

Clinical use of Exosomes

Edward Park, MD, MPH

Integrative Healthcare
Symposium 2024

Name that movie...



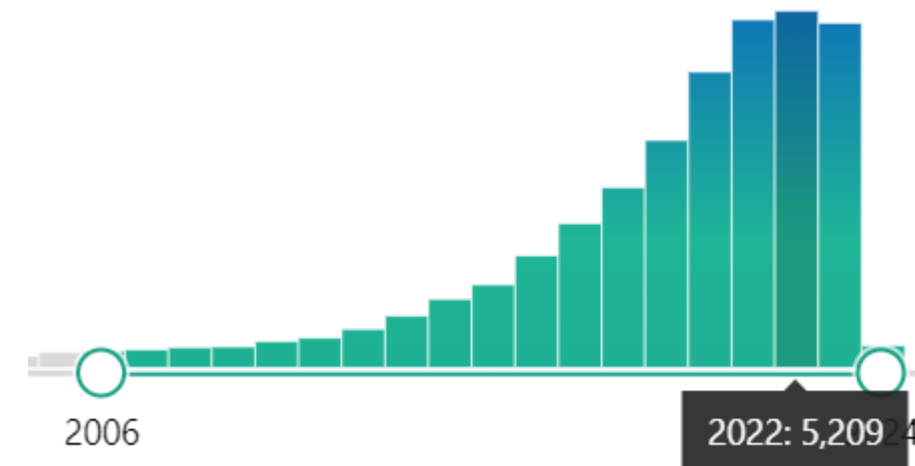
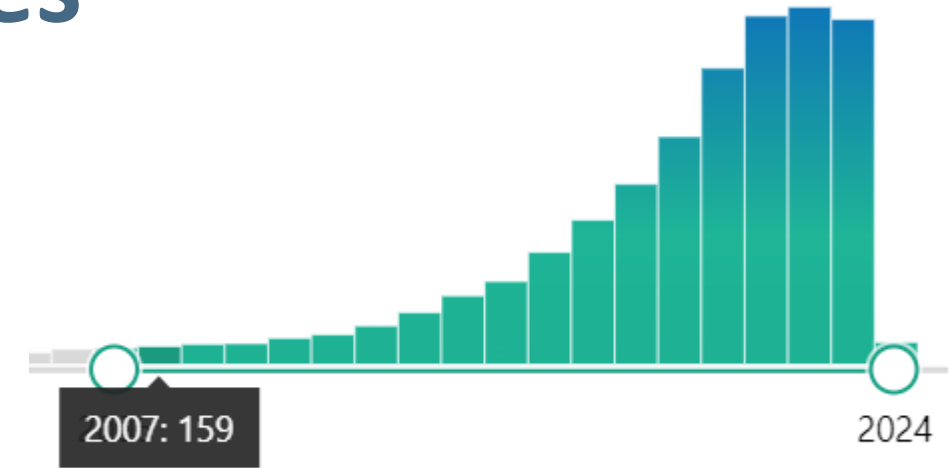


Disclosures

- Spoke once for Kimera Labs at a SCN (stem cell mtg 2022)
- Distributor for Kimera Labs exosomes (non-exclusive)
- Have a provider online training course for using exosomes
- I wrote a book about exosomes

Learning Objectives

- Compare the distinctions between exosomes and stem cells
- Assess the benefits of MSC exosomes
- Determine methods to learn more about exosome use

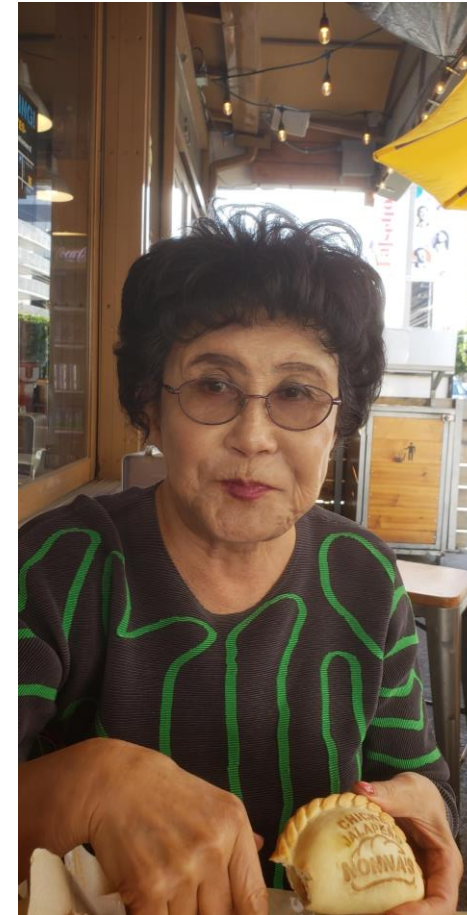


What song do you hear? (Gen X: 1965-80)

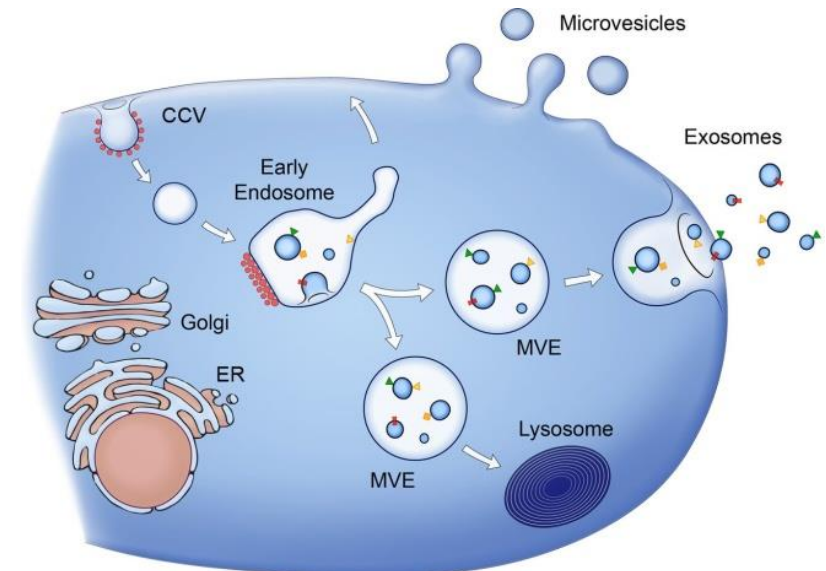
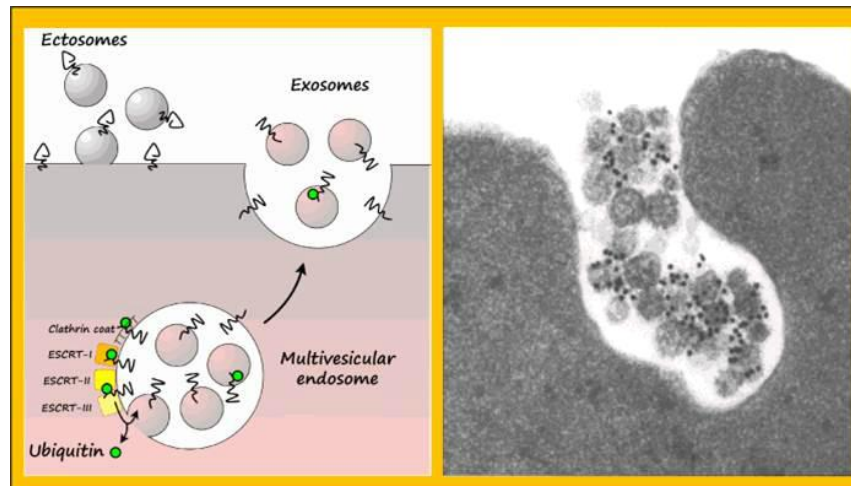
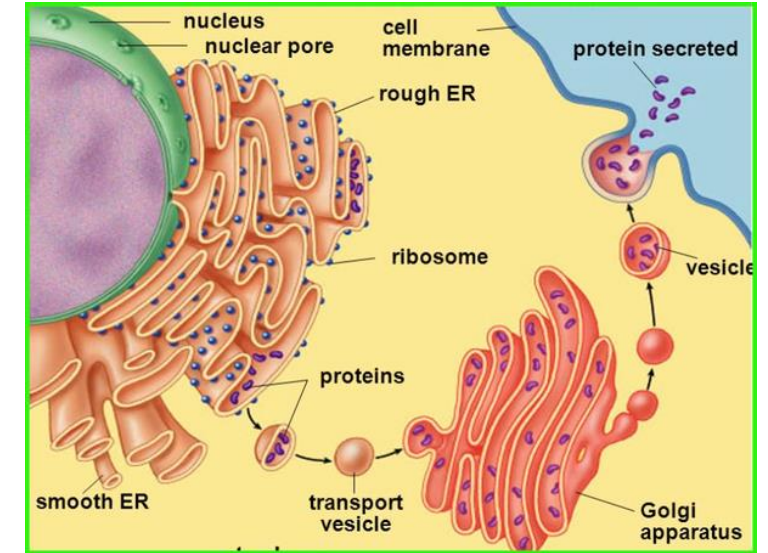
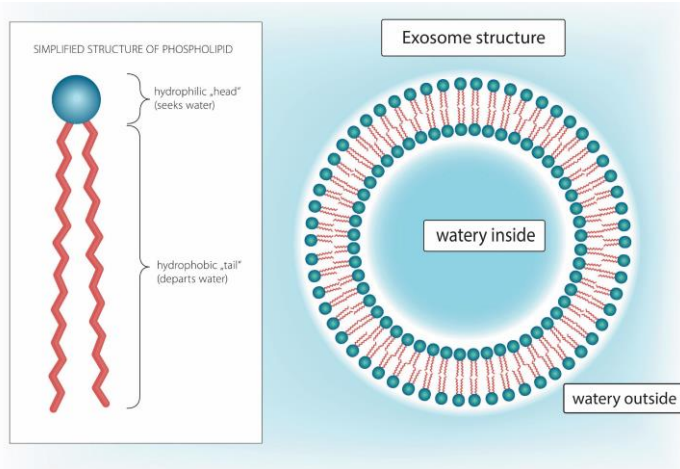


Who am I?

- Harvard (BA/residency) and Columbia (MD/MPH)
- In 12/2018, I attended a lecture from an MD/patient
- ~2,000 treatments, 800 encounters, 400 patients – CA, HI, TX, FL, NY
- Speaker and author
- Online 12hr education course for providers

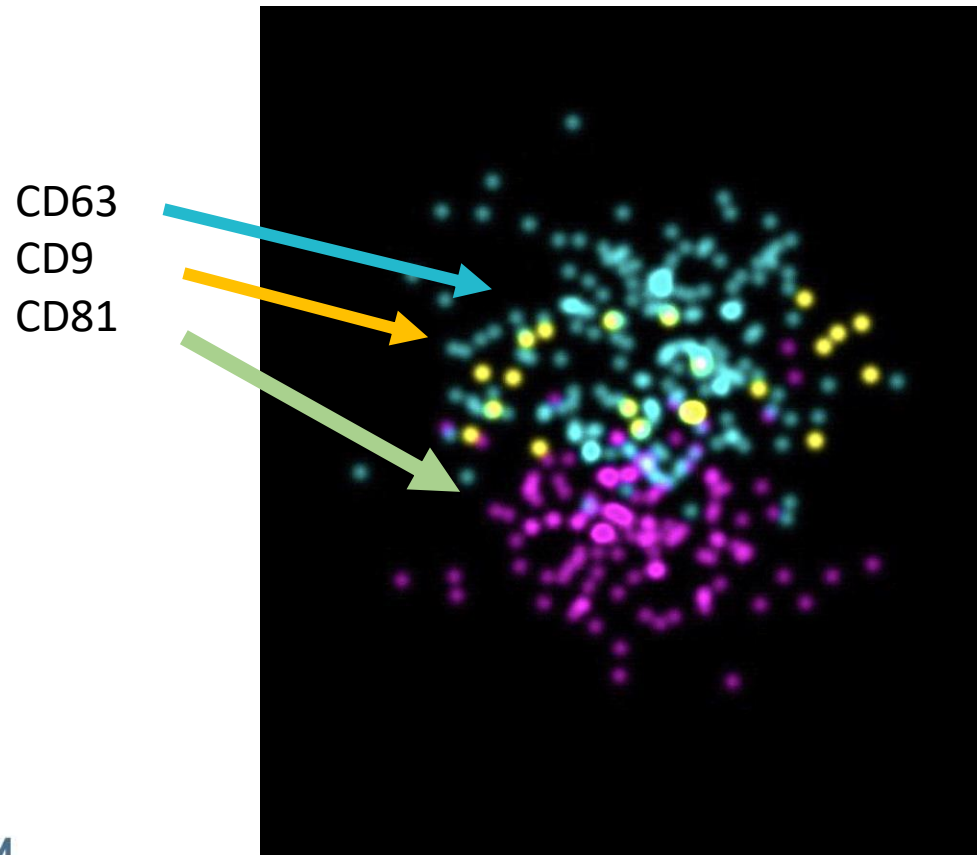


What is an exosome?





Why are there exosomes?



Proteins (gas)

miRNA (brakes)

mRNA (clutch)

Primary means of cell
communication

They are songs...notes,
motifs, harmonies



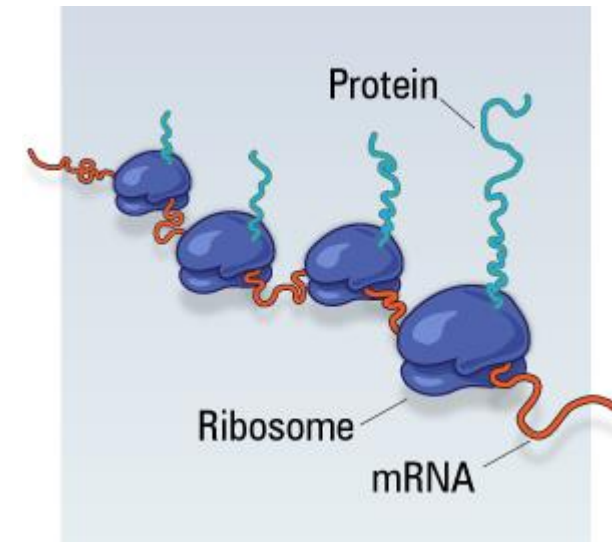
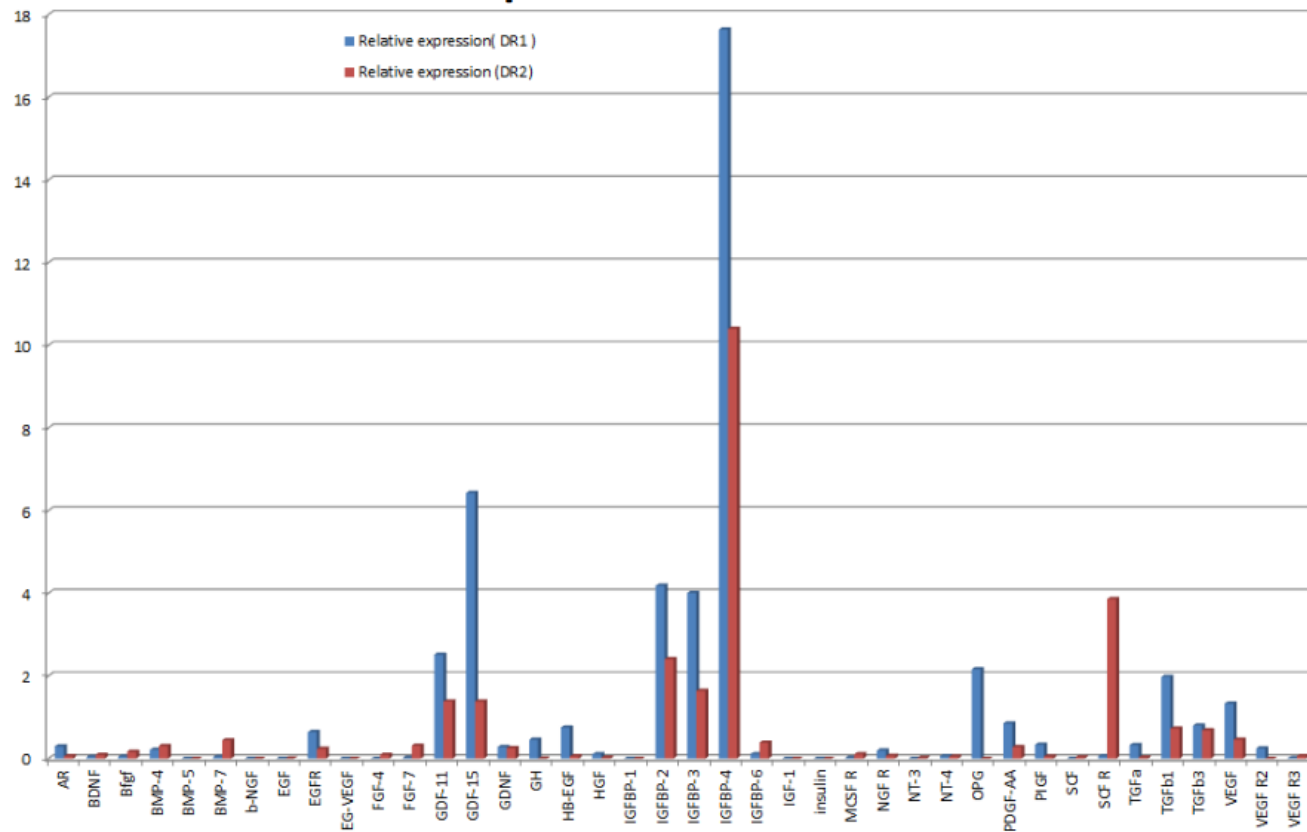
Proteomics

(pg/ml)	2017-006-0045	Amnio 20284	Red 5 ml
AR	0.0	23.2	16.0
BDNF	6.0	34.0	0.4
bFGF	8.3	5.6	4.2
BMP-4	0.0	0.0	0.0
BMP-5	0.0	847.7	3,763.5
BMP-7	0.0	527.7	0.0
b-NGF	0.0	0.0	0.0
EGF	269.3	53.0	3.8
EGF R	798.4	824.8	55.4
EG-VEGF	85.1	1,421.5	0.0
FGF-4	0.0	0.0	0.0
FGF-7	0.0	9.9	15.8
GDF-15	607.5	2,642.2	5,801.1
GDNF	2.3	8.3	14.1
GH	16.9	128.0	204.1
HB-EGF	0.0	0.0	0.0
HGF	1,923.0	3,015.6	161.7
IGFBP-1	734.5	16,644.0	178.9
IGFBP-2	88.7	5,898.7	1,751.1
IGFBP-3	14,599.9	227,006.2	5,444.5
IGFBP-4	0.0	13,579.5	0.0
IGFBP-6	0.0	80,901.4	267.6
IGF-1	0.0	0.0	0.0
Insulin	0.0	370.1	493.1
MCSF R	0.0	9,933.3	24.2
NGF R	0.0	110.4	3.2
NT-3	0.0	0.0	4.5
NT-4	0.0	0.0	0.0
OPG	0.0	43.9	6,817.7
PDGF-AA	45.9	440.7	36.4
PIGF	25.2	13.3	72.9
SCF	13.3	9.7	120.0
SCF R	0.0	342.4	14.2
TGFa	12.7	0.0	0.0
TGFb1	0.0	941.7	0.0
TGFb3	0.0	0.0	340.5
VEGF	58.1	5.1	182.8
VEGF R2	0.0	33.1	0.0
VEGF R3	0.0	23.2	13.6
VEGF-D	0.0	0.0	0.0



RNAomics

Relative expression of mRNA to HPRT



all known physics

$$\Psi = \int e^{\frac{i}{\hbar} \int (\frac{R}{16\pi G} - F^2 + \bar{\psi} i \not{D} \psi - \lambda \varphi \bar{\psi} \psi + |D\varphi|^2 - V(\varphi))}$$

Schrodinger
 Feynman
 Einstein
 Maxwell-Yang-Mills
 Yukawa
 Dirac
 Higgs
 Newton
 Planck

What does Captain Renault say?

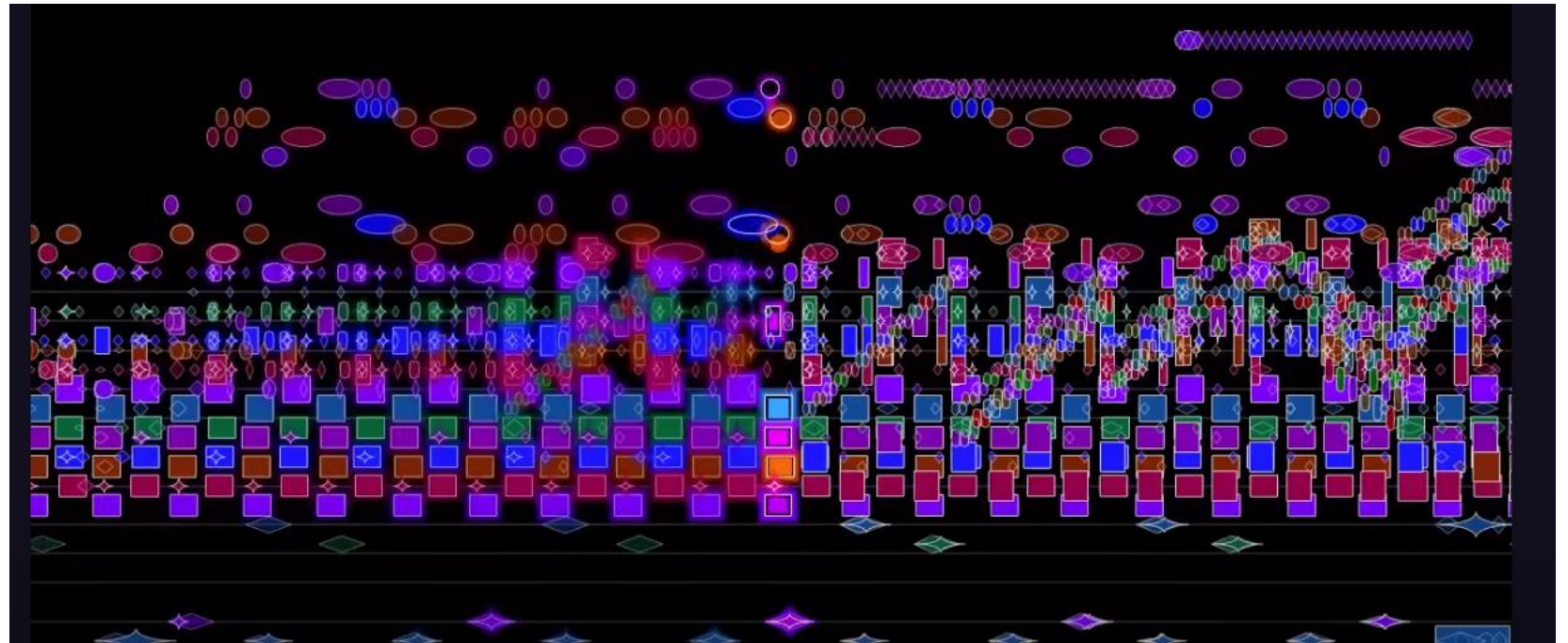




- miRNA-34a and miRNA-146a: convert M1 inflammatory macrophages to M2 regenerative type
- miRNA-100 – inhibits immune cells from attaching to blood vessels
- VEGF (vascular endothelial growth factor) – promotes new blood vessel growth
- IGFBP/types 1,2,3,5 (insulin-like growth factor binding proteins) – carries and potentiates actions of IGF (insulin-like growth factor)
- GDF11- (growth differentiation factor) enhances stem cell DNA repair
- GDF15- decreases inflammation, influences apoptosis and cell growth and repair
- TIMP1&2 (tissue inhibitor of metalloproteinase) – helps limit tissue destruction
- SCF – (stem cell factor) – increases survival of blood-producing stem cells
- GM-CSF (granulocyte-macrophage colony-stimulating factor)
- BMP-5 (bone morphogenetic protein 5) – induces bone and cartilage growth
- GH (growth hormone) – stimulates cell growth and reproduction
- HGF (hepatocyte growth factor) – promotion of epithelial cell replication and migration for new vessels and tissue regeneration
- OPG (osteoprotegerin) – inhibits the cells which normally absorb bone



Where and when do exosomes work?



“Rite of Spring” by Igor Stravinsky (per Stephen Malinowski)

Where and when do exosomes work?

The role of exosomes in hepatitis, liver cirrhosis and hepatocellular carcinoma

Jiliang Shen ¹, Chiung-Kuei Huang ², Hong Yu ¹, Bo Shen ¹, Yaping Zhang ³, Yuelong Liang ¹, Zheyong Li ¹, Xu Feng ¹, Jie Zhao ¹, Lian Duan ¹, Xiujuan Cai ¹

Affiliations + expand

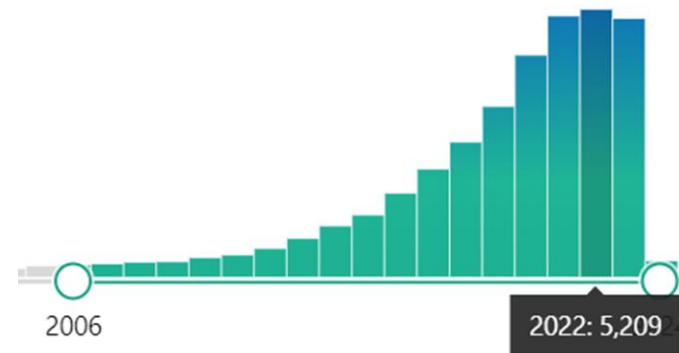
PMID: 28224705 PMCID: PMC5387156 DOI: 10.1111/jcmm.12950

[Free PMC article](#)

MicroRNA expression profile of urinary exosomes in Type IV lupus nephritis complicated by cellular crescent

Yi Li, Xiaosong Xu, Xiaopeng Tang, Xiuwu Bian, Bingbing Shen, Hongwen Zhao, Shiyuan Luo, Zhiwen Chen & Kegin Zhang

Journal of Biological Research-Thessaloniki 25, Article number: 16 (2018) | [Cite this article](#)



Name that movie...



23 years of aging

22 YRS OF AGING ON
TELOMERASE ACTIVATORS!

Scan QR for my contact info and
to download all my Exosome
Educational information



2000 (Ages 1 & 33)



2010 (Ages 43 & 10)



2016 (Ages 13, 17 & 49)

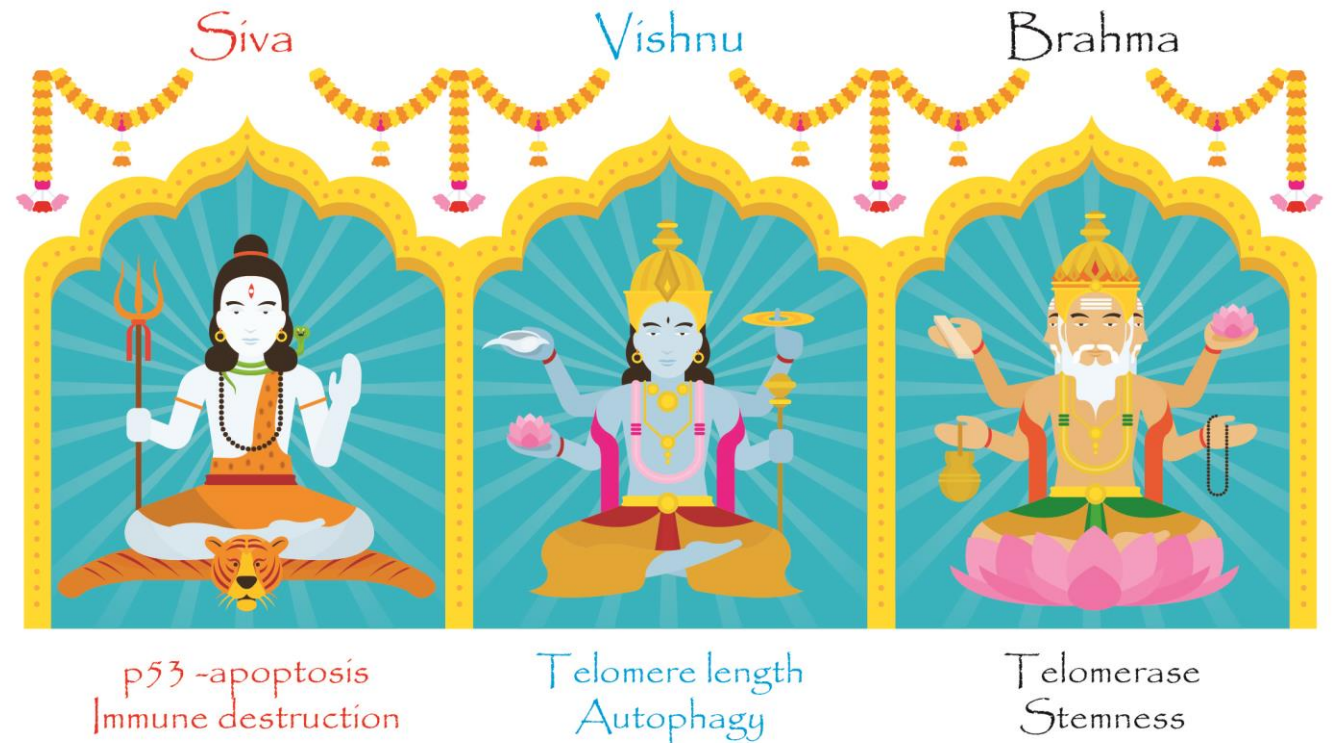


2022 (Ages 23 & 85)



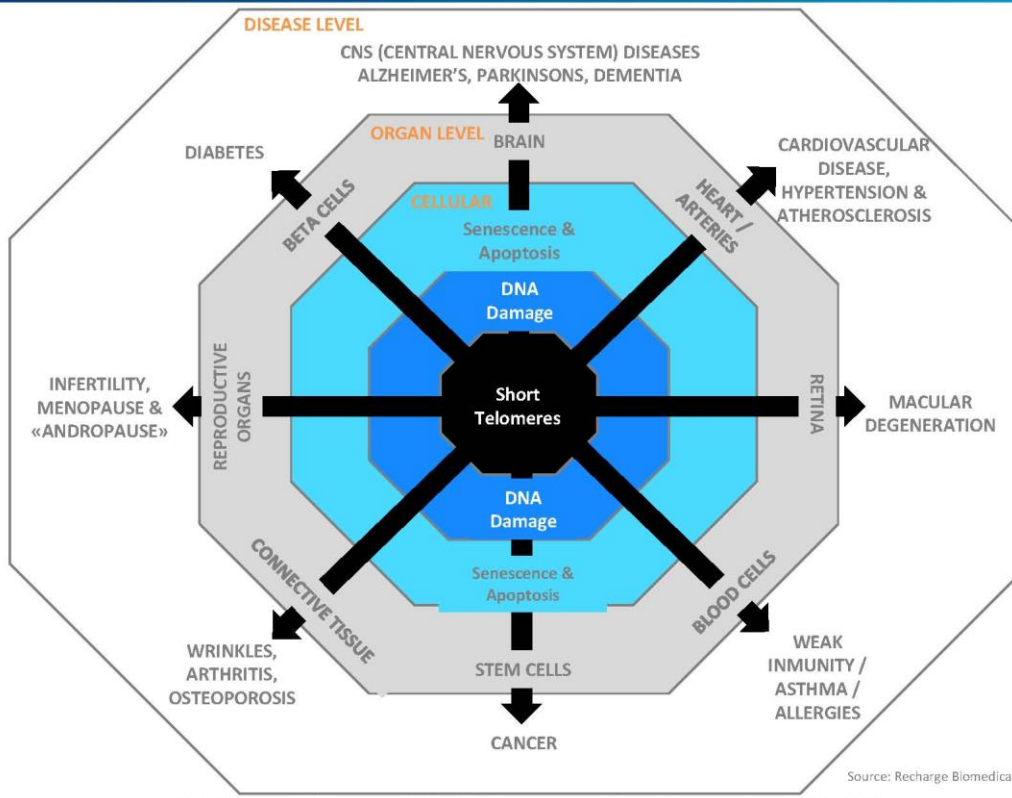
2022 (Ages 19, 23 & 55)

What is aging?



Stem cell depletion and dysfunction

Short telomeres play a central role in the development of age-related diseases



Source: Recharge Biomedical Clinic & DR. Ed Park

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Page 1

Some local stem cells that should be copying are making error-ridden copies or unable to copy at all (tendinitis and OA of knees)

One disease, many faces

All around body, genes are silenced in cells, leading to "senescence" and poor cellular milieu

Depletion, Dysfunction, Inflammation



Disclaimer

- The use of MSC exosomes has not been approved by the FDA for the treatment or prevention of any disease. (Covid-19 mRNA)
- The clinical practice of medicine involves autonomy, informed consent, and critical thinking





Real world applications

- Local regeneration of depleted/damaged stem cell niches with high therapeutic index
- “Osis” is simply depleted stem cell niches arthroses (cartilage), tendinosis (muscle), osteoporosis (bone)
- Vasculogenesis

➤ [Am J Respir Crit Care Med](#). 2018 Jan 1;197(1):104-116. doi: 10.1164/rccm.201705-0925OC.

Mesenchymal Stromal Cell Exosomes Ameliorate Experimental Bronchopulmonary Dysplasia and Restore Lung Function through Macrophage Immunomodulation

Gareth R Willis^{1 2}, Angeles Fernandez-Gonzalez^{1 2}, Jamie Anastas^{1 3}, Sally H Vitali^{4 2}, Xianlan Liu¹, Maria Ericsson³, April Kwong¹, S Alex Mitsialis^{1 2}, Stella Kourembanas^{1 2}

Affiliations + expand

PMID: 28853608 PMCID: [PMC5765387](#) DOI: [10.1164/rccm.201705-0925OC](#)

[Free PMC article](#)



Long Covid

- **Anti-inflammatory action in organs and vessels**
- **Stem cell dedifferentiation and copying**
- **New vessel creation**
- **Empiric success**

PERSPECTIVE article

Front. Nanotechnol., 04 October 2022

Sec. Biomedical Nanotechnology

Volume 4 - 2022 | <https://doi.org/10.3389/fnano.2022.987117>

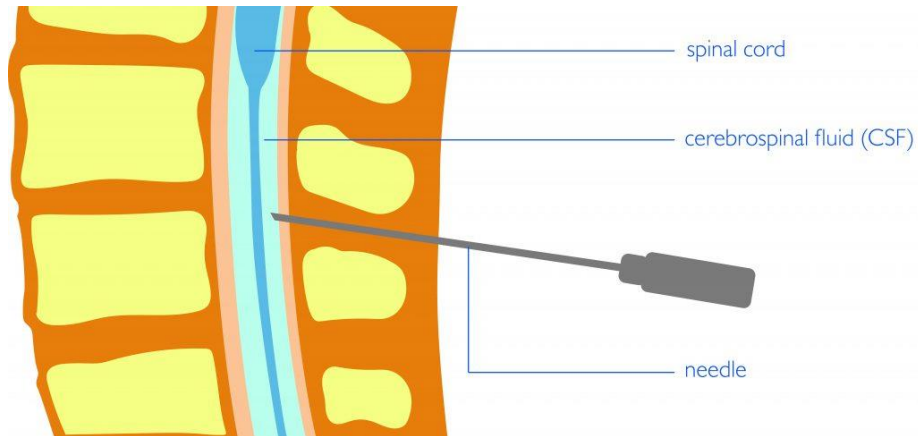
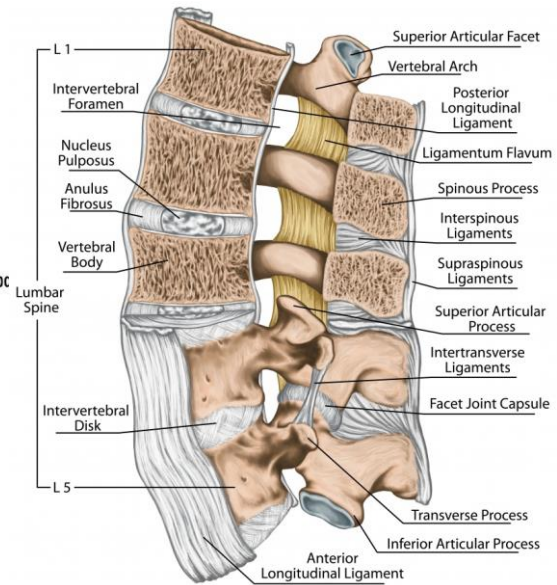
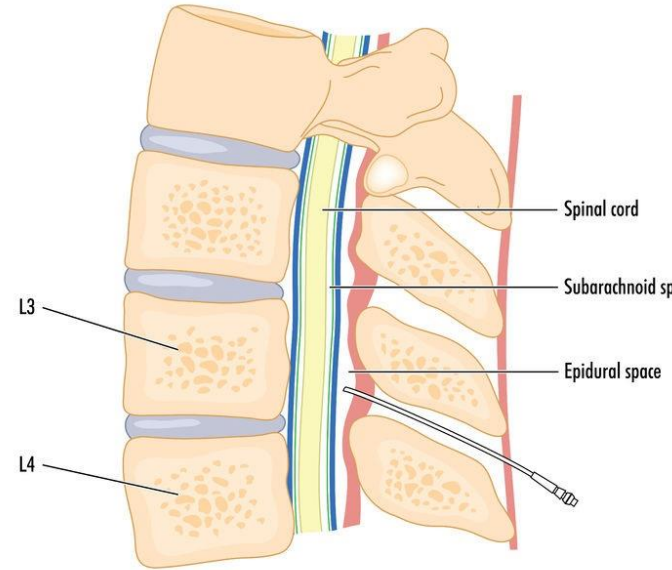
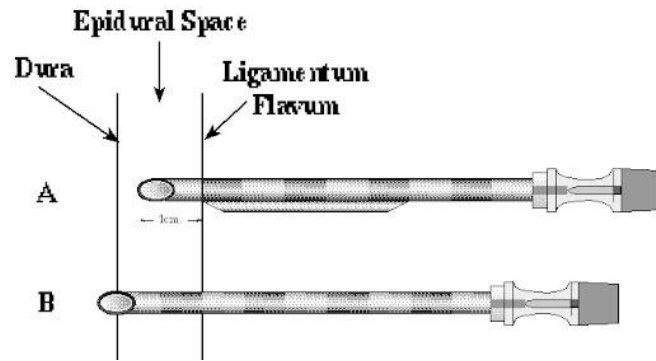
Recommendation: Treatment of clinical long COVID encephalopathies with nasal administered mesenchymal stromal cell extracellular vesicles



Philip W. Askenase*

Section of Rheumatology, Allergy and Clinical Immunology, Department of Internal Medicine, Yale University School of Medicine, New Haven, CT, United States

Back Pain

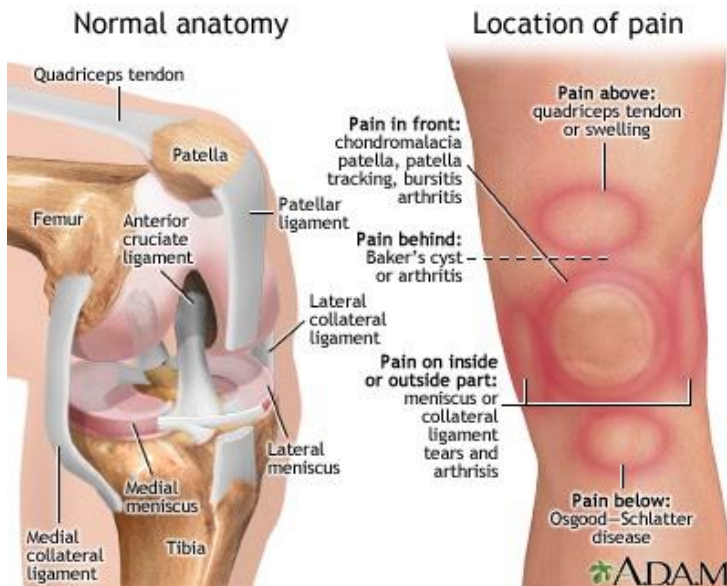


FDA issues “black box warning” for epidural steroid spinal injections

The U.S. Food and Drug Administration (FDA) is warning that injection of corticosteroids into the epidural space of the spine may result in rare but serious adverse events, including loss of vision, stroke, paralysis, and death...

Knees

- In 15%, the bursa doesn't communicate with the knee joint

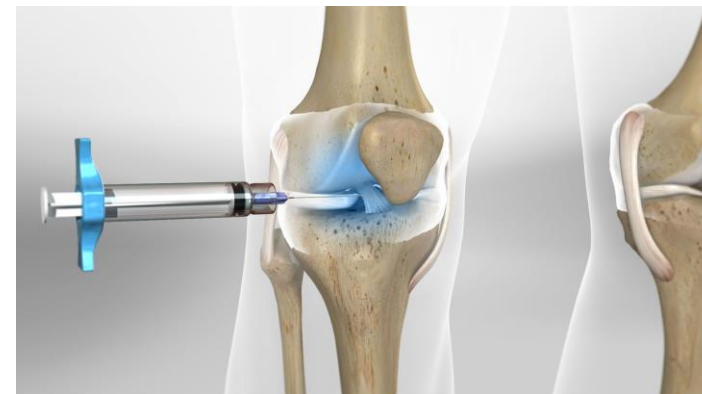


MSC exosome as a cell-free MSC therapy for cartilage regeneration: Implications for osteoarthritis treatment

Wei Seong Toh ¹, Ruenn Chai Lai ², James Hoi Po Hui ³, Sai Kiang Lim ⁴

Affiliations + expand

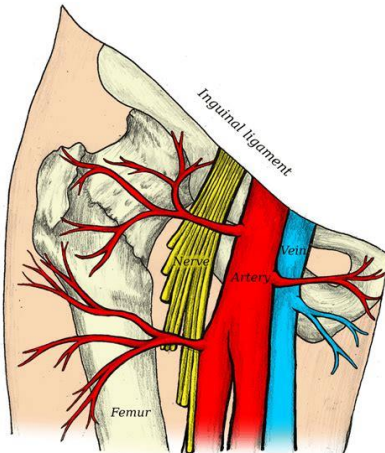
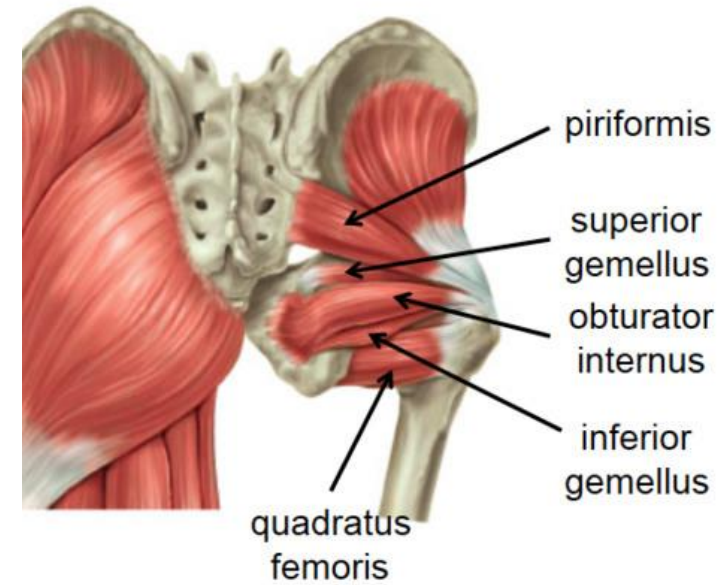
PMID: 27674002 DOI: 10.1016/j.semcdb.2016.11.008





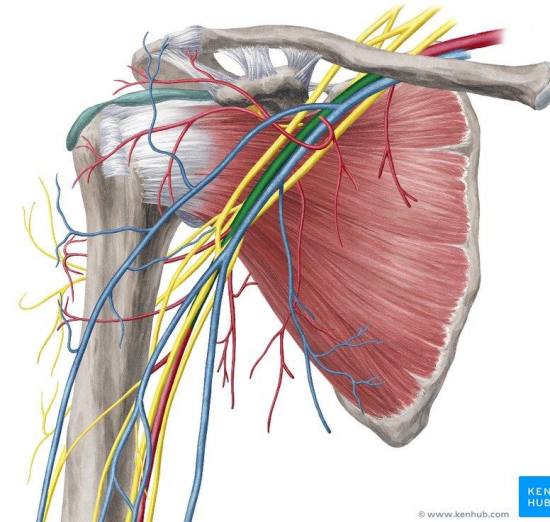
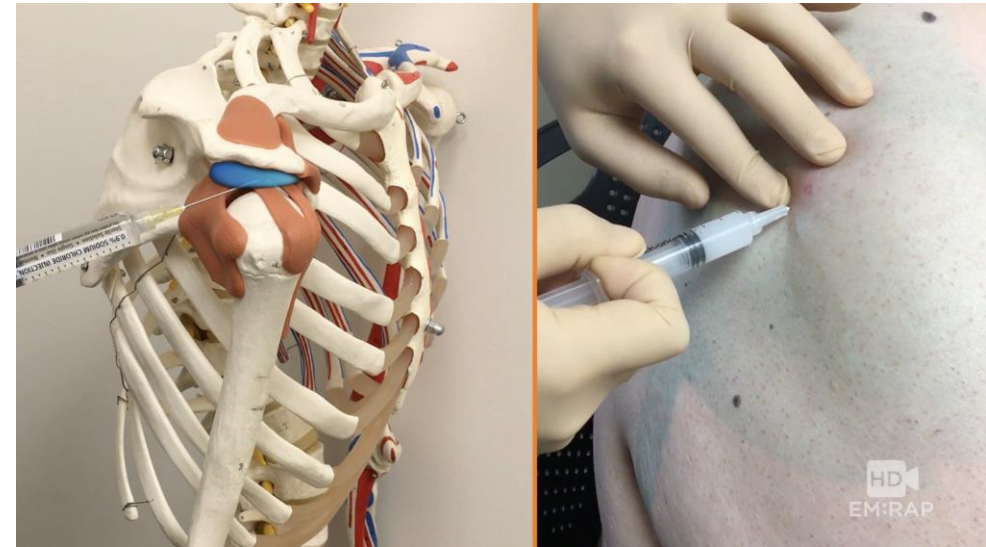
Hips

- For the joint, U/S is needed
- “bursitis”

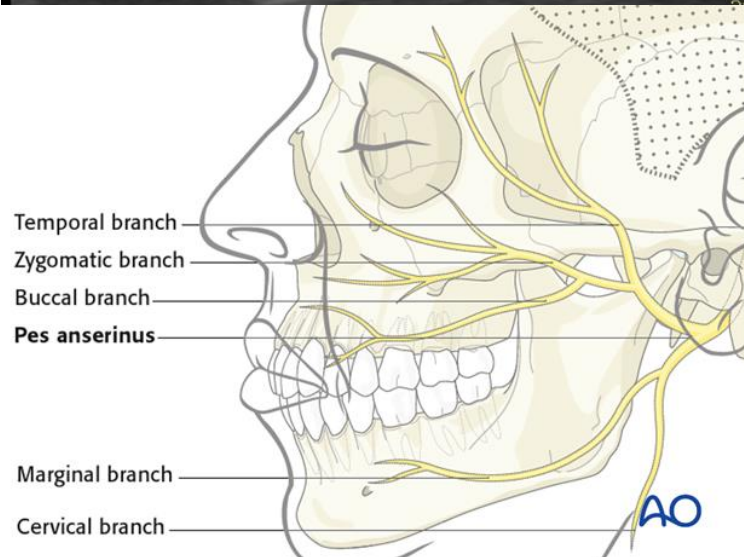


Shoulders

- Most common is the rotator cuff injected at SAB
- Slight pain touching bone
- Little risk from post approach



Nerves and Arteries



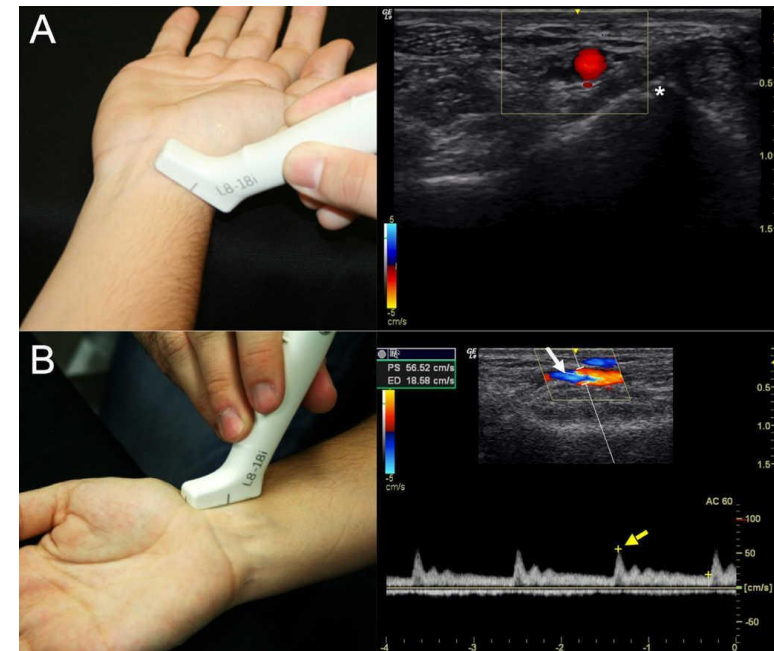
[Neural Regen Res.](#) 2015 May; 10(5): 743–747.

doi: [10.4103/1673-5374.156968](#)

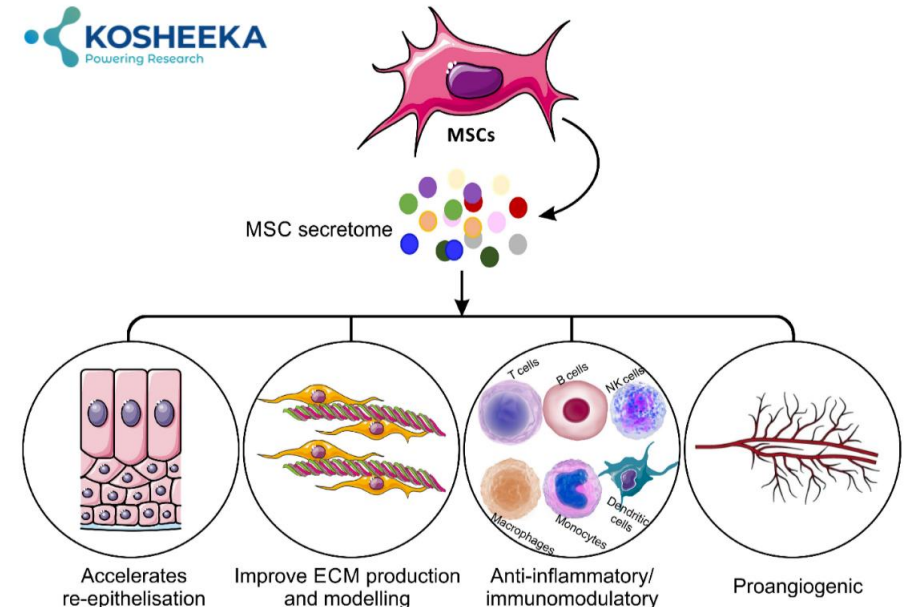
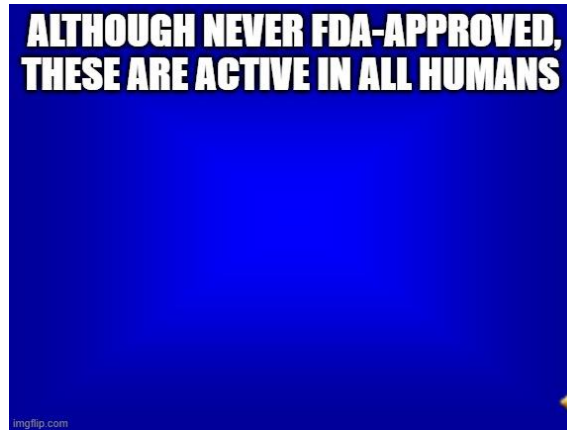
The role of exosomes in peripheral nerve regeneration

[Rosanna C. Ching](#)^{1,2} and [Paul J. Kingham](#), Ph.D.^{1,*}

► [Author information](#) ► [Article notes](#) ► [Copyright and License information](#) ► [Disclaimer](#)

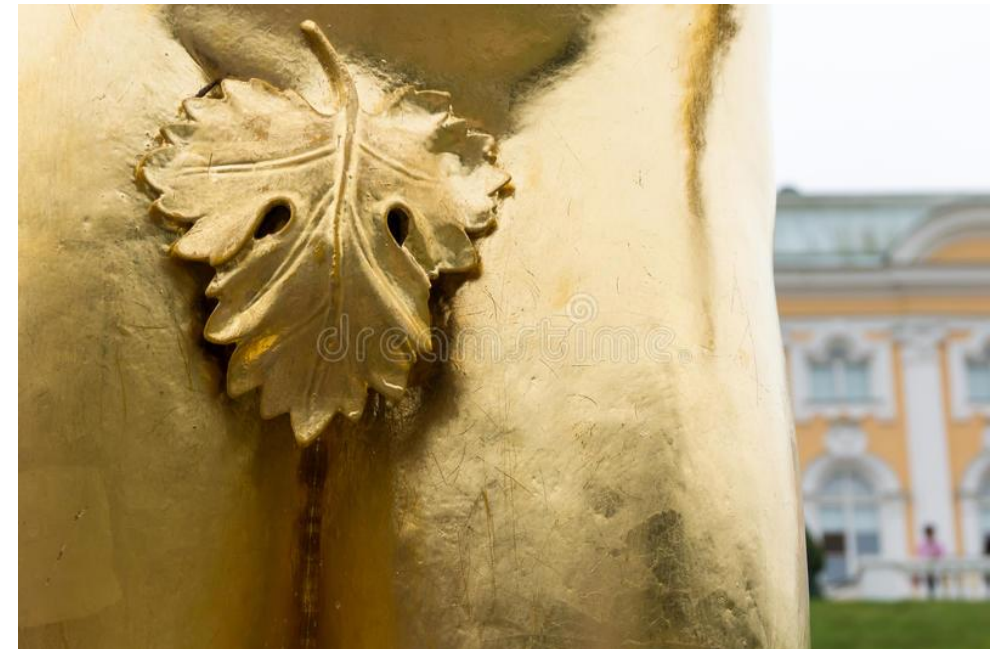


- Local injury, bleeding, infection
- Contamination (from donor or handling)
- Recovery of organ function
- Herpes reactivation
- Pt dissatisfaction – managing expectations



FDA trials

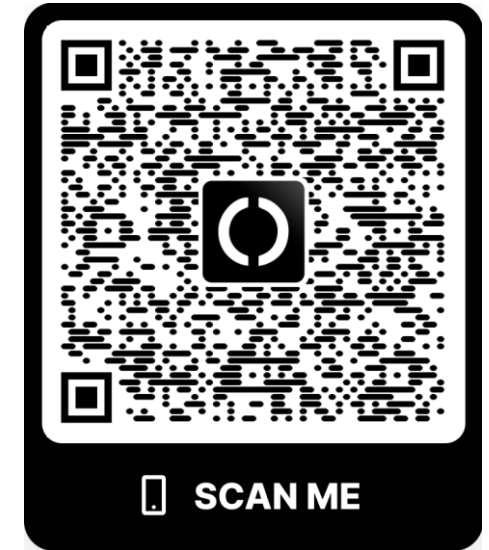
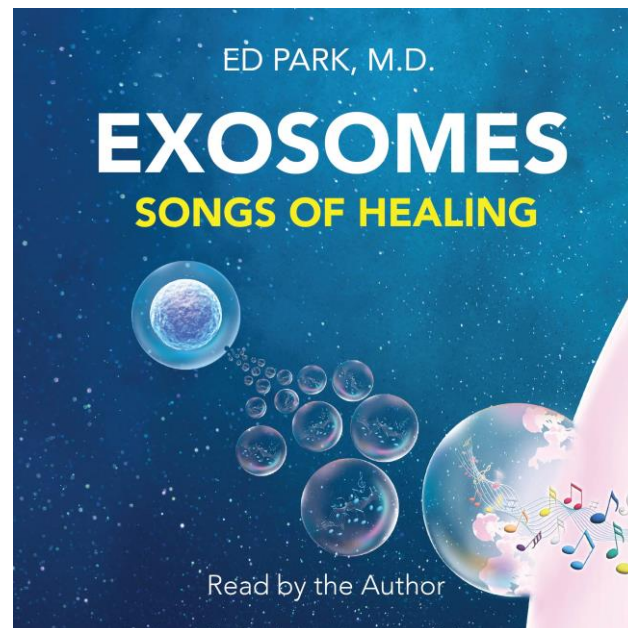
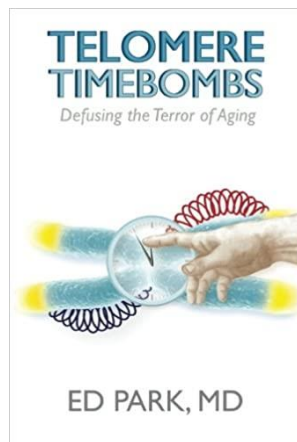
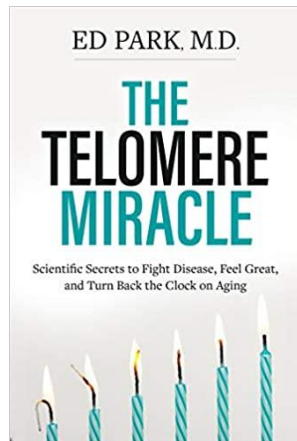
- There are multiple companies with INDs filed with FDA
- Indications are Covid, Long Covid, Crohn's disease, Infertility, Pulmonary Fibrosis, Acute Respiratory Distress Syndrome
- Intellectual Property issues?
- Animal studies in preemies, MI, CVA...



“the future is already here...” - Gibson



How to learn more – say “hi”



<https://ovou.me/edwardpark>

“This book is a must for any regenerative medicine specialist as it reviews the fundamentals of the disease of aging at the cellular, epigenetic, and genetic levels in a way I have never seen before”

Vince Giampapa, MD
Founder of A4M and CEO RMI-institute



Thursday 11:00am – 12:00pm

Clinical Use of MSC Exosomes

Please scan this QR code on you mobile
or tablet device to access the session feedback survey



Clinical Use of MSC Exosomes