Tabriz University of Medical Sciences

ویژگیهای سلول های بنیادی مزانشیمی و پرایمینگ آنها جهت استخراج سکرتوم و اگزوزوم

ارایه:

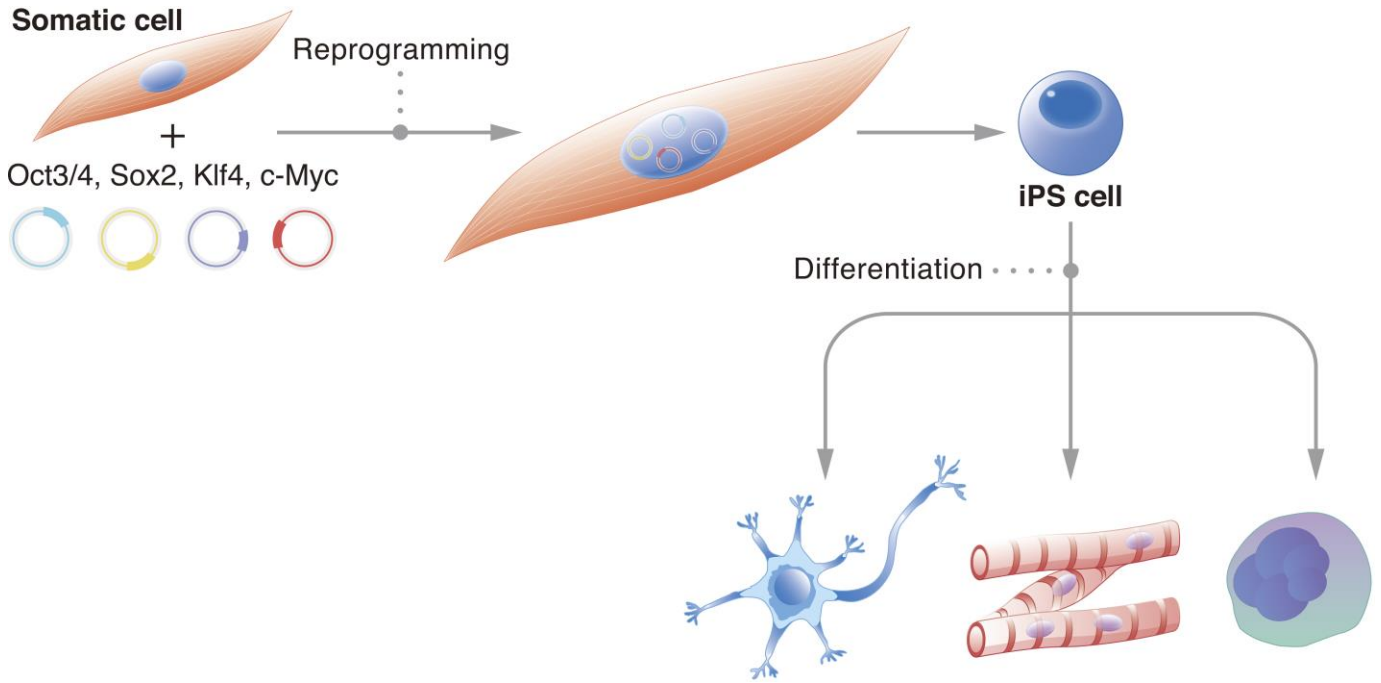
دکتر ابوالفضل برزگری

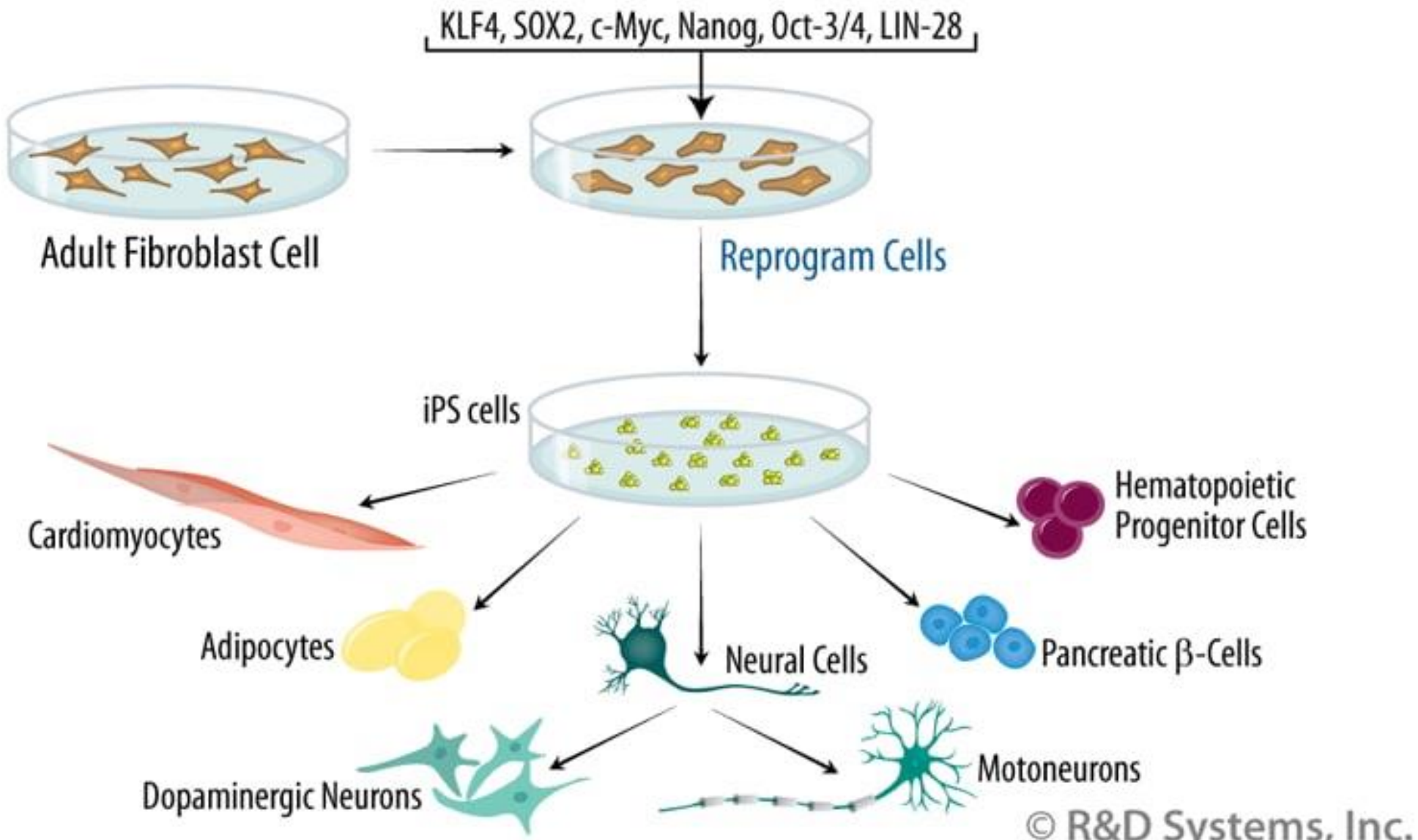
هیات علمی مرکزجامع سلو های بنیادی و پزشکی بازساختی

Regenerative medicine

- ✓Regenerative medicine is the branch of medicine that focused on developing and applying new treatments to heal tissues and organs and restore function lost due to aging, disease, damage or defects.
- ✓ *The human body has the natural ability to heal itself in many ways.*

Nobel Prize winner
Sir John Gurdon and
Shinya Yamanaka




KLF4, SOX2, c-Myc, Nanog, Oct-3/4, LIN-28
Adult Fibroblast Cell
Reprogram Cells
iPS cells
Cardiomyocytes
Hematopoietic
Progenitor Cells
Adipocytes
Neural Cells
Pancreatic β-Cells
Dopaminergic Neurons
Motoneurons
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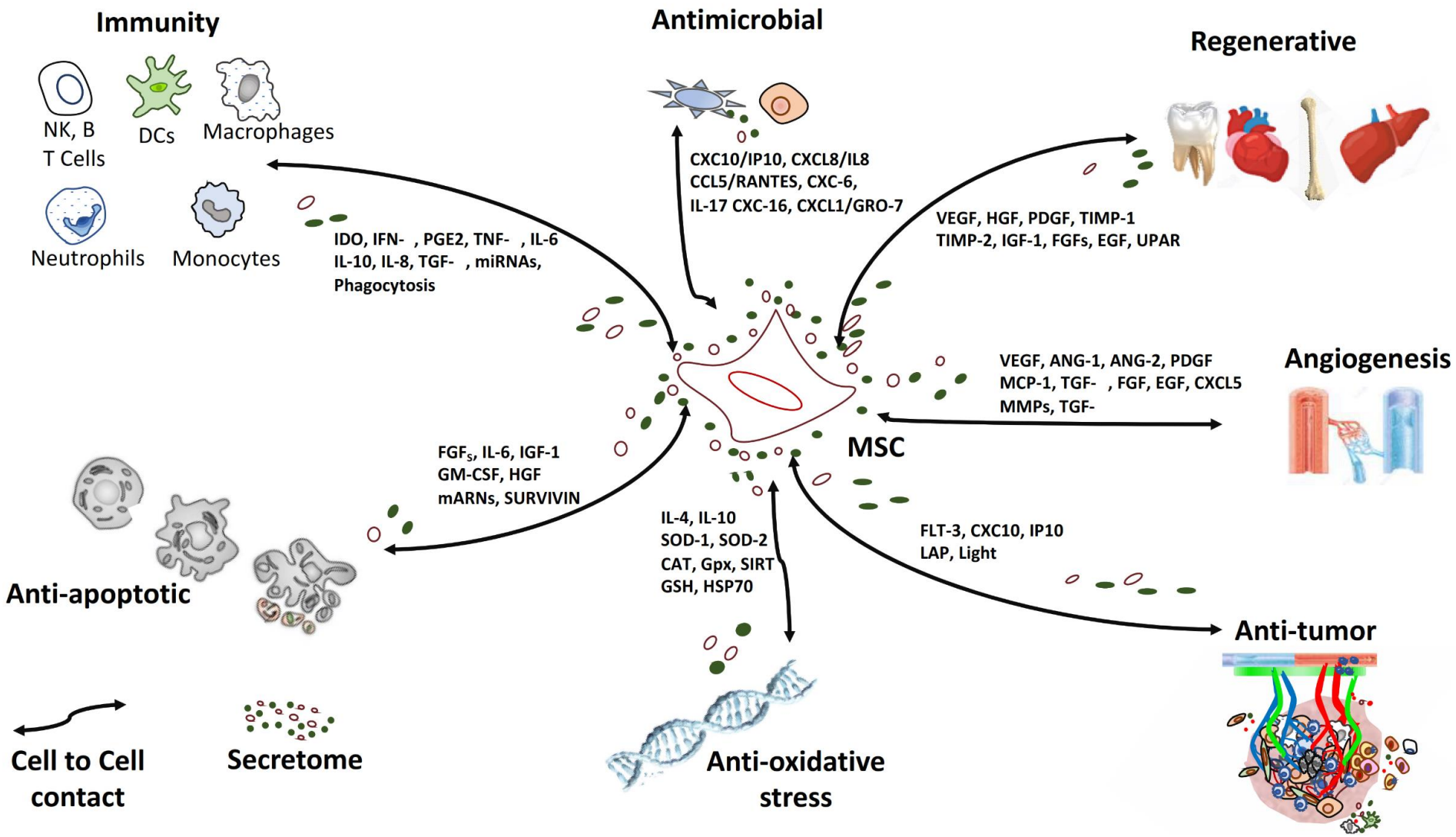
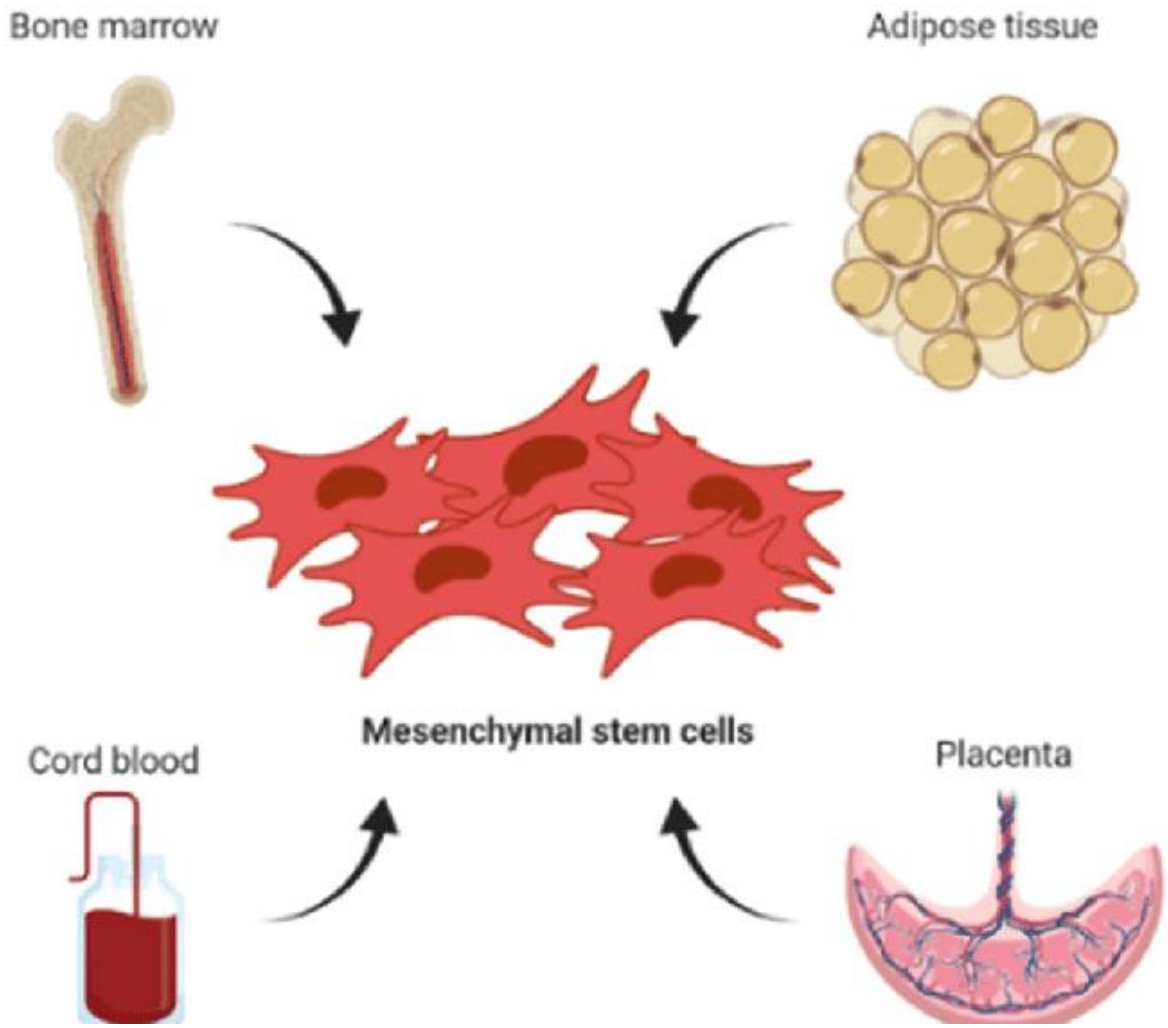
Mesenchymal Stem Cells as a Cornerstone in a Galaxy of Intercellular Signals: Basis for a New Era of Medicine

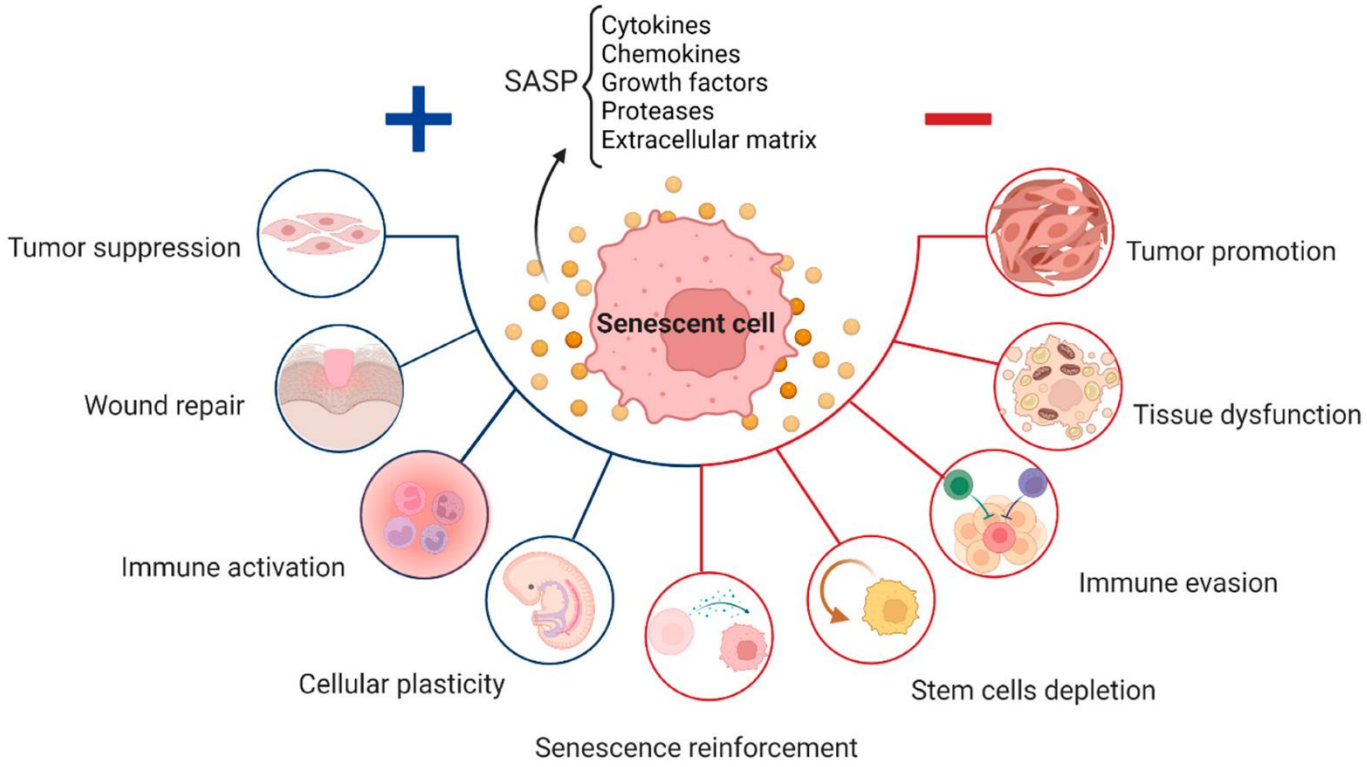


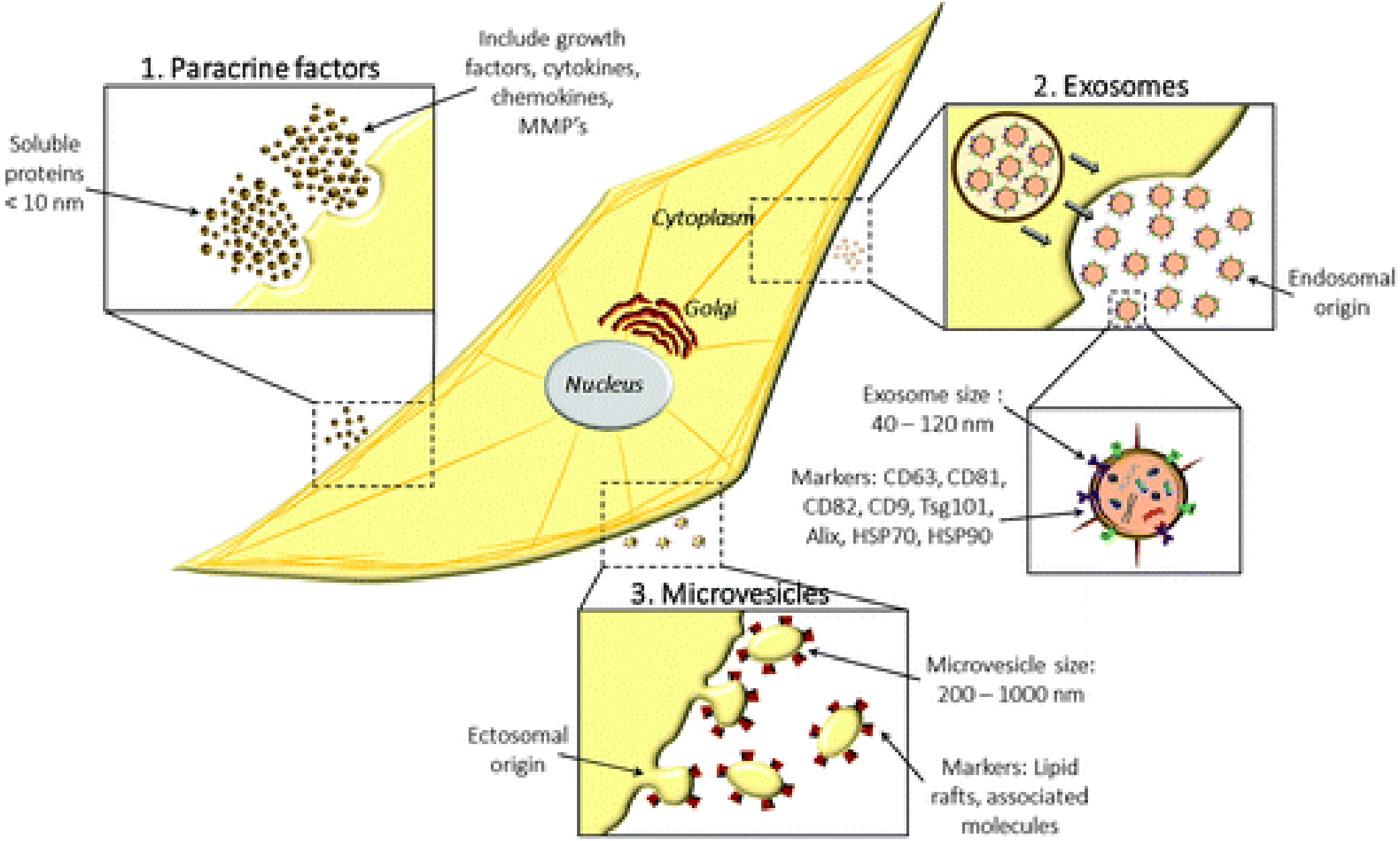
The main source of MSCs

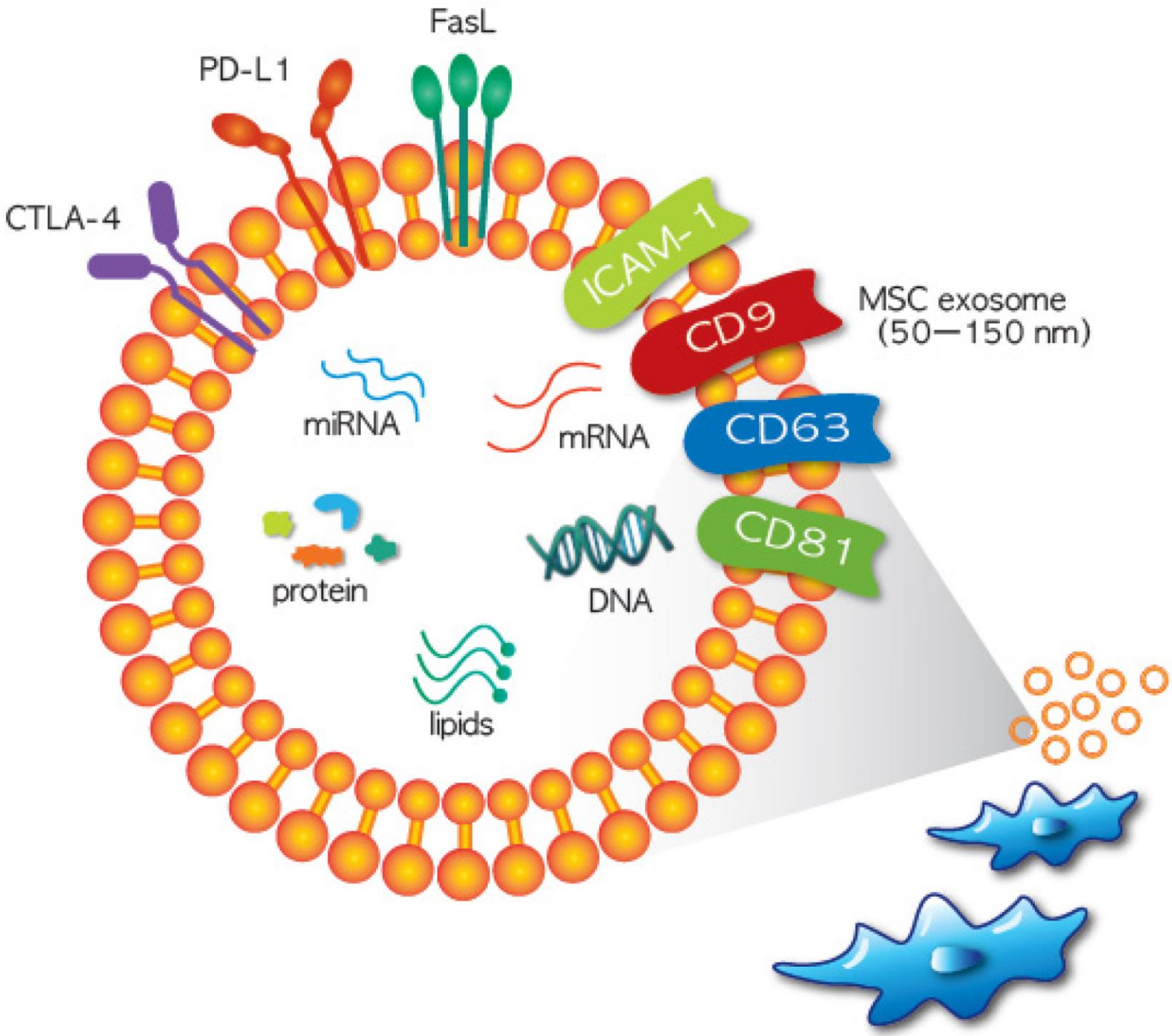


Senescence-associated secretory phenotype (SASP)
'senescence-messaging secretome' or SMS

I. Rapamycin and its analogs (so-called ‘rapalogs’) suppress the SASP by inhibiting mTOR and appear to extend healthspan.
II. The antidiabetic drug metformin, which, among other activities, inhibits the SASP, alleviates several age-related conditions and chronic dis




1. Paracrine factors
Include growth factors, cytokines, chemokines, MMP's
Soluble proteins < 10 nm
Cytoplasm
Golgi
Nucleus
2. Exosomes
Endosomal origin
Exosome size : 40 – 120 nm
Markers: CD63, CD81, CD82, CD9, Tsg101, Alix, HSP70, HSP90
3. Microvesicles
Microvesicle size: 200 – 1000 nm
Ectosomal origin
Markers: Lipid rafts, associated molecules



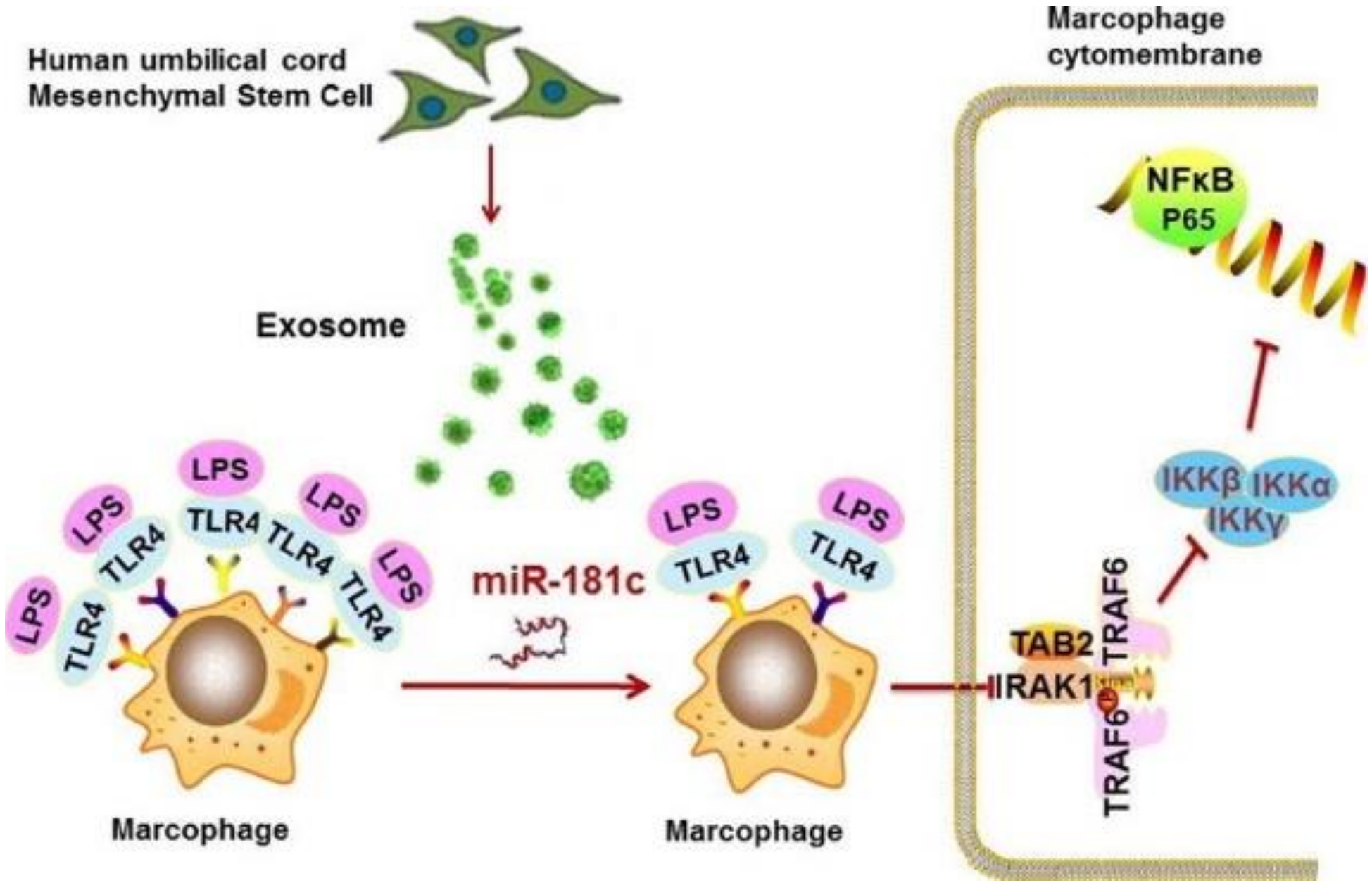
MSC Exosome Contents

Growth factors
Cytokines
Lipids
mRNAs
miRNAs
mtRNAs

Role of MSC Exosomes

Cell migration ↑
Matrix synthesis ↑
Anti-apoptosis ↑
Immunomodulation ↑

Inflammation ↓
Collagen deposition ↓

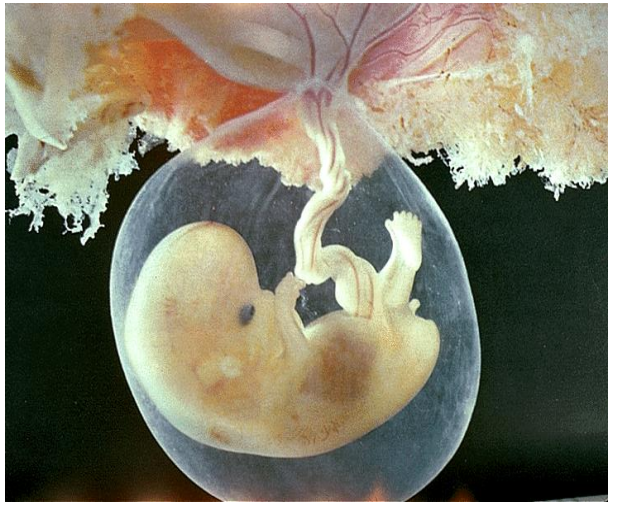

Human umbilical cord
Mesenchymal Stem Cell
Exosome
Marcophage
cytomembrane
NFκB
P65
IKKβ
IKKα
IKKγ
TRAF6
TAB2
IRAK1
TRAF6
LPS
TLR4
miR-181c
Marcophage
Marcophage

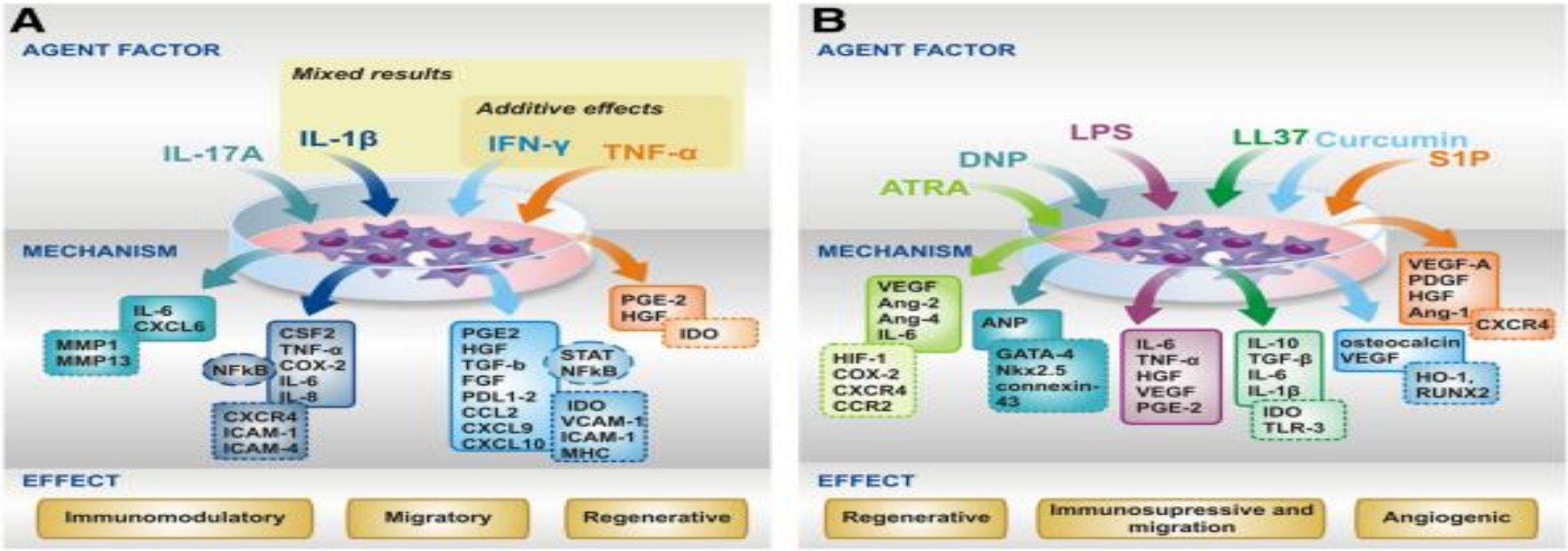
AMNIOTIC STEM CELL BANKS

- Biocell center, European biotechnology company is the first firm to harvest and preserve amniotic stem cells

- Biocell Center captures the stem cells from amniotic fluid if the family requests and pays for the preservation of the stem cells

- Amniotic fluid withdrawn during amniocentesis is sent to the Biocell Center laboratory. The stem cells are frozen in liquid nitrogen and preserved in the company's state-of-the-art cryo-bank.




A
AGENT FACTOR
Mixed results
Additive effects
IL-17A
IL-1β
IFN-γ
TNF-α
MECHANISM
IL-6
CXCL6
MMP1
MMP13
NFkB
CSF2
TNF-α
COX-2
IL-6
IL-8
CXCR4
ICAM-1
ICAM-4
PGE2
HGF
TGF-b
FGF
PDL1-2
CCL2
CXCL9
CXCL10
STAT
NFkB
IDO
VCAM-1
ICAM-1
MHC
PGE-2
HGF
IDO
EFFECT
Immunomodulatory
Migratory
Regenerative
B
AGENT FACTOR
LPS
LL37
Curcumin
S1P
DNP
ATRA
MECHANISM
VEGF
Ang-2
Ang-4
IL-6
HIF-1
COX-2
CXCR4
CCR2
ANP
GATA-4
Nkx2.5
connexin-43
IL-6
TNF-α
HGF
VEGF
PGE-2
IL-10
TGF-β
IL-6
IL-1β
IDO
TLR-3
osteocalcin
VEGF
HO-1,
RUNX2
VEGF-A
PDGF
HGF
Ang-1
CXCR4
EFFECT
Regenerative
Immunosupressive and migration
Angiogenic
C
AGENT FACTOR
Hypoxia
MECHANISM
HGH
VEGF
HGF
HIF1-α
stabilization
GLUT1-2-3
LDHA
ICAM
CXCR3
CXCR7
CXCR4
GSH
SOD
NOTCH
pAKT
BAD
BCL-XL
BAG-1
EFFECT
Angiogenic
Survival and engraftment
Anti-apoptotic
D
AGENT FACTOR
3D Culture
MECHANISM
FGF-2
HGF
Ang
TGF-ß1
PGE-2
HGH
TSG-6
STC-1
IL-1
IL-6
IL-8
CCL2
CCL7
Oct-4
SOX2
Nanog
CXCR-4
EFFECT
Angiogenic
Immunomodulatory
Increase stemness

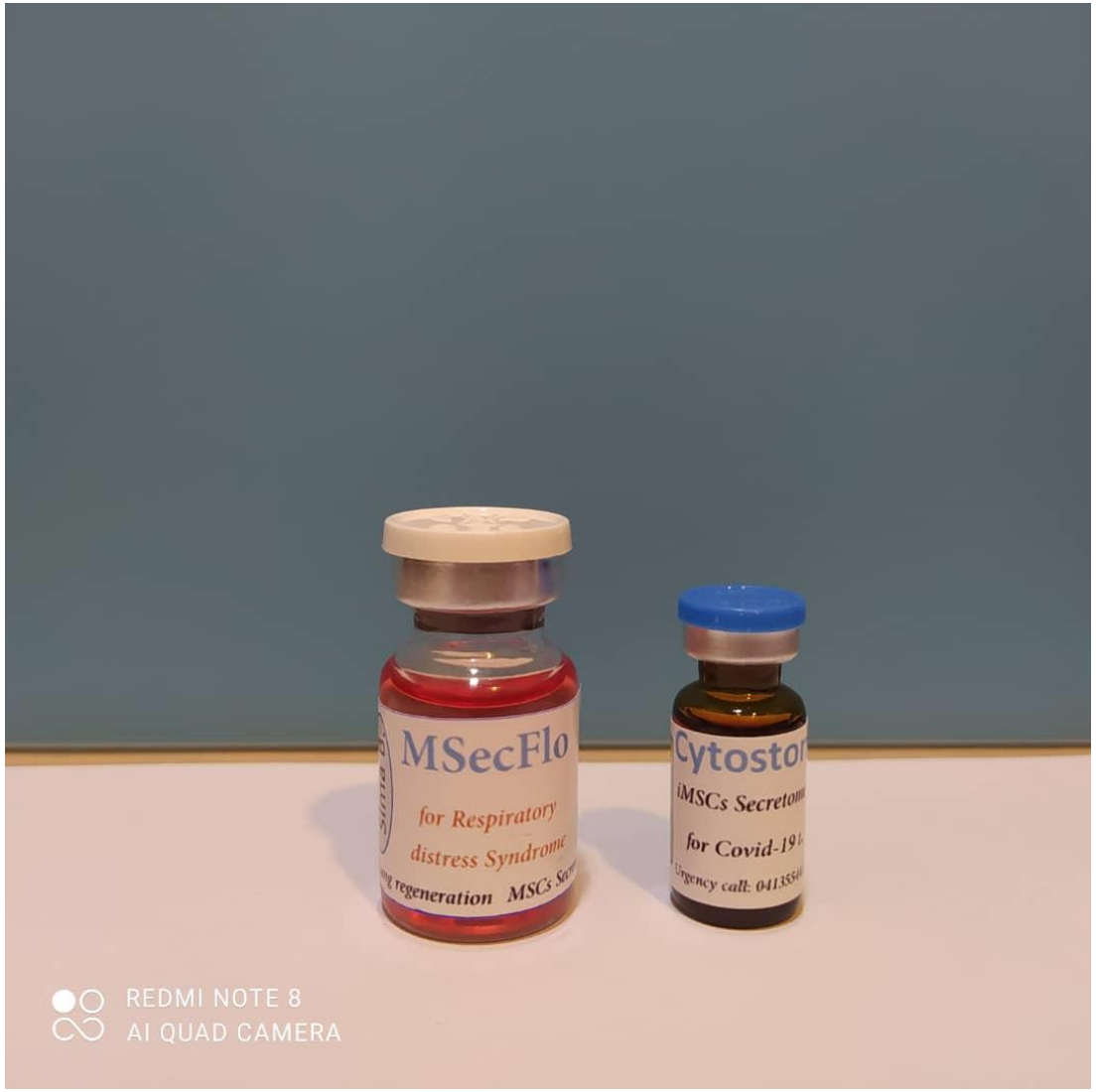
Although MSC-secretome efficacy has been widely established in numerous preclinical models, the development of large-scale GMP-grade secretome-based pharmaceuticals is still missing.

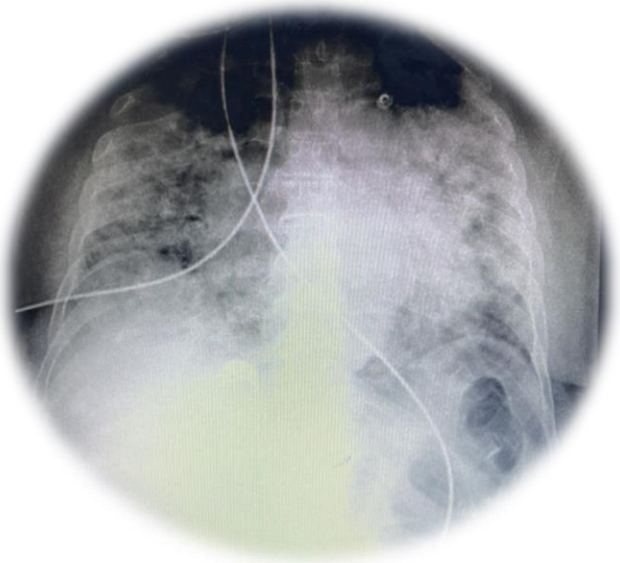
The use of **MSC-secretome** as a cell-free therapy is being studied in a number of disorders

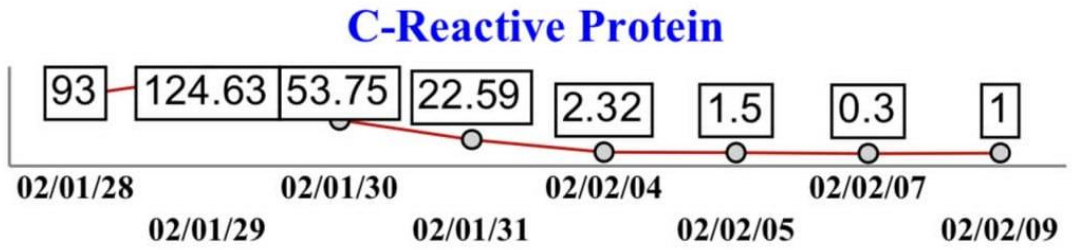
- It is also important to establish the optimal milking timing, transport, storage, and delivery protocols of MSC secretion as MSC secretome is a highly dynamic product .
- Furthermore, dosage amount, the optimum volume of injection, the route of administration (intramuscular, intravenous, or subcutaneous, etc.), and administration frequency are unknown for the different diseases.
- An experimental good manufacturing protocol (GMP) was planned to transform MSC-secretome/lysate into a pharmaceutical product, combining freeze-drying and ultrafiltration procedures

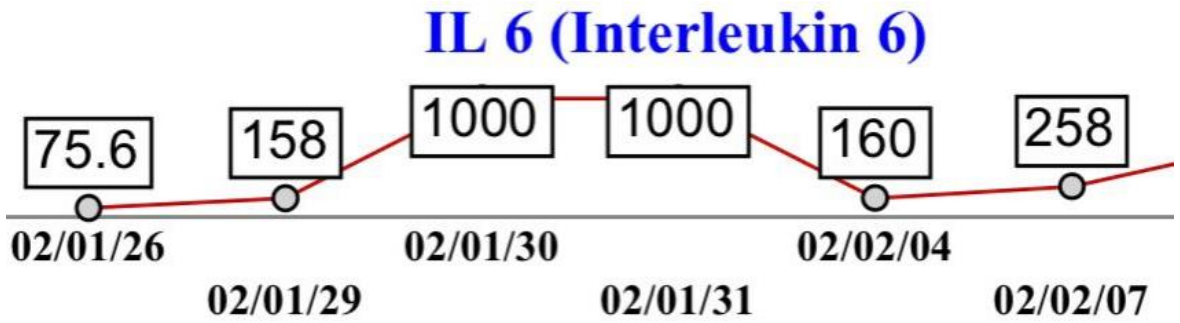
Mesenchymal stem cell-based therapy for burn wound

Immunomodulatory, anti-inflammatory, and regenerative properties of MSCs' Secretome

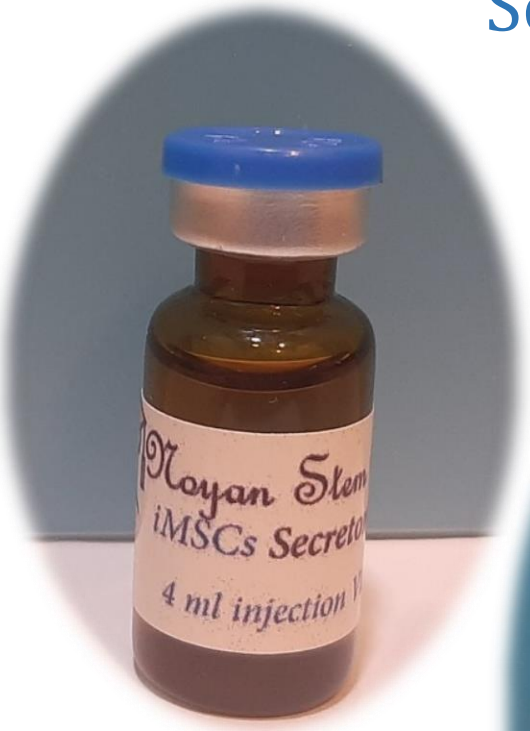


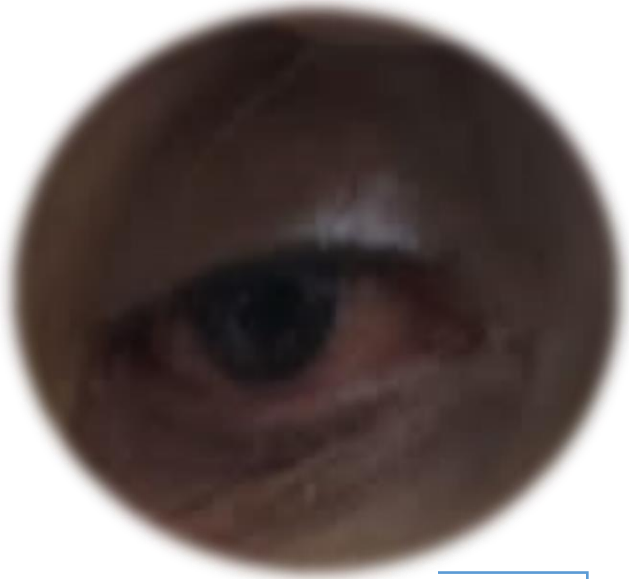



C-Reactive Protein
93
124.63
53.75
22.59
2.32
1.5
0.3
1
02/01/28
02/01/29
02/01/30
02/01/31
02/02/04
02/02/05
02/02/07
02/02/09


IL 6 (Interleukin 6)
75.6
158
1000
1000
160
258
02/01/26
02/01/29
02/01/30
02/01/31
02/02/04
02/02/07

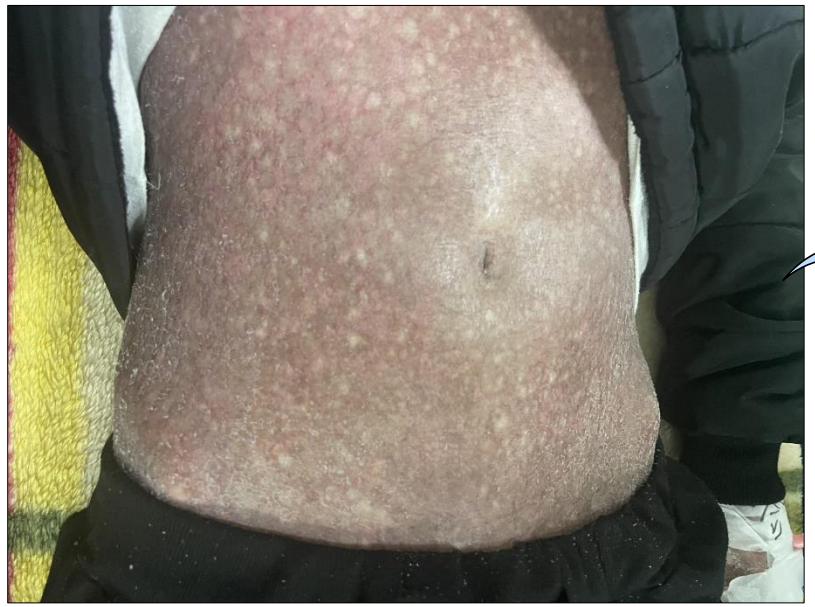
The **immunosuppressive and regeneration activity** of Secretome in graft versus host disease (GvHD)

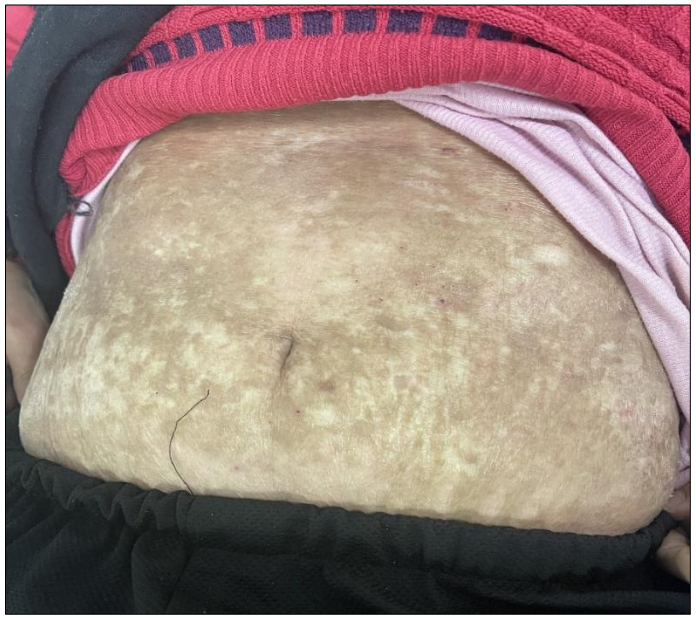


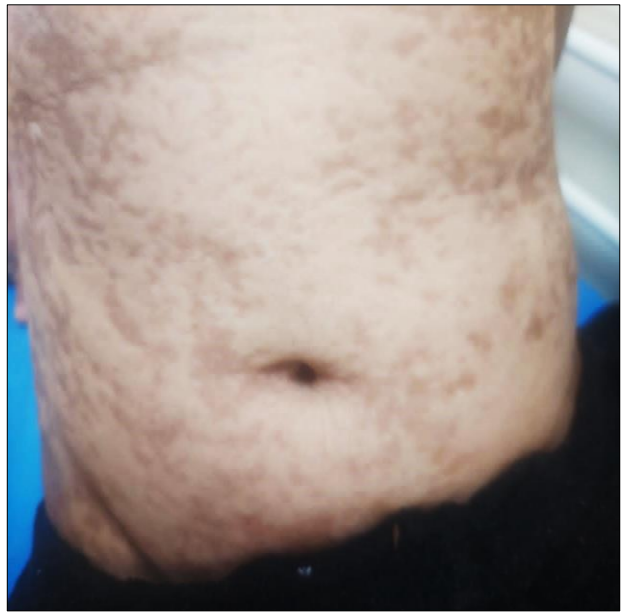


Before

After








Custom

Thanks for Your Attention

"We can't solve problems by using the same kind of thinking we used when we created them."
Albert Einstein