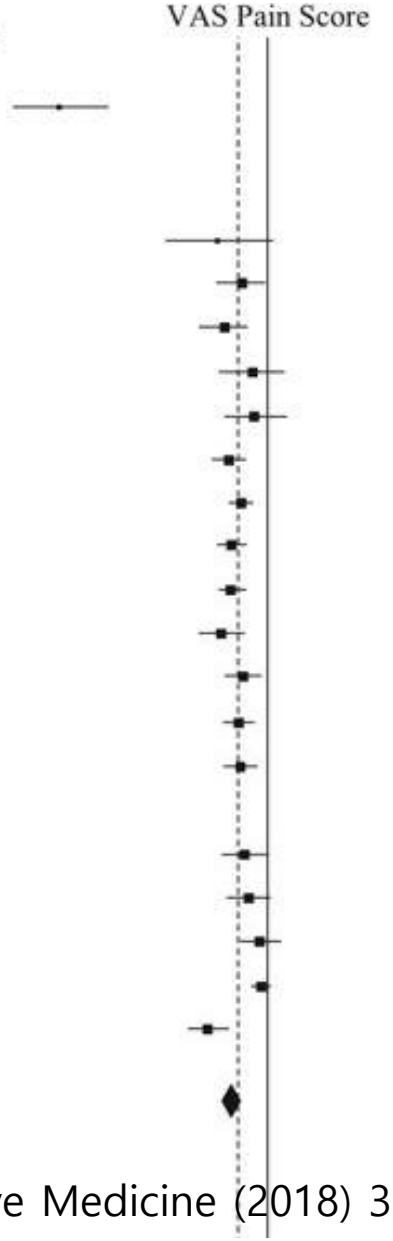
Clinical MSC-based study for RA & OA

Rheumatic disease	Type of study	Intervention	Comparator	Reference
RA	Clinical phase I/II; follow-up at 3, 6 and 8 months	136 patients, i.v. injection of 4×10^7 UC-MSCs and DMARDs	36 patients, intravenous injection of DMARDs and cell medium	Wang *et al.*[58]
	Clinical phase Ib/IIa; follow-up at 6 months	3 i.v. injection of allogeneic Ad-MSCs: 16 patients, 1×10^6 cells/kg; 19 patients, 2×10^6 cells/kg; four patients, 4×10^6 cells/kg	Four patients, placebo (Ringer's lactate solution)	Álvaro-Gracia *et al.*[80]
OA	Clinical phase I/II; follow-up at 2 years	12 patients, i.a. injection of 40×10^6 autologous BM-MSCs	None	Orozco *et al.*[105]
	Clinical phase I/II; follow-up at 12 months	50 patients, i.a. injection of 40×10^6 autologous BM-MSCs	None	Rich *et al.*[106]
	Clinical phase I/II; follow-up at 6 months	i.a. injection of autologous Ad-MSCs: 3 patients, 1×10^7 cells; 3 patients, 5×10^7 cells; 12 patients, 1×10^8 cells	None	Jo *et al.*[107]
	Clinical phase I/II; follow-up at 12 months	15 patients, i.a. injection of 40×10^6 cells	15 patients, intra-articular injection of hyaluronic acid	Vega *et al.*[108]

Ad-MSCs, adipose tissue mesenchymal stem cells; BM-MSCs, bone marrow mesenchymal stem cells; DMARDs, disease-modifying anti-rheumatic drugs; i.a., intra-articular; i.v., intravenous; UC-MSCs, umbilical cord mesenchymal stem cells.

MSC (IA or arthroscopic Tx) improve knee pain

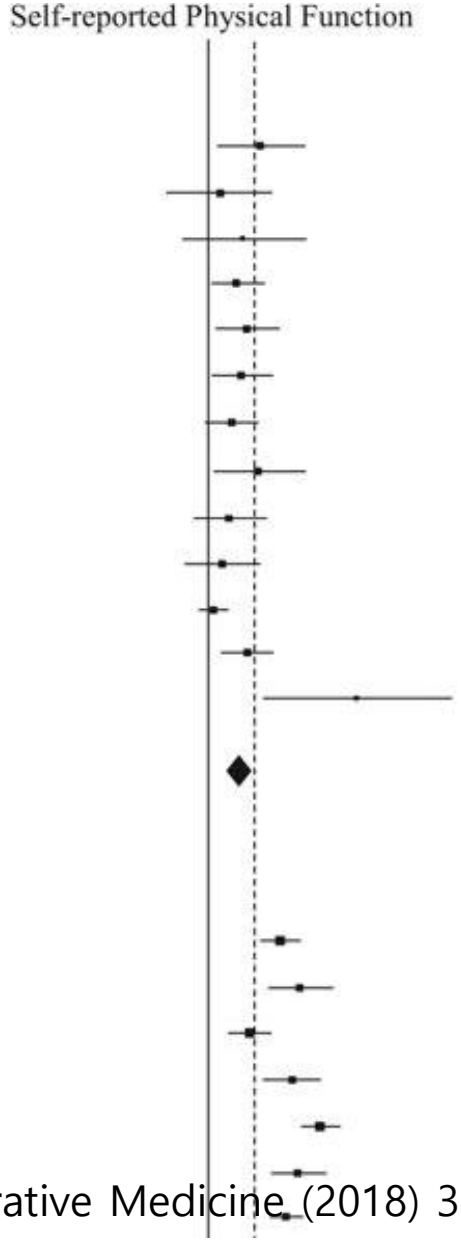
Study	n	SMD (95% CI)	Weight, %
Autologous			
Bui, 2014 (Vietnam)	21	-11.97 (-14.73, -9.21)	2.0
Centeno, 2008a (Unites states)	1	Not estimable	
Centeno, 2008b (Unites states)	1	Not estimable	
Davatchi, 2016 (Iran)	3	-2.75 (-5.86, 0.35)	1.7
Emardin, 2012 (Iran)	6	-1.45 (-2.79, -0.12)	3.9
Fodor, 2016 (Unites states)	8	-2.41 (-3.78, -1.04)	3.8
Jo, 2014; Low-dose (Korea)	3	-0.79 (-2.57, 0.98)	3.2
Jo, 2014; Mid-dose (Korea)	3	-0.61 (-2.31, 1.10)	3.3
Jo, 2014; High-dose (Korea)	12	-2.09 (-3.12, -1.06)	4.4
Koh, 2012 (Korea)	25	-1.42 (-2.04, -0.79)	5.0
Koh, 2013 (Korea)	18	-1.99 (-2.81, -1.18)	4.7
Koh, 2015 (Korea)	30	-1.97 (-2.59, -1.35)	5.0
Lamo-Espinosa, 2016; Low-dose (Spain)	10	-2.54 (-3.78, -1.30)	4.0
Lamo-Espinosa, 2016; High-dose (Spain)	10	-1.29 (-2.28, -0.31)	4.5
Nguyen, 2017 (Vietnam)	15	-1.46 (-2.28, -0.64)	4.7
Orozco, 2013 (Spain)	12	-1.48 (-2.40, -0.55)	4.6
Pak, 2011 (Korea)	2	Not estimable	
Pers, 2016; Low-dose (France)	6	-1.19 (-2.46, 0.08)	4.0
Pers, 2016; Mid-dose (France)	6	-1.00 (-2.23, 0.23)	4.1
Pers, 2016; High-dose (France)	6	-0.34 (-1.48, 0.81)	4.2
Soler Rich, 2015 (Spain)	50	-0.22 (-0.62, 0.17)	5.3
Soler, 2016 (Spain)	15	-3.28 (-4.42, -2.14)	4.2
Subtotal (Random effects model)	263	-1.82 (-2.41, -1.24)	76.7
Test for heterogeneity: $Chi^2 = 119.01$ ($P < 0.001$), $I^2 = 85\%$			
Allogeneic			



npj Regenerative Medicine (2018) 3:15

MSC improve knee Functional Score (partially)

Study	n	SMD (95% CI)	Weight, %
Autologous			
WOMAC Physical Functional Score			
Emardin, 2012 (Iran)	6	1.70 (0.29, 3.10)	2.9
Jo, 2014; Low-dose (Korea)	3	0.45 (-1.21, 2.10)	2.6
Jo, 2014; Mid-dose (Korea)	3	1.17 (-0.79, 3.12)	2.2
Jo, 2014; High-dose (Korea)	12	0.91 (0.06, 1.76)	3.6
Lamo-Espinosa, 2016; Low-dose (Spain)	10	1.29 (0.31, 2.27)	3.5
Lamo-Espinosa, 2016; High-dose (Spain)	10	1.05 (0.10, 2.00)	3.5
Orozco, 2013 (Spain)	12	0.77 (-0.07, 1.60)	3.7
Pers, 2016; Low-dose (France)	6	1.69 (0.29, 3.09)	2.9
Pers, 2016; Mid-dose (France)	6	0.75 (-0.44, 1.94)	3.2
Pers, 2016; High-dose (France)	6	0.52 (-0.64, 1.68)	3.2
Soler Rich, 2015 (Spain)	50	0.14 (-0.26, 0.53)	4.1
Soler, 2016 (Spain)	15	1.31 (0.51, 2.10)	3.7
Turajane, 2013 (Thailand)	5	4.79 (1.82, 7.76)	1.3
Subtotal (Random effects model)	144	0.97 (0.56, 1.38)	40.3
Test for heterogeneity: $Chi^2 = 23.91$ ($P = 0.020$), $I^2 = 50\%$			
IKDC Score			
Kim, 2015a-1 (Korea)	39	2.39 (1.80, 2.98)	4.0
Kim, 2015a-2 (Korea)	17	2.99 (1.98, 4.00)	3.4
Kim, 2015b-1 (Korea)	20	1.38 (0.69, 2.08)	3.8
Kim, 2015b-2 (Korea)	20	2.74 (1.85, 3.63)	3.6
Kim, 2015c (Korea)	55	3.65 (3.03, 4.26)	3.9
Kim, 2016 (Korea)	24	2.94 (2.10, 3.77)	3.7
Koh, 2014a (Korea)	60	2.54 (2.06, 3.03)	4.1



npj Regenerative Medicine (2018) 3:15

Summary 2

Present feasible & regenerative therapeutic option

Chondrocyte treatment
Autologous chondrocyte
Proliferate & transplant

Chondrocyte harvest

Culture & expansion

Auto-transplant

A

Intra-articular injection

Repeat surgical operation
Repaired cartilage: fibrosis

Chondrocyte treatment
Allogenic chondrocyte
Proliferate & transplant

Polydactily

C

live Chondrocyte

+

irradiated Chondrocyte
+ **TGFb gene**

Inflammation suppression
Cartilage regeneration?

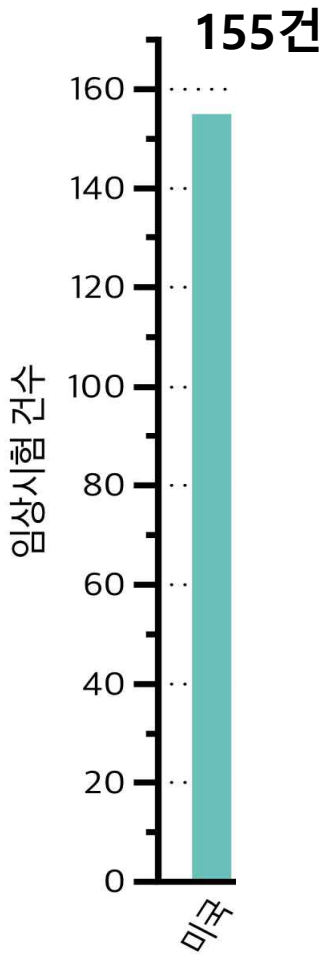
목 차

The stronger the light source,
the darker the shadow.

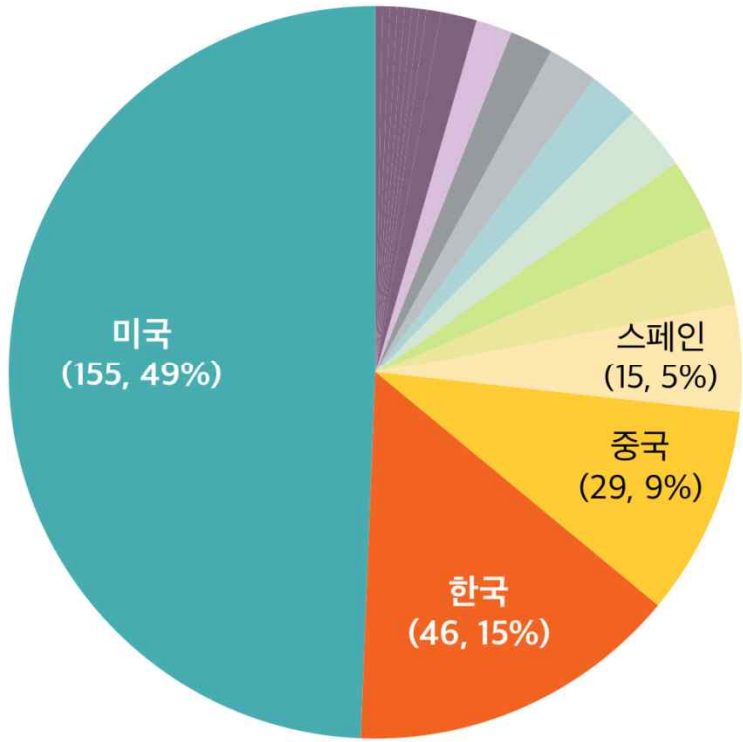

明
暗

Light

Stem cell R&D in South Korea



국가별 줄기세포치료제 임상연구 건



2017.04.24, 식약처 첨단바이오제품과

Light

Stem cell R&D in South Korea

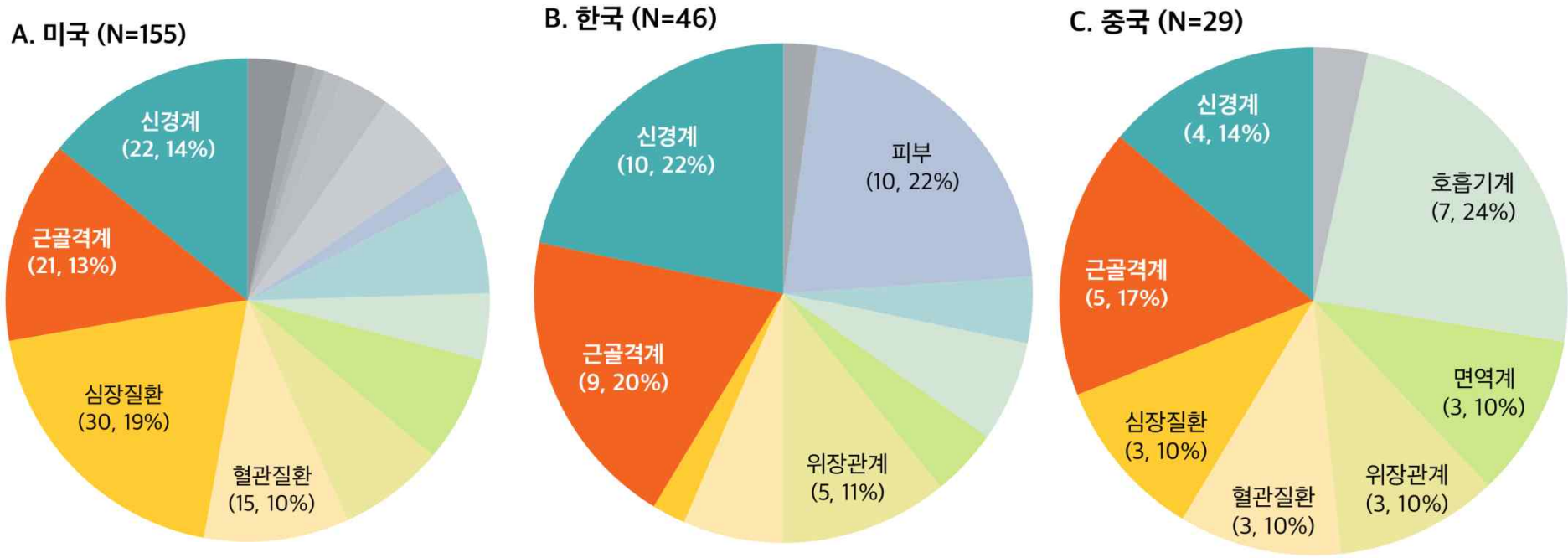
4/7

	허가국	제품 (허가 기업)
줄기세포 치료제	한국	하티셀그램-AMI(파미셀)
		카티스템(메디포스트)
		큐피스템(안트로젠)
		뉴로나타-R(코아스템)
	캐나다/뉴질랜드/일본	프로키말(Osiris Therapeutics)
	이탈리아	홀로클라(Chiesi)
	유럽	스트림벨리스(GSK)
면역세포 치료제	한국	이뮨셀-LC(녹십자셀)
		크레아박스-RCC(JW 크레아젠)
		NKM(엔케이바이오)
	미국	프로벤지(Dendreon)
		킴리아(Novartis)
		예스카타(Kite Pharma)

2017.04.24, 식약처 첨단바이오제품과 & 2017.11 LG경제연구원

계통별 개발현황

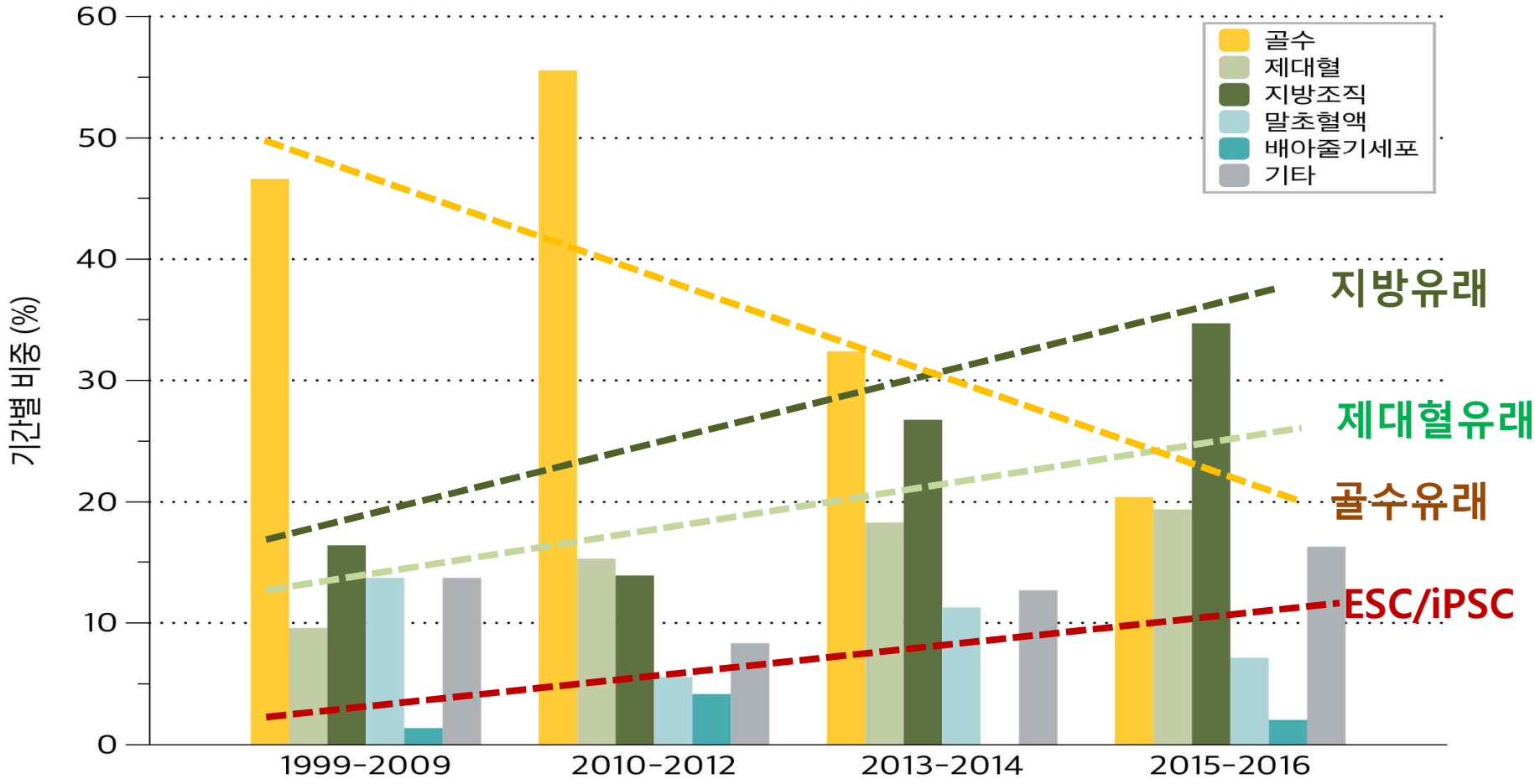
Stem cell R&D in South Korea



2017.04.24, 식약처 첨단바이오제품과

줄기세포기원별 현황

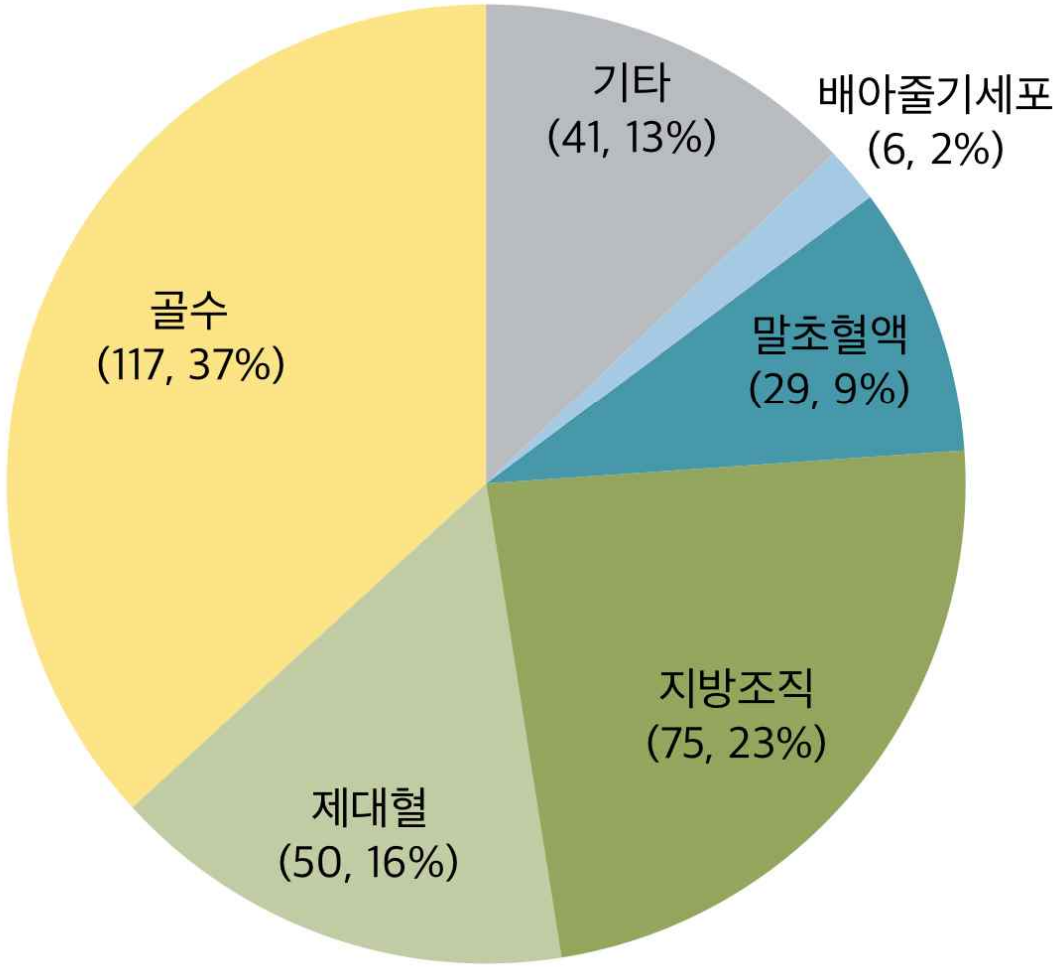
Stem cell R&D in South Korea



2017.04.24, 식약처 첨단바이오제품과

줄기세포기원별 현황

Stem cell R&D in South Korea



2017.04.24, 식약처 첨단바이오제품과


明
暗

Shadow

Stem cell R&D in South Korea

개발국(건수)	미국	중국	한국	대만	스페인	인도	이스라엘
2014	21	5	5	0	3	0	1
2015	16	11	10	3	2	2	2
2016	23	8	5	3	2	0	2

2016년 신규등록 줄기세포치료제 임상시험건수

2017.04.24, 식약처 첨단바이오제품과

Shadow

Stem cell R&D in South Korea

	허가국	제품 (허가 기업)	
줄기세포 치료제	한국	하티셀그램-AMI(파미셀)	(2012년) 1~5천만원
		카티스템(메디포스트)	
		큐피스템(안트로젠)	
		뉴로나타-R(코아스템)	
	캐나다/뉴질랜드/일본	(2013년) GVHD 2억	
	이탈리아	(2014년) 각막윤부줄기세포소실 2억	
	유럽	(2016년) ADA HSC 7억	

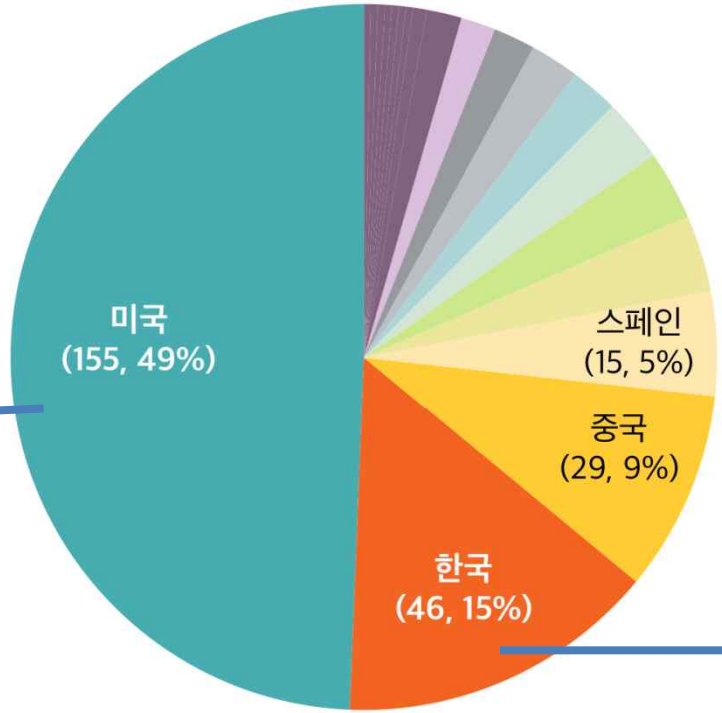
2017.11 LG경제연구원

Shadow

Stem cell R&D in South Korea

제품허가

"0건"



제품허가

"4건"

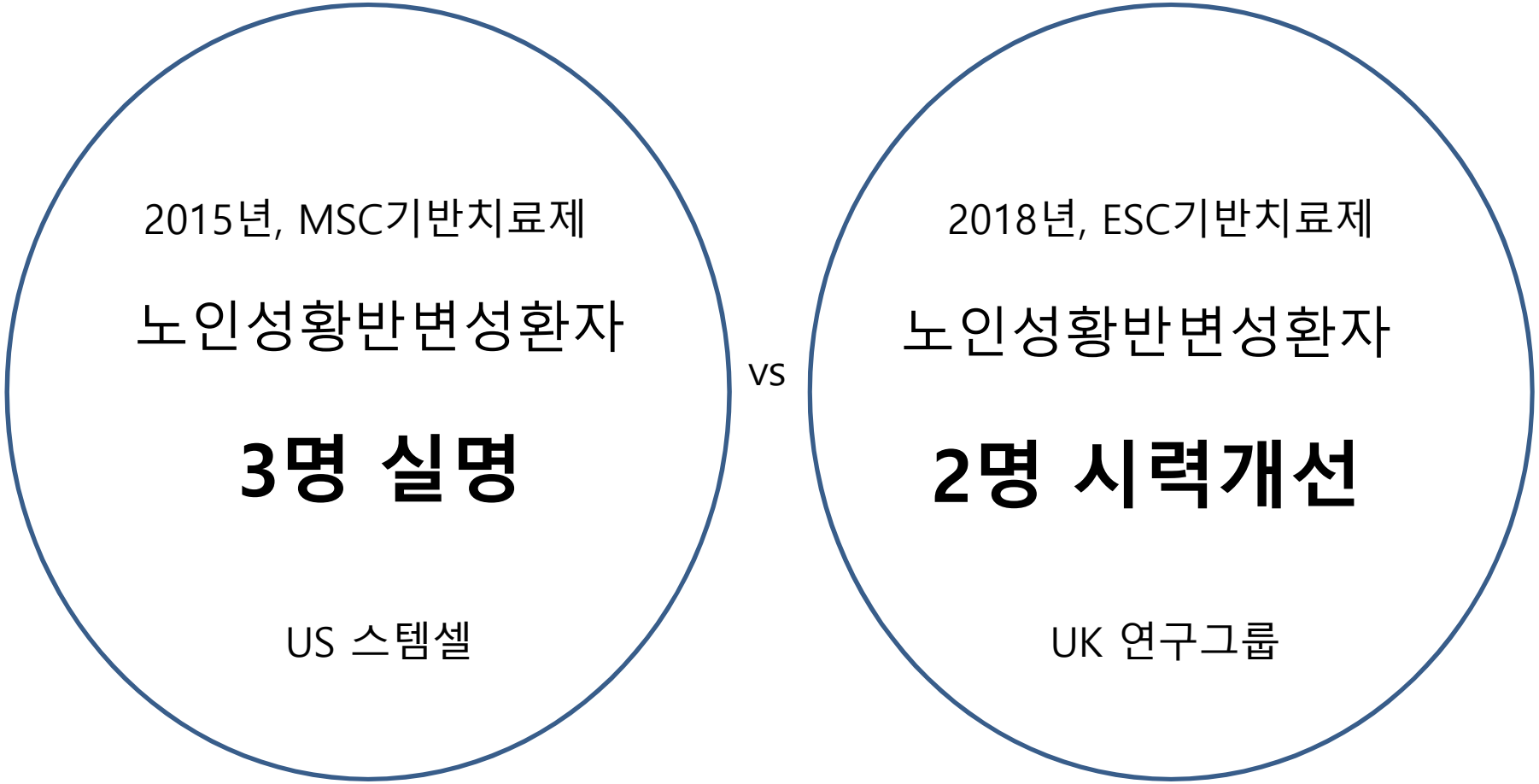
"한국에서 허가된 줄기세포 치료제에 대해 알려진 정보는 식약처의 보도자료를 통해 전파된 것" (Nature 2012.6)

"과학적 근거가 부족한 성체줄기세포 시술·치료 단속이 강화돼야 한다." (Nature 2018.5)

2018.5 Nature 리뷰

Shadow

Stem cell R&D in South Korea



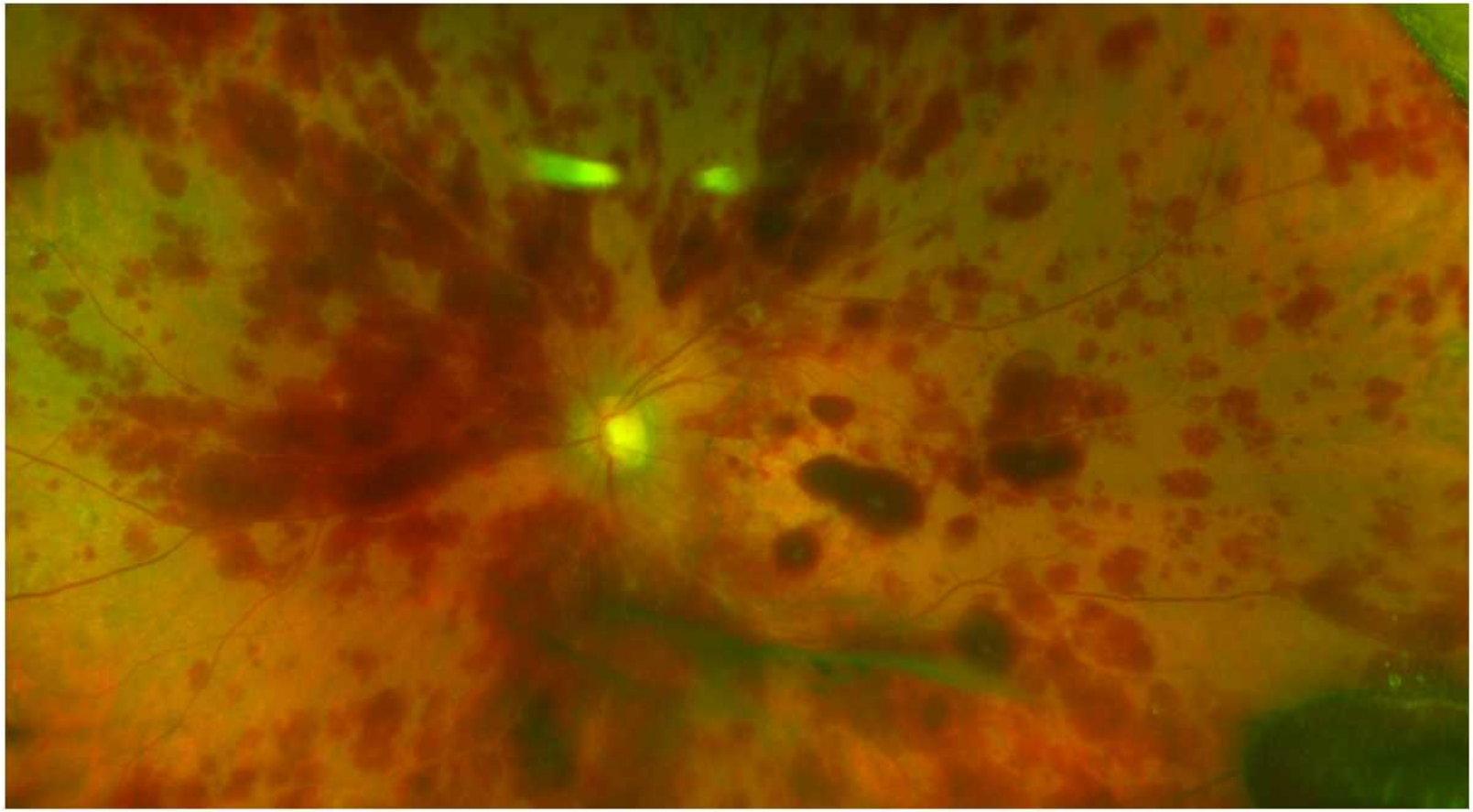
2018.5 Nature 리뷰

HEALTH

The New York Times

Patients Lose Sight After Stem Cells Are Injected Into Their Eyes

Adipose tissue-derived stem cell



The left eye of a patient showing hemorrhages 13 days after stem-cell injection. Dr. Thomas Albini

Retinal hemorrhage & blindness after MSC Intra-ocular injection

Commented in "Nature" editorial

The New York Times, March 15, 2017

-0.38% ▼ Nasdaq **7816.28** -1.04% ▼ U.S. 10 Yr **-0/32 Yield** 2.393% ▼ Crude Oil **62.71** -0.25% ▼ Euro **1.1159** -0.18%

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HEALTH | YOUR HEALTH

Stem Cells for Knee Problems? U.S. Doctors Investigate

Demand is high from patients with osteoarthritis, meniscus tears and other maladies, but studies haven't reached firm conclusions yet

By *Sumathi Reddy*

Updated Jan. 8, 2018 3:29 p.m. ET

The Wall Street Journal, Jan. 8, 2018

The New York Times

12 People Hospitalized With Infections From Stem Cell Shots

Cord blood-Derived stem cell

FDA commissioner

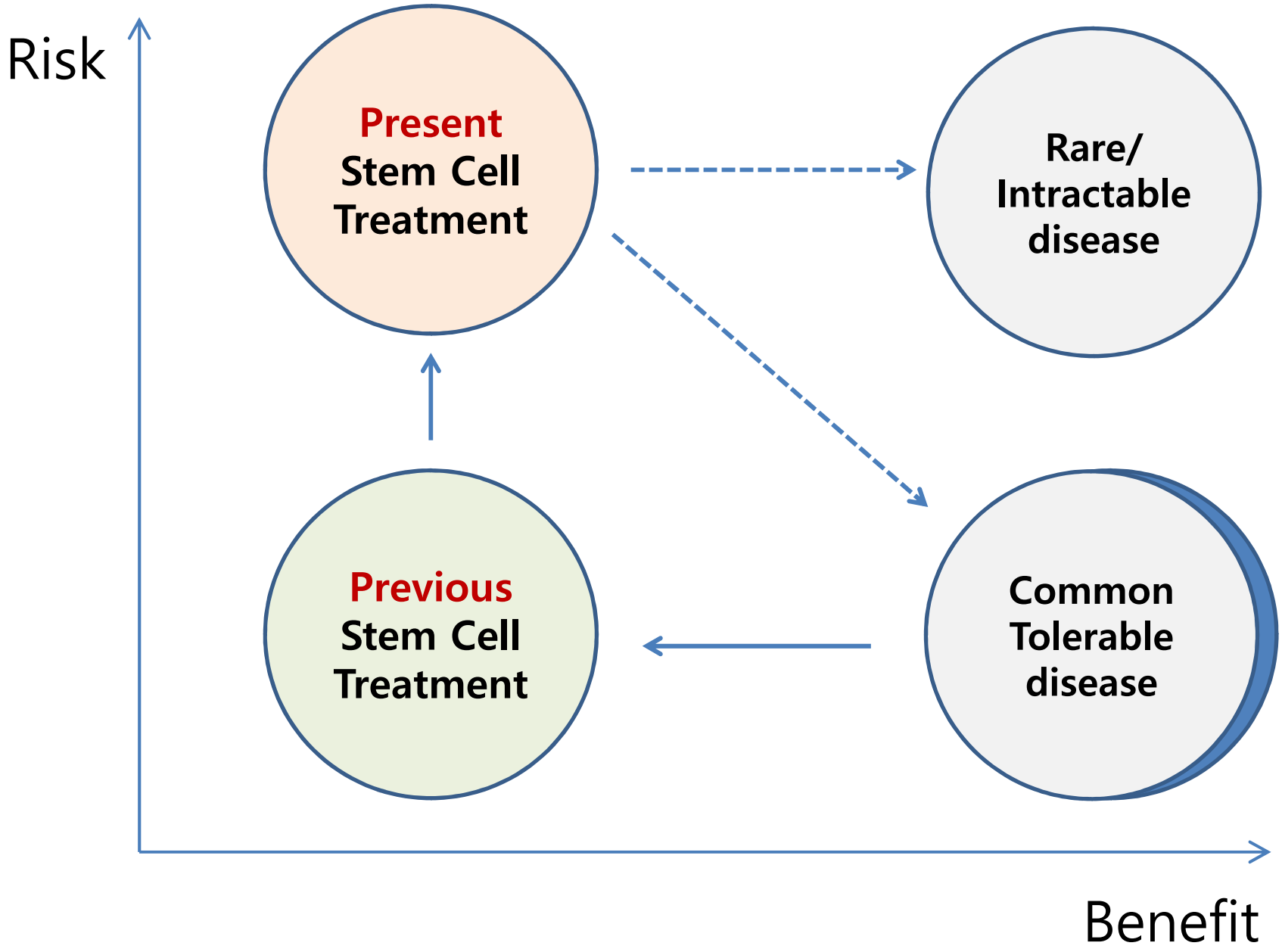
Infections after MSC IA Knee injection

Commented in "NEJM" editorial

The New York Times, Dec. 20, 2018

How much did you pay for your stem cell Tx?

Perspective



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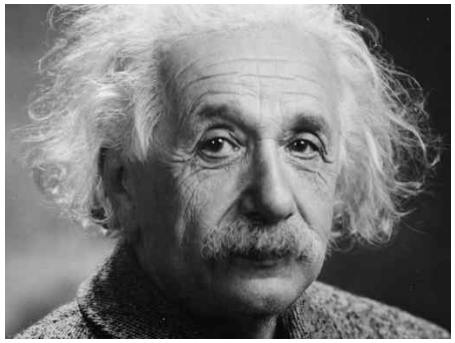
의학적 수요
학문적 근거

산업적 수요
생산물 공급

R&D

학계(과학자)



기술이전
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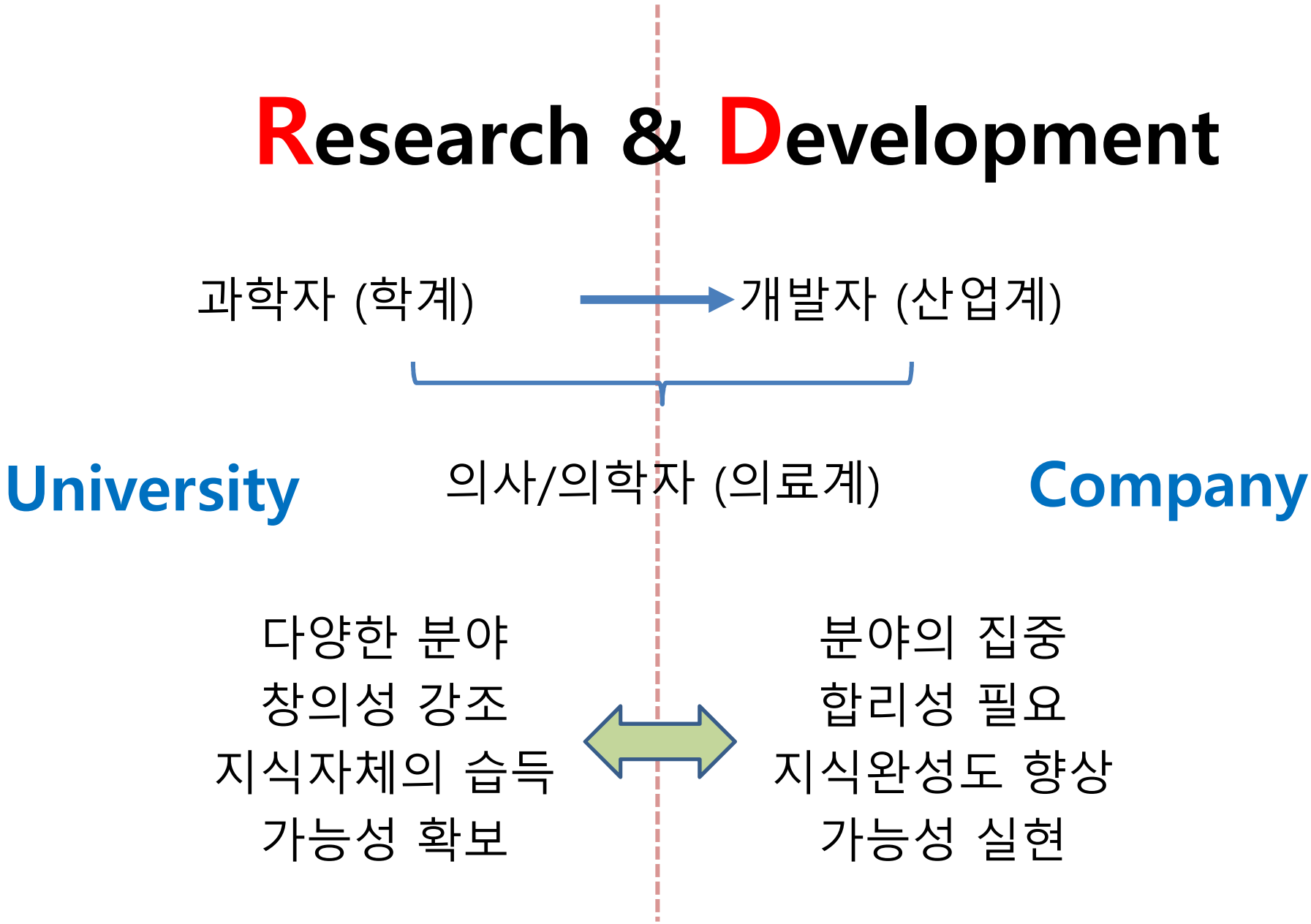
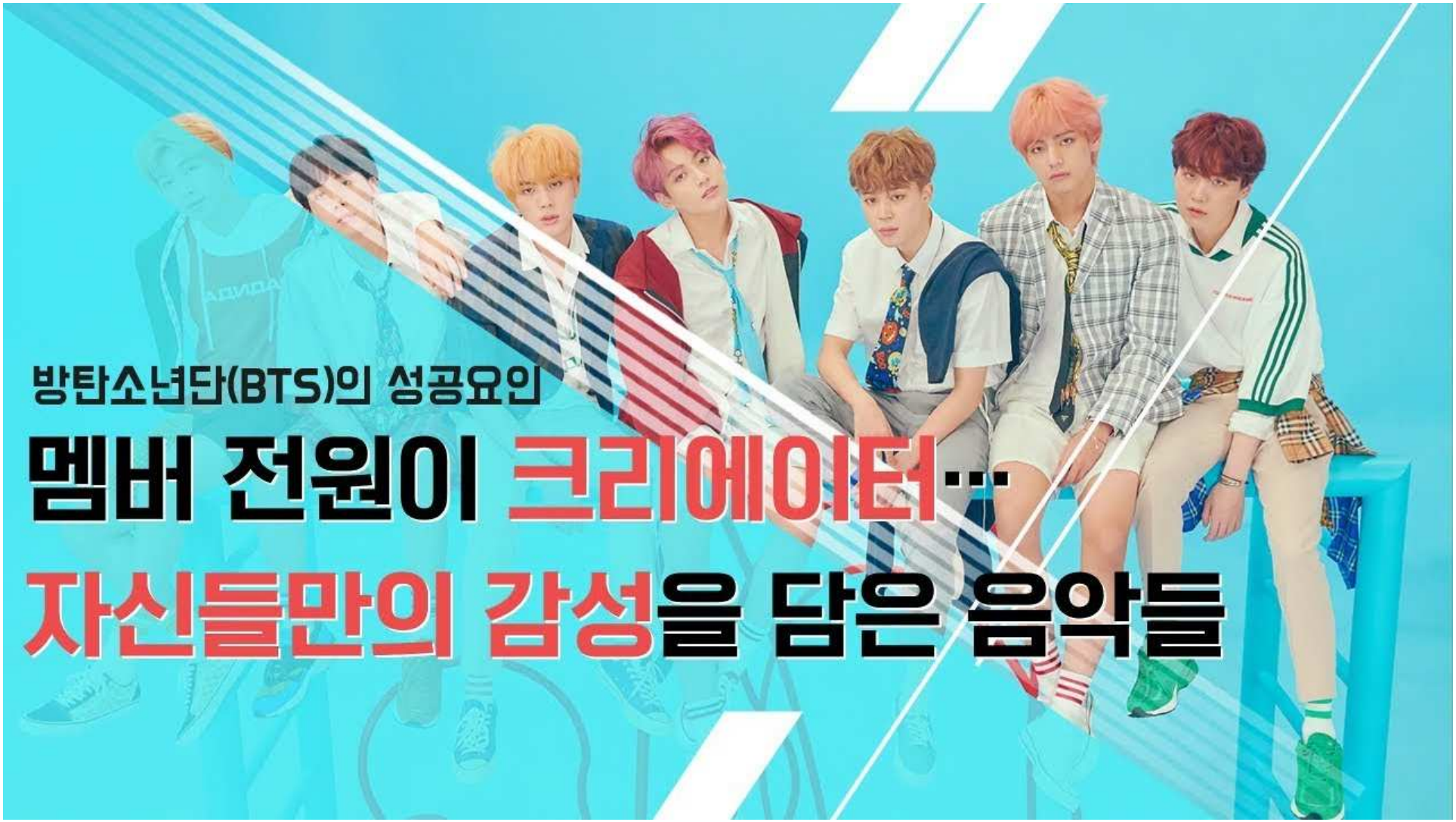

Research & Development
과학자 (학계)
개발자 (산업계)
University
의사/의학자 (의료계)
Company
다양한 분야
창의성 강조
지식자체의 습득
가능성 확보
분야의 집중
합리성 필요
지식완성도 향상
가능성 실현


대학
(과학자)
병원
(의사)
기업
(회사)

차원이 다른 BTS 의 생산방식 7계명

- 유명 작사·작곡가 도움 안받기
- '뜨내기 손님' 보다 '단골 손님'
- 품앗이 미학… "멤버들끼리 가르치고 배운다"
- '밑바닥' 까지 보여주는 실시간 SNS 활동
- BTS ↔ ARMY(BTS 팬덤), 생산방식 '공유'
- "내 스토리는 내가 짠다"
- '아티스트 + 아이돌' 제작방식 결합


방탄소년단(BTS)의 성공요인
멤버 전원이 크리에이터…
자신들만의 감성을 담은 음악들

줄기세포/세포치료제의 개발 및 치료환경?

알래스카

척박한 개발/치료환경
짧은 여름, 긴 겨울

학문적근거확보 목적
환경의존적/수동적
학계의 구조적 위기

생존을 위한 전략

지구온난화
"2.0"

빨리
빨리

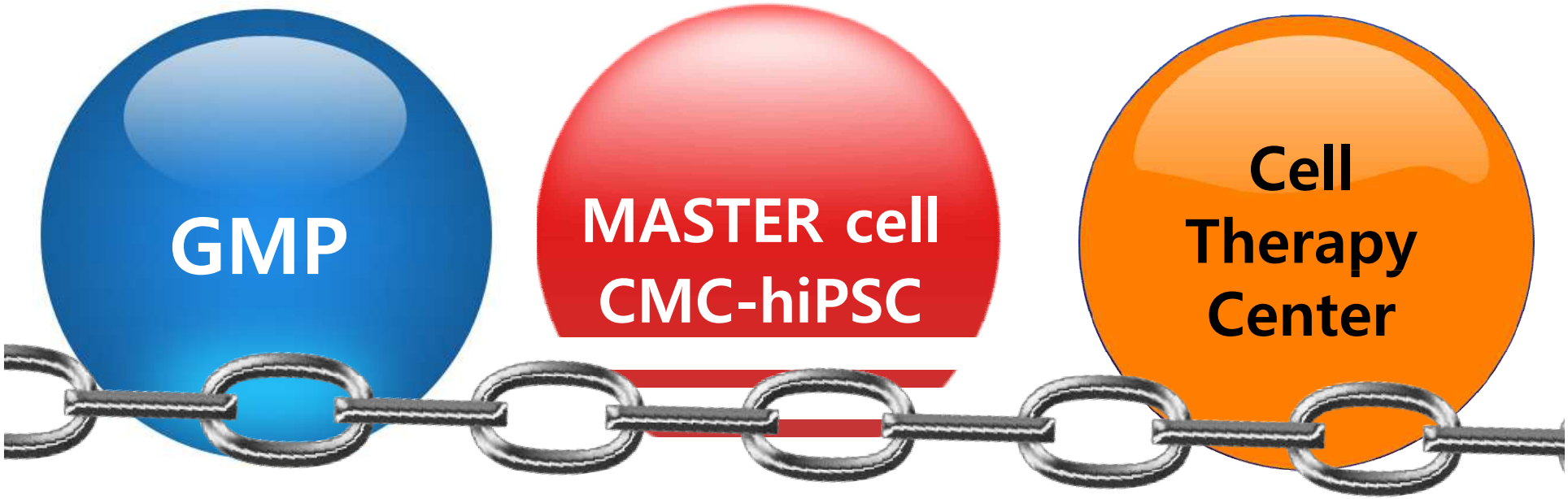
아프리카 초원

약육강식의 세계
승자독식의 논리

근원적인 경쟁력 확보
이익의 극대화 능동적
한국 R&D 능동적 시장개척

지속/안정적 성장전략

성공적인 줄기세포 임상연구를 위한 지원 분야



A bird in the hand is worthier than two in the bush (Proverb)
한국속담: 구슬이 서 말이라도 꿰어야 보배

한국 줄기세포 R&D 활성화를 위해....

좋은 재료

MASTER세포
CMC-iPS세포

성체줄기세포치료제 표준화/상업화/실용화 제도/정책적 지원

좋은 생산환경

Institutional GMP

학술기관/병원에서 세포생산에 대한 제도/정책적 지원

치료적용

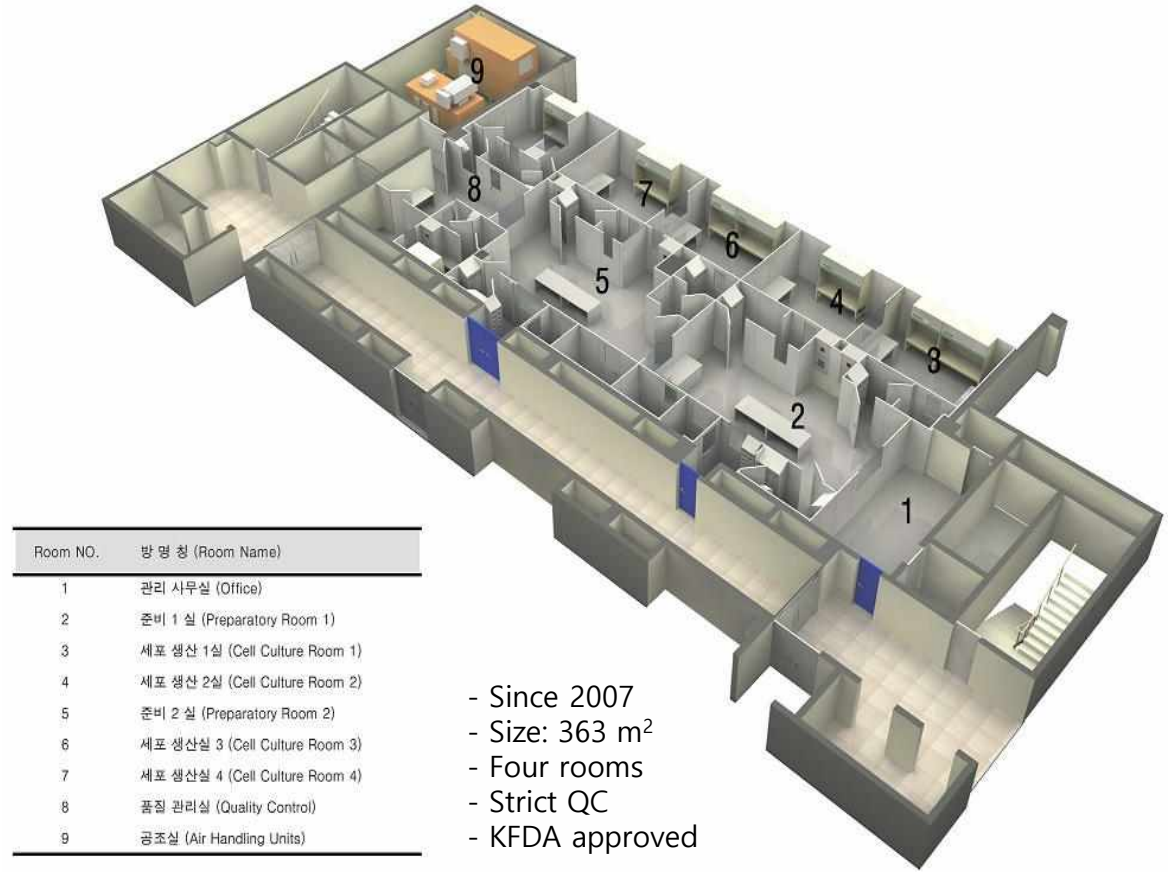
Cell Therapy Center

병원에서 줄기세포 치료제 사용에 대한 제도/정책적 지원

슬프게도... 첨단재생의료법
국회 법안심사소위원회 통과(2019.3.25)
-> 국회법제사법위원회 보류(2019.4.4)

세포생산시설 (GMP) 운영

- GMP(Good Manufacturing Practice) 시설 : 세포생산 인프라



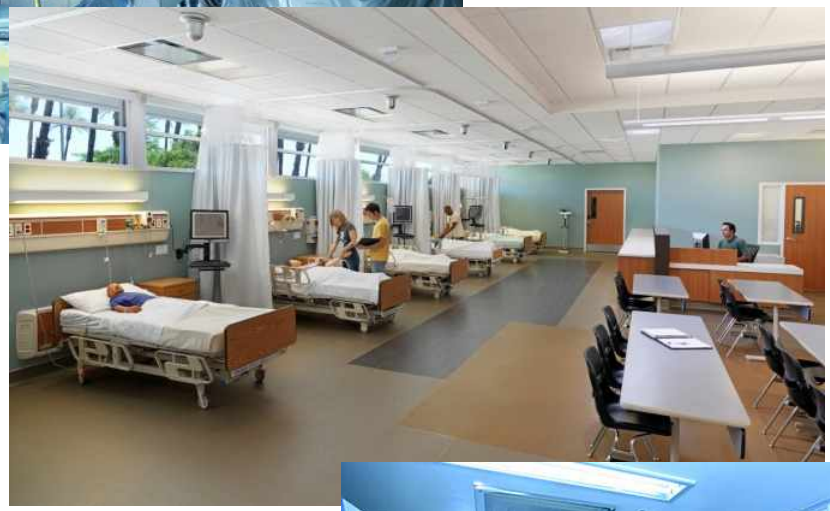
Room NO.	방 명 칭 (Room Name)
1	관리 사무실 (Office)
2	준비 1 실 (Preparatory Room 1)
3	세포 생산 1실 (Cell Culture Room 1)
4	세포 생산 2실 (Cell Culture Room 2)
5	준비 2 실 (Preparatory Room 2)
6	세포 생산실 3 (Cell Culture Room 3)
7	세포 생산실 4 (Cell Culture Room 4)
8	품질 관리실 (Quality Control)
9	공조실 (Air Handling Units)

- Since 2007
- Size: 363 m^2
- Four rooms
- Strict QC
- KFDA approved

- GMP는 가톨릭생명윤리에 부합하는 성체줄기세포 연구발전에 꼭 필요한 시설
- GMP를 통해서만 줄기세포 연구를 완성할 수 있음

Bench
(Lab)

가톨릭세포치료 사업단은 이미 성체줄기세포 연구 임상에 이미 "**B-B-B**" 성공 경험을 보유.



Bed
(Clinic)

Business
(GMP)

결 론

줄기세포 R&D가 어떻게 되어야하나 ?

Industry's eye

Scientist's eye

FDA eye

앞으로 K-Bio의 성공을 위해서....

Industry's eye

Scientist's eye

FDA's eye

Rio Olympic Story

줄기세포 R&D란?

기술전달 하는 party (연구자)　　기술전달 받는 party (기업)

줄기세포 R&D란?

기술전달 하는 party (연구자)

기술전달 받는 party (기업)

줄기세포 R&D란?

2016년 리우올림픽, 여자 미국팀 계주예선

2016년 리우올림픽, 여자 미국팀 계주예선

연구자 & 기업의 역할, PICK & RUN!!!!

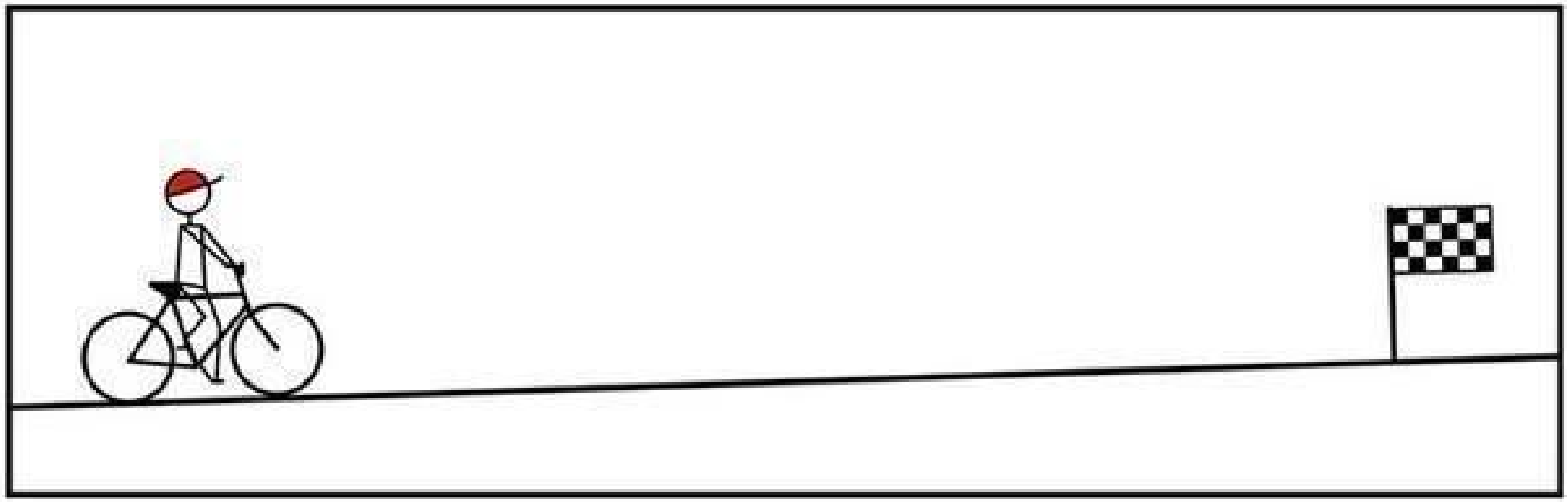
식약처 및 정부의 역할: 2016리우올림픽 심판의 역할

Story from CCTV NEWS.


FELIX
GARDNER
1
AFP BBNews


줄기세포 R&D의
발전과 성공....
연구자
학자
관찰
표현

Your plan : 이론적으로 줄기세포 치료제는 이럴까?



치료관련 부작용

비용 상승

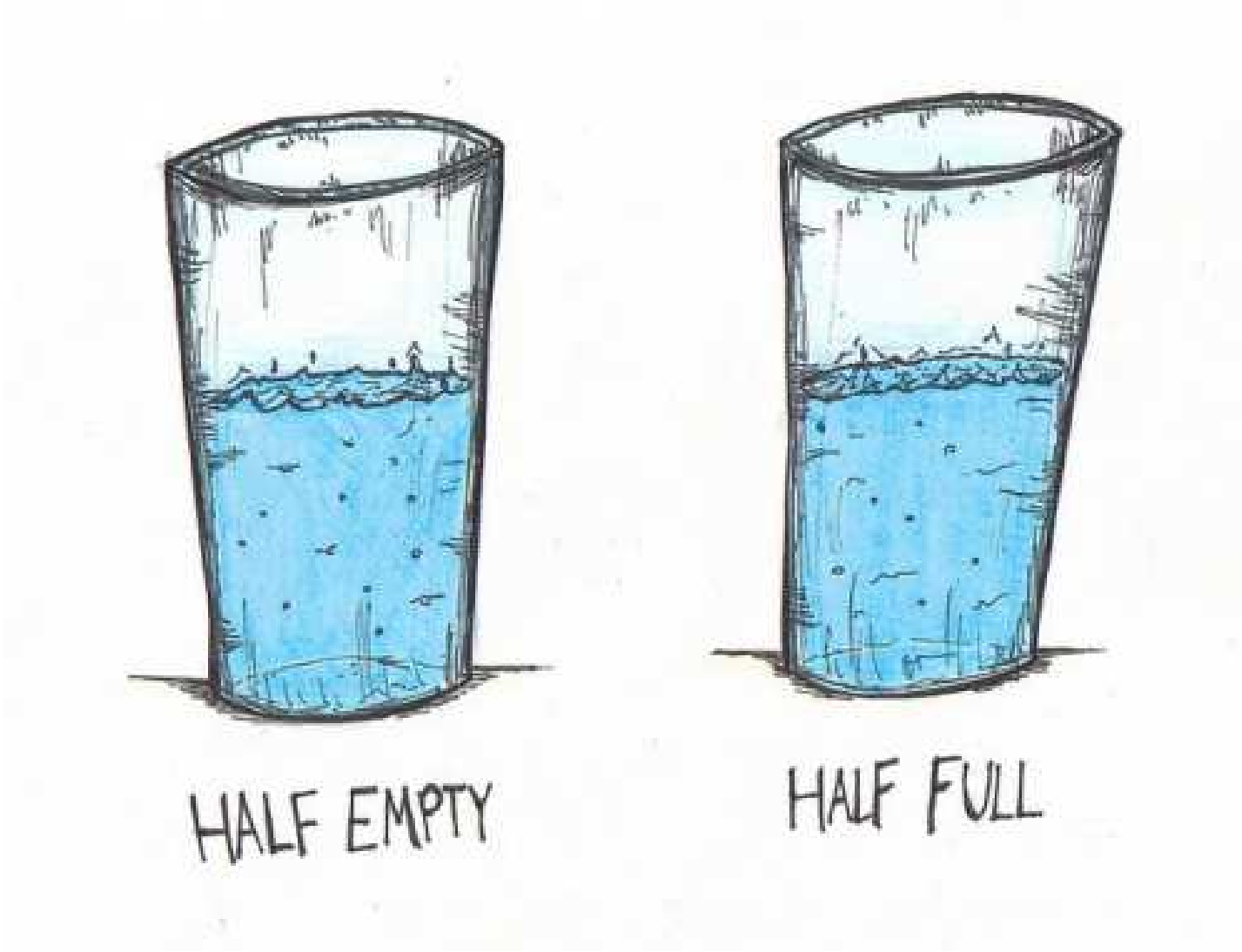
생산표준 확보

새로운 경쟁약제!

Conclusion

- 줄기세포치료제는 앞으로 큰 가능성이 있음
- 앞으로 고령화 사회에서 특히 더 필요한 치료형태
- 그러나 학문적인 근거를 확실히 만들어야 할 필요성
- 줄기세포 치료제 개발의 명과 암이 존재
- 전략적 접근이 필요한 시점 "**Risk hedge**" & "**Benefit ensure**"
- 줄기세포치료제 개발의 성공: 가장 한국적인 개념이 필요한 시점 (신속성, 업무의 분담, 업무의 통섭)

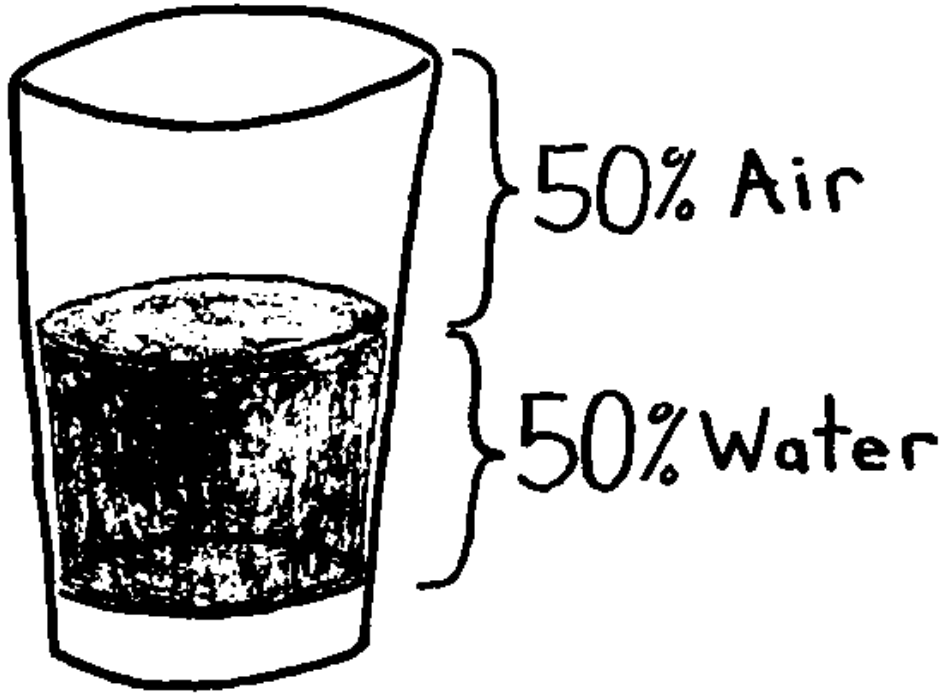
줄기세포치료제에 대한 시각



비관론자

낙관론자

현실주의자의 입장...



Technically,
The Glass is Completely Full.

경청해 주셔서 감사합니다