Symposium: “Stem Cells-based Renal Therapy”
Date: December 6, 2025
Time: 17:05-18:20

MSC Exosomes in Renal Disease Modulation: Immunity as the Common Denominator

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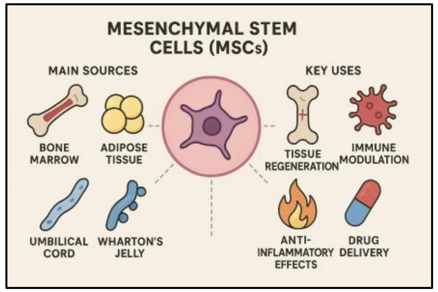
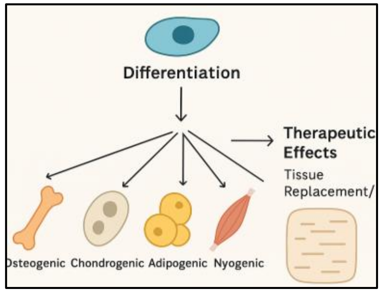
Member, ISCT/ICCBBAA/ISEV Extracellular Vesicle Nomenclature Committee
Member, ISEV Task Force on Regulatory Affairs and Clinical Use of EV-based Therapeutics

NUS National University of Singapore
Yong Loo Lin School of Medicine
Department of Surgery
Paracrine Therapeutics
"Living well with stem cell exosomes"

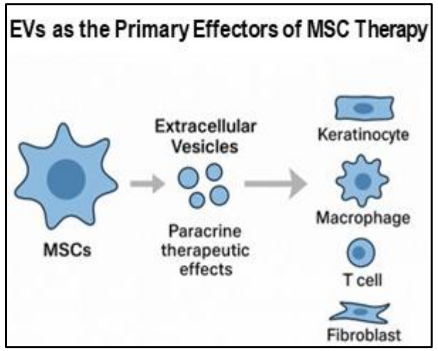
MSC and MSC exosomes in Renal Disease

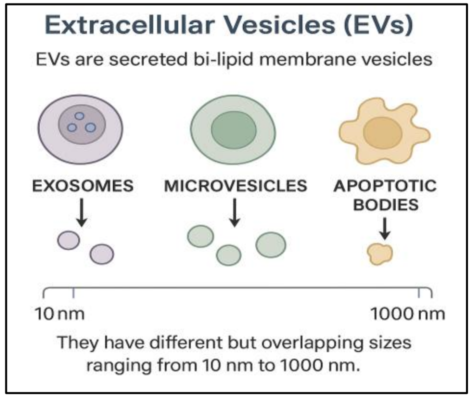


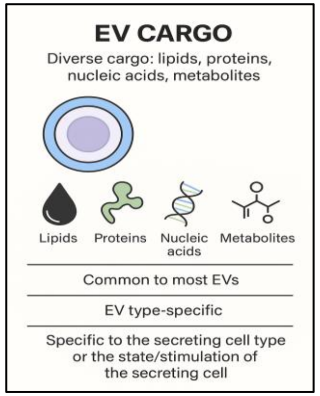


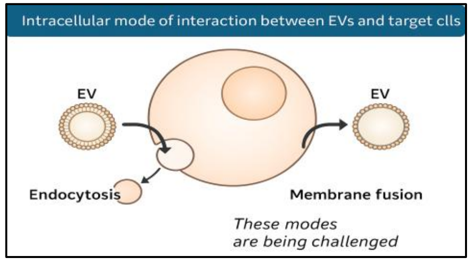
MSC kidney trials from ClinicalTrials.gov

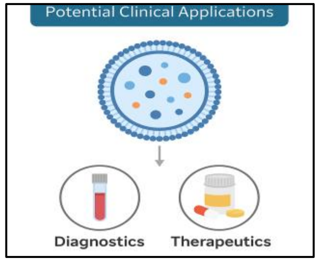
NCT ID	Indication Group	Indication Detail
NCT04869761	CKD	Chronic Kidney Disease
NCT05362786	CKD/DKD	Diabetic Kidney Disease (NEPHSTROM extension/US)
NCT03321942	CKD	Chronic renal failure / renal interstitial fibrosis
NCT05042206	CKD	Cellgram-CKD (safety)
NCT03460223	CKD	CKD/kidney failure (general)
NCT02585622	DKD	Type 2 diabetes with DKD (NEPHSTROM)
NCT03288571	DKD	Diabetic nephropathy
NCT03673748	Lupus Nephritis	Active/refractory LN
NCT06485648	Lupus Nephritis	Refractory LN
NCT02693366	FSGS	Focal segmental glomerulosclerosis
NCT01275612	AKI	Cisplatin-induced AKI
NCT04194671	AKI	General AKI
NCT03015623	AKI/CRRT	SBI-101 (MSC bioreactor) in patients requiring CRRT
NCT04445220	AKI/CRRT	COVID-19-related AKI on CRRT
NCT01429038	Transplant	Post-kidney transplant adjunct MSCs
NCT00752479	Transplant	Pre-transplant MSCs to induce tolerance
NCT00734396	Transplant	Subclinical rejection after kidney transplant
NCT03478215	Transplant/DGF	MSC adjunct to reduce DGF/rejection
NCT02492490	Transplant/DCD	DCD kidney transplant adjunct (SVF-MSC)
NCT04388761	Transplant	Allogeneic adipose-MSC intra-op adjunct
NCT02057965	Transplant	MSC therapy in renal recipients

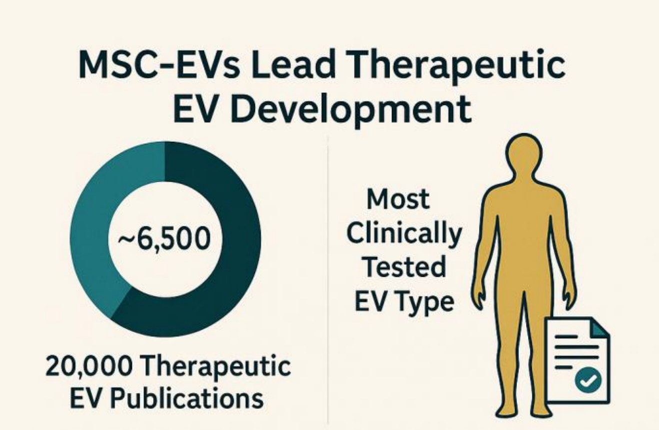




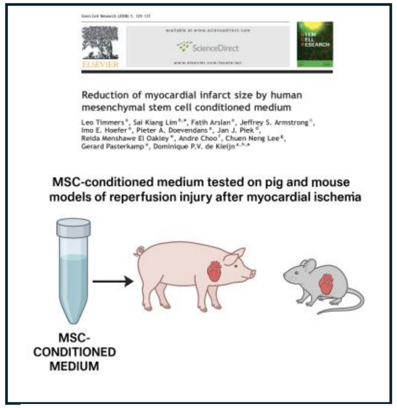


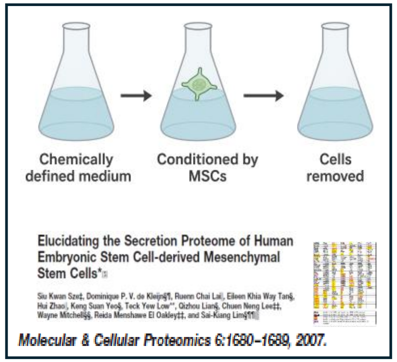


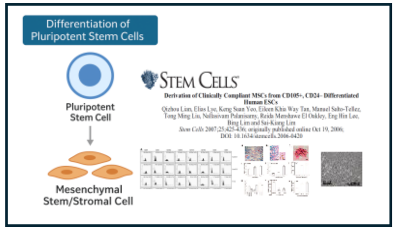




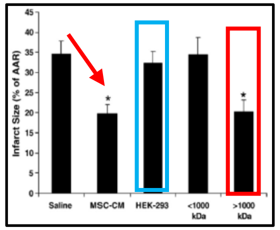
MSC exosomes/sEVs: discovery

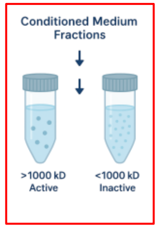


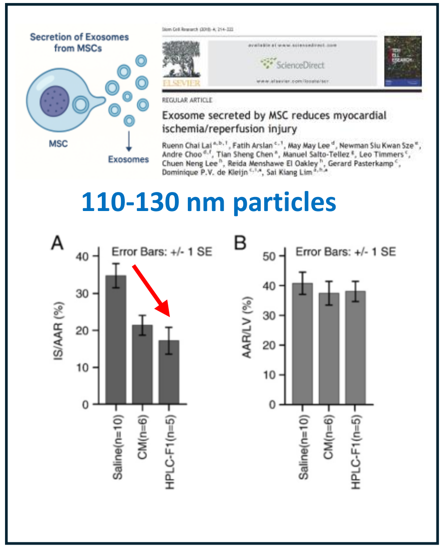


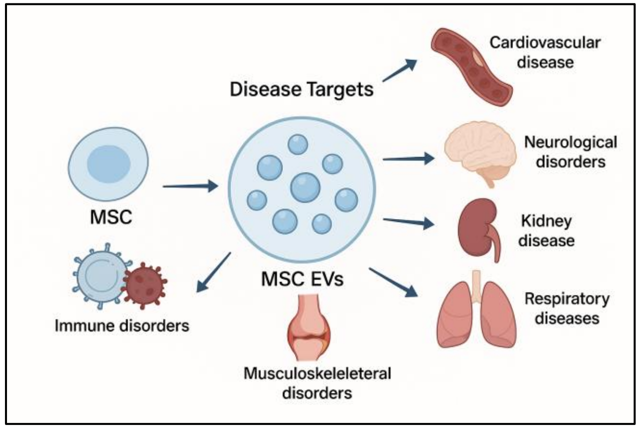


HEK CM did not work



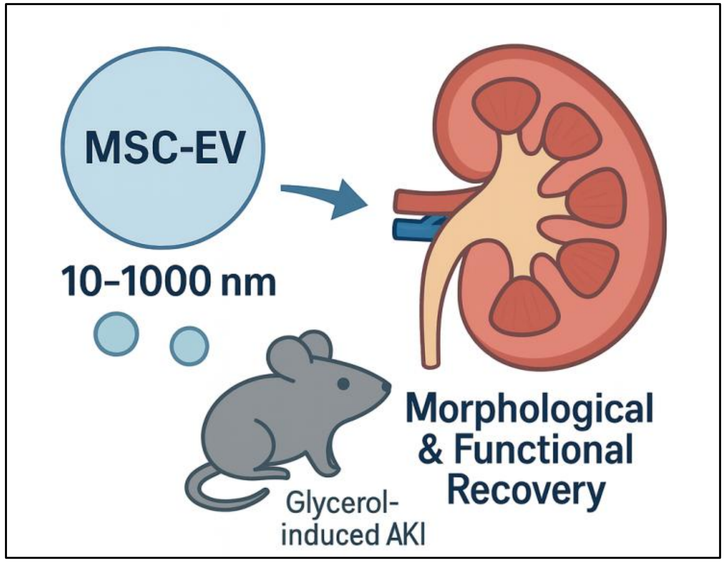






1. Myocardial reperfusion injury
2. Psoriasis
3. Liver fibrosis
4. Acute GVHD
5. Osteochondral defect
6. Osteoarthritis
7. Drug-induced hepatotoxicity
9. Aging-associated senescence
10. Radiation-induced intestinal toxicity
11. Corneal scarring

Renal protective MSC EVs



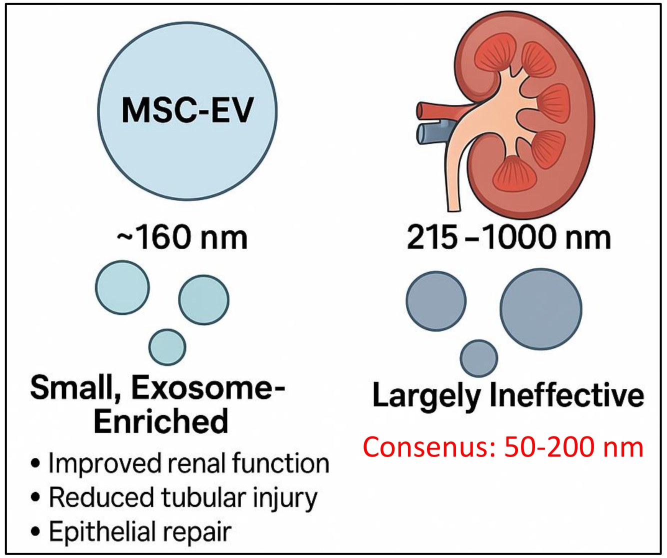
BASIC RESEARCH

Mesenchymal Stem Cell-Derived Microvesicles Protect Against Acute Tubular Injury

Bruno, Stefania; Grange, Cristina; Deregibus, Maria Chiara; Calogero, Raffaele A.; Saviozzi, Silvia; Collino, Federica; Morando, Laura; Busca, Alessandro; Falda, Michele; Bussolati, Benedetta; Tetta, Ciro; Camussi, Giovanni

Author Information

Journal of the American Society of Nephrology 20(5):p 1053-1067, May 2009. | ***DOI:*** 10.1681/ASN.2008070798



TISSUE ENGINEERING: Part A
Volume 23, Numbers 21 and 22, 2017
Mary Ann Liebert, Inc.
DOI: 10.1089/ten.tea.2017.0069

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Tissue Engineering & Regenerative Medicine International Society

SPECIAL FOCUS: EMERGING IMPACT OF EXTRACELLULAR VESICLES ON TISSUE ENGINEERING AND REGENERATION*

Renal Regenerative Potential of Different Extracellular Vesicle Populations Derived from Bone Marrow Mesenchymal Stromal Cells

Stefania Bruno, PhD,[1] Marta Tapparo, PhD,[2] Federica Collino, PhD,[2,3] Giulia Chiabotto, PhD,[2] Maria Chiara Deregibus, MD,[2] Rafael Soares Lindoso, PhD,[2,3] Francesco Neri, PhD,[4,5] Sharad Kholia, PhD,[2] Sara Giunti, MD,[2] Sicheng Wen, PhD,[6] Peter Quesenberry, MD,[6] and Giovanni Camussi, MD[2]

MSC exosomes in Renal Diseases

MSC EVs: most studied therapeutic EVs in pre-clinical studies of renal diseases

Table 1. Therapeutic application of extracellular vesicles from various origins in different kidney diseases

Disease Model	Origin	EV type	Mechanism	Ref.
AKI	hWJMSCs	MVs	• hWJMSC-derived MVs improve renal function in ischemic AKI model by facilitating the proliferation of renal tubular cells and alleviating the apoptosis and fibrosis of renal cells *in vivo* (rats).	(9)
	hWJMSCs	Not specified	• hWJMSC-derived EVs ameliorate ischemic AKI by inhibition of mitochondrial fission through miR-30 *in vivo* (rats).	(44)
	hWJMSCs	MVs	• hWJMSC-derived MVs alleviate the oxidative stress through suppressing NOX2 expression in both *in vitro* (HUVEC) and *in vivo* (rats) IRI model. • hWJMSC-derived MVs reduce apoptosis and enhanced proliferation in renal IRI.	(10)
	hWJMSCs	MVs	• hWJMSC-derived MVs induce HGF synthesis in damaged tubular cells via RNA transfer, facilitating tubular cell dedifferentiation and regeneration in unilateral AKI model *in vivo* (rats).	(45)
	hUC-MSCs	MVs	• hUC-MSC-derived MVs mitigate epithelial cell apoptosis in low oxygen environment *in vitro* (HK-2) and ameliorated renal IRI *in vivo* (rats) via delivery of miR-21.	(46)
	hUSCs	Exosomes	• hUSC-derived exosomes ameliorate ischemic AKI *in vivo* (rats). • hUSC-derived exosomes inhibit oxidative stress after H/R injury *in vitro* (HK-2). • *miR-146a-5p* targets *interleukin-1 receptor-associated kinase 1* mRNA and subsequently inhibited the activation of NF-κB signaling *in vitro* (HK-2).	(11)
	hBM-derived MSCs	Exosomes	• Exosomes from hBM-derived MSCs play a protective role in H/R injury *in vitro* (HK-2) as well as in renal IRI *in vivo* (mice). • *miR-199a-3p* is involved in the renal protective effects of exosomes from hBM-derived MSCs by regulating Sema3A and activating the AKT and ERK pathways.	(12)
	Adipose-derived MSCs	Not specified	• Hypoxia-preconditioning increase the antiapoptotic, immune-modulatory, and anti-oxidative properties of adipose-derived MSC-EVs *in vitro*. • Adipose-derived MSC-EVs improve recovery of renal function in ischemic AKI *in vivo* (rats).	(47)
	Mouse serum	Exosomes	• Delayed remote ischemic preconditioning exerts renoprotection in septic AKI through exosomal *miR-21* derived from preischemic limbs *in vivo* (mice). • Exosomal *miR-21* attenuates septic AKI both *in vivo* (mice) and *in vitro* (mTECs) through PDCD4/NF-κB and PTEN/AKT pathways inducing anti-inflammatory and anti-apoptotic effects.	(13)
	Human urine	Not specified	• Urinary EVs alleviate AKI generated by glycerol injection and accelerate renal recovery *in vivo* (mice). • The protective role of urinary EV is mediated through repletion of Klotho in injured renal tissue.	(14)
	Human renal tubular cells	Exosomes	• Exosomes from human renal tubular cells prevent ischemic renal injury in Nude rats by preventing renal oxidant stress and apoptosis and suppressing pro-inflammatory and pro-fibrotic pathways.	(16)
Diabetic nephropathy	Rat BM-derived MSCs	Exosomes	• BM-derived exosomes improve renal function, morphology, and fibrosis in streptozotocin-induced diabetic nephropathy model *in vivo* (rats) in parallel with increased autophagy markers, LC3 and Beclin-1, and decreased mTOR and fibrotic markers expression in renal tissue.	(18)
	Rat BM-derived MSCs	Exosomes	• Exosomes from BM-derived MSCs ameliorate renal inflammation and fibrosis while protecting tight junction structure in streptozotocin-induced diabetic nephropathy *in vivo* (rats). • Exosomes from BM-derived MSCs suppress apoptosis and degeneration of tubular epithelial cells in primary renal cell culture of streptozotocin-induced diabetic rats *in vitro*.	(19)
	hUC-MSCs	Exosomes	• hUC-MSC-derived exosomes decrease the production of pro-inflammatory and pro-fibrotic cytokines in high glucose-injured renal tubular epithelial cells and renal glomerular endothelial cells *in vitro*.	(48)
	hBM-derived MSCs and HLSCs	Not specified	• EVs from hBM-derived MSCs and HLSCs alleviate renal fibrosis and proteinuria in streptozotocin-induced diabetic nephropathy model *in vivo* (mice).	(49)
Hypertensive nephropathy	Adipose-derived MSCs	Not specified	• Adipose-derived MSC-EVs improve renal function, decreased urinary protein excretion, and renal fibrosis while preventing cardiac tissue fibrosis and inducing better blood pressure control in DOCA-salt hypertensive model *in vivo* (rats).	(20)
	Cardiosphere-derived cells	Exosomes	• Administration of exosomes from cardiosphere-derived cells attenuate renal injury and cardiac hypertrophy in angiotensin II-induced hypertension model *in vivo* (mice), which appears to be associated with changes in the expression of interleukin-10.	(21)

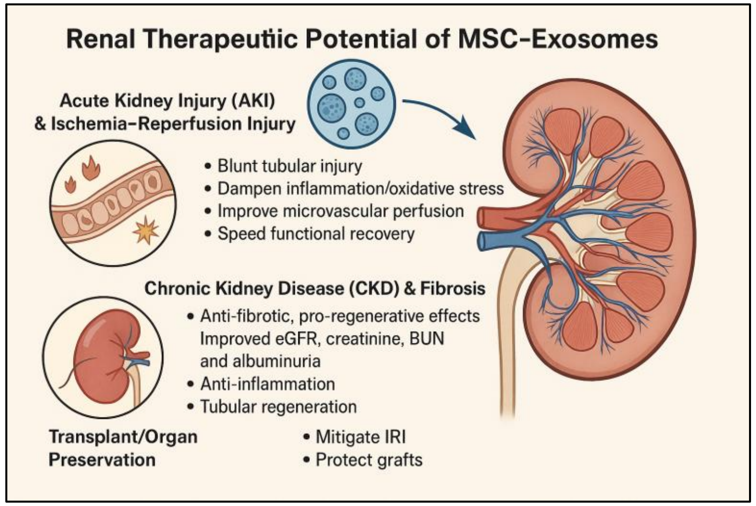
Table 1. Continued

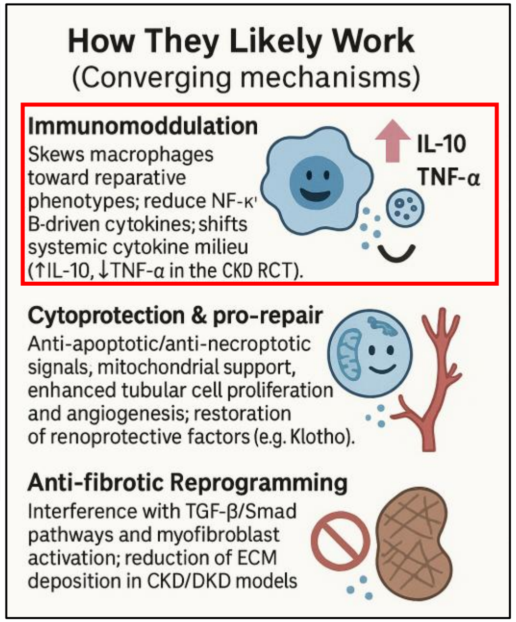
Disease Model	Origin	EV type	Mechanism	Ref.
Glomerulonephritis	hEPC	Not specified	• hEPC-derived EVs alleviate complement-mediated mesangial injury in anti-Thy1.1-induced glomerulonephritis model *in vivo* (rats) by inhibiting mesangial cell activation, leukocyte infiltration, and apoptosis. • hEPC-derived EVs inhibit complement-mediated renal mesangial cell injury and C5b-9 deposition *in vitro*.	(22)
Other CKD	Adipose-derived autologous MSCs	Not specified	• Autologous MSCs-derived EVs restore renal function through attenuation of renal inflammation, tissue hypoxia, and fibrosis in metabolic syndrome and renal artery stenosis model *in vivo* (pigs). • These protective effects are blunted in pigs treated with interleukin-10-depleted EVs.	(23)
	MSCs	Not specified	• MSC-derived EVs from lean pigs more effectively improve renal function and decrease tubular injury and fibrosis compared to those from pigs with metabolic syndrome. • The beneficial effect of MSC-derived EVs appears to be associated with up-regulated TGF-β signaling and enriched regulatory T cells.	(24)
	hCB-MSCs	Not specified	• Cell-free hCB-MSCs-EVs ameliorate the inflammatory immune reaction and transiently improve the overall kidney function in CKD patients. • Cell-free hCB-MSCs-EVs do not induce any significant adverse events throughout the study period (one year).	(50)
	hBM-derived MSCs	Exosomes	• MSCs-derived exosomal anti-let-7i-5p attenuates the pro-fibrotic response induced by TGF-β1 *in vitro* (NRK52E cells). • MSC-derived exosomal anti-let-7i-5p improves renal function and attenuates renal fibrosis in UUO-induced renal fibrosis model *in vivo* (mice).	(51)
	hWJMSCs	MV	• hWJMSC-derived MVs attenuate ischemia-induced renal fibrosis *in vivo* (rats) and promote M2 macrophage polarization *in vitro* (THP-1 macrophages) via transferring HGF.	(52)
	Human adipose-derived MSCs	Exosomes	• GDNF-modified human adipose-derived MSCs ameliorate renal fibrosis in murine UUO model. • GDNF-modified human adipose-derived MSCs exert cytoprotective effect on HUVEC in hypoxia/serum deprivation injury model by promoting angiogenesis through activation of SIRT1/eNOS signaling pathway.	(53)
Graft dysfunction after renal transplantation	Tregs	Exosomes	• Treg-derived exosomes can postpone allograft rejection and prolong the survival time of transplanted kidney *in vivo* (rats). • Treg-derived exosomes suppress T cell proliferation *in vitro*.	(26)
	Mouse immature DCs	Exosomes	• Immature DC-derived exosomes improve the survival in isograft mice by alleviating inflammatory response, reducing CD4 T cell infiltration, and increasing regulatory T cells in spleen and kidney tissues. • miR-682 is highly expressed in immature DC-derived exosomes which can promote regulatory T cell differentiation and immune tolerance in renal allograft *in vivo* (mice).	(27)
	hWJMSCs	MV	• hWJMSC-derived MVs improve survival rate and renal function after renal transplantation *in vivo* (rats). • hWJMSC-derived MVs mitigate renal cell apoptosis and inflammation and enhance proliferation in the acute stage while abrogating renal fibrosis in the late stage.	(28)

BMB Reports
BMB Rep. 2022; 55(1): 3-10
www.bmbreports.org
Invited Mini Review

Therapeutic application of extracellular vesicles for various kidney diseases: a brief review

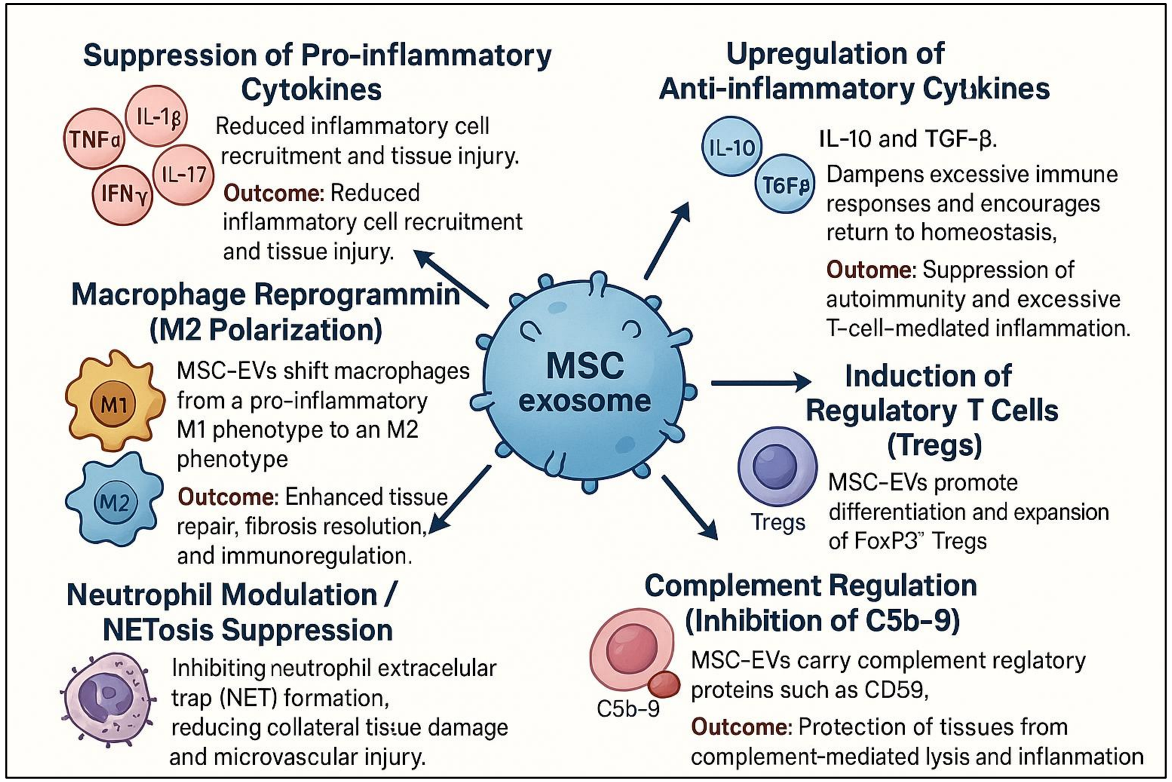
Sul A Lee[1] *& Tae Hyun Yoo*[2,*]
[1]Department of Medicine, MetroWest Medical Center/Tufts University School of Medicine, Framingham, MA 01702, USA, [2]Department of Internal Medicine, College of Medicine, Institute of Kidney Disease Research, Yonsei University, Seoul 03722, Korea



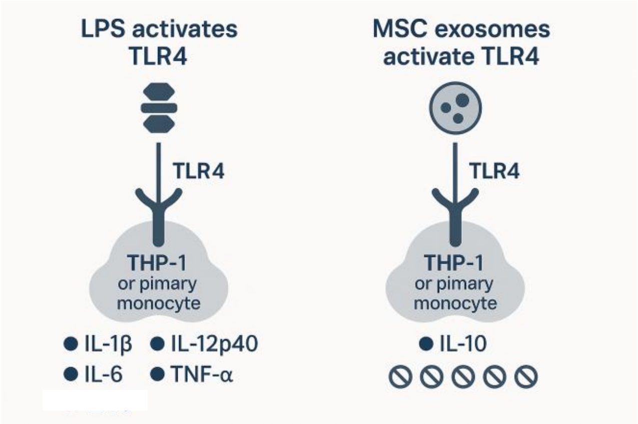


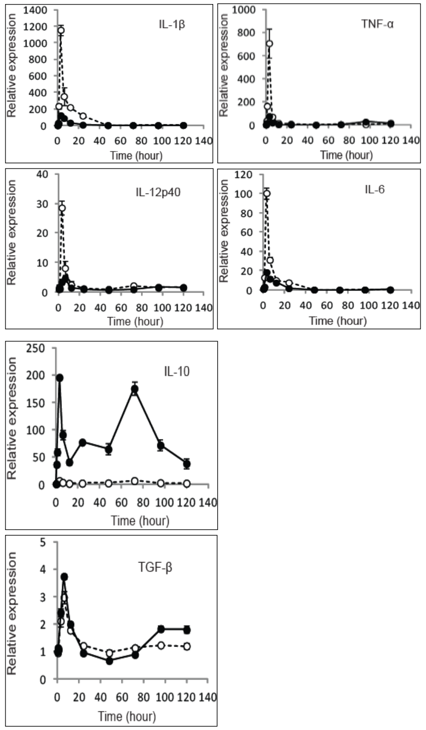
Key mechanism: immunomodulatory activities

Immunomodulatory activities of MSC exosomes



MSC exosomes:
↓inflammatory but ↑anti-inflammatory cytokines





STEM CELLS AND DEVELOPMENT
Volume 23, Number 11, 2014
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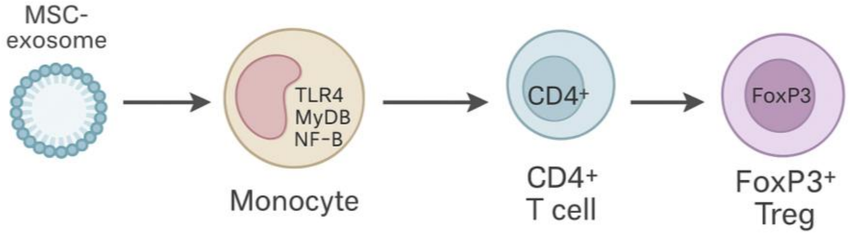
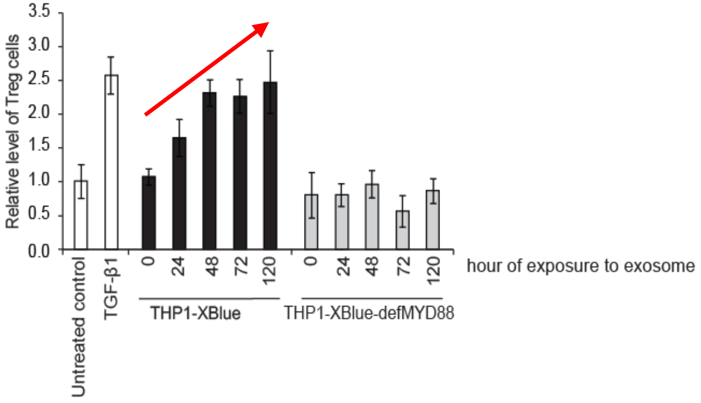
DOI: 10.1089/scd.2013.0479

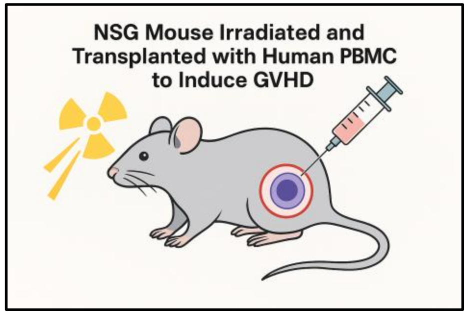
Mesenchymal Stem Cells Secrete Immunologically Active Exosomes

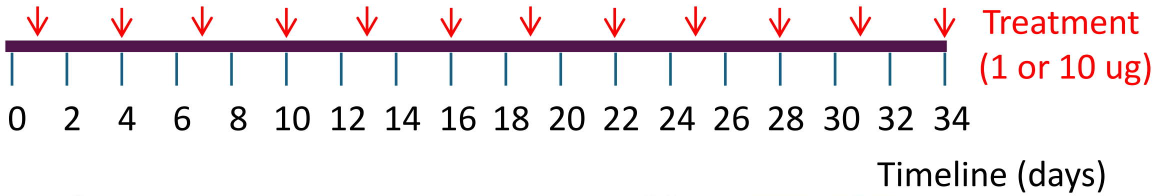
Bin Zhang,[1,*] Yijun Yin,[1,*] Ruenn Chai Lai,[1] Soon Sim Tan,[1] Andre Boon Hwa Choo,[2] and Sai Kiang Lim[1,3]

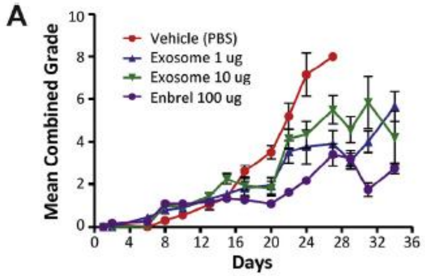




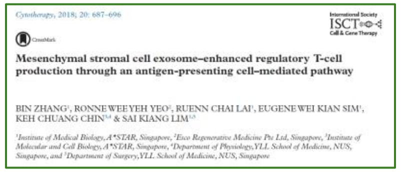
MSC exosome increase Treg in a mouse GVHD model







MSC exosomes
A) Alleviate GVHD


Cytotherapy, 2018; 20: 687–696

International Society ISCT Cell & Gene Therapy

Mesenchymal stromal cell exosome–enhanced regulatory T-cell production through an antigen-presenting cell–mediated pathway

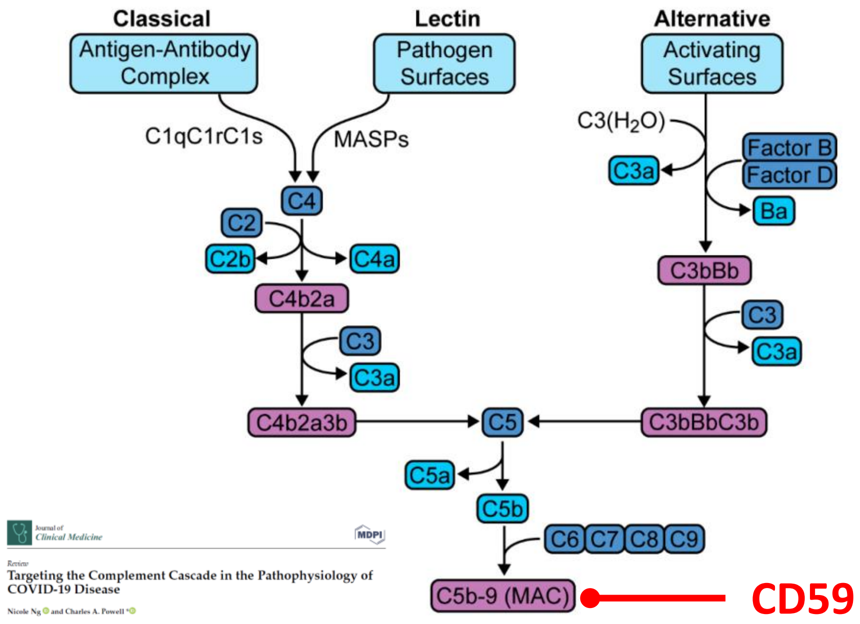
BIN ZHANG[1], RONNE WEE YEH YEO[2], RUENN CHAI LAI[1], EUGENE WEI KIAN SIM[1], KEH CHUANG CHIN[3,4] & SAI KIANG LIM[1,5]

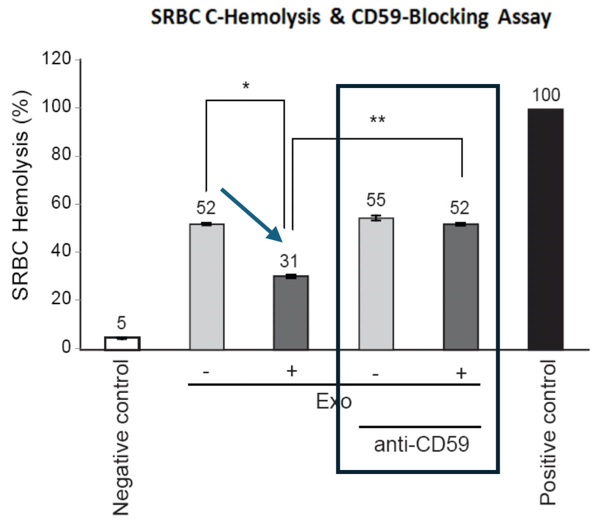
[1]Institute of Medical Biology, A*STAR, Singapore, [2]Esco Regenerative Medicine Pte Ltd, Singapore, [3]Institute of Molecular and Cell Biology, A*STAR, Singapore, [4]Department of Physiology, YLL School of Medicine, NUS, Singapore, and [5]Department of Surgery, YLL School of Medicine, NUS, Singapore

NUS National University of Singapore | Yong Loo Lin School of Medicine Department of Surgery

Paracrine Therapeutics "Living well with stem cell exosomes"

Complement inhibition by MSC exosome



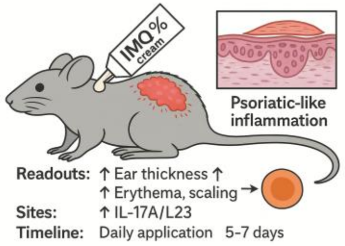


C5b9 activity assay (sheep rbc lysis assay)

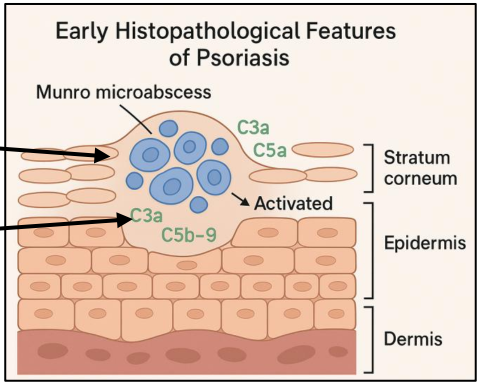
- MSC exosome inhibits formation of C5b9 complex (MAC)
- Inhibition is abrogated by a neutralising CD59 antibody

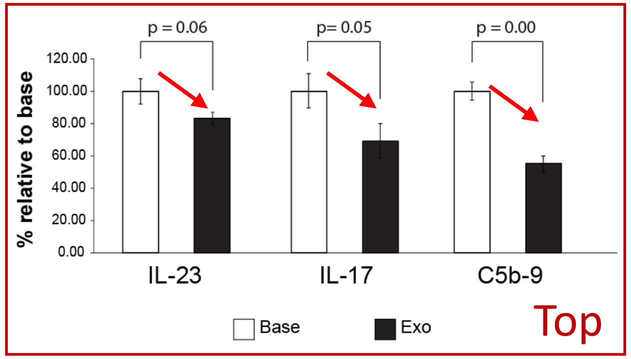
MSC exosome inhibit C5b9 formation though **CD59** on the exosome membrane

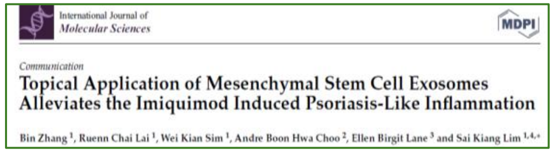
MSC exosome alleviate psoriasis via complement



- Mouse model of IMQ-induced psoriatic inflammation
  - Topically applied but not IP/SC injected MSC-sEVs
    - reduce IL17 and IL23, and C5b9 (terminal complement complex)
  - Topical MSC-sEVs confined to SC
- Background Information
  - Characteristics of Psoriatic SC
    - Munro microabscess of neutrophils (ca 1898)
      - Neutrophils: major source of psoriatic IL-17
    - Rich in activated complements





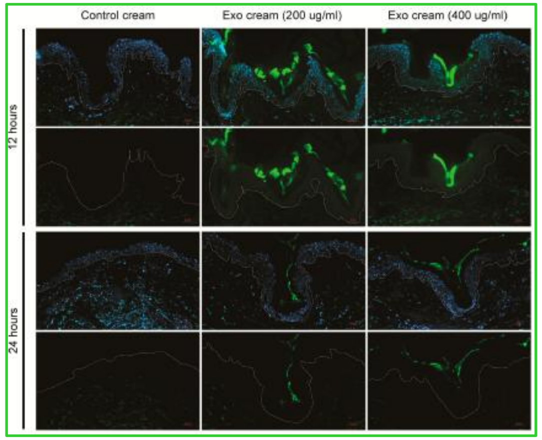

International Journal of Molecular Sciences

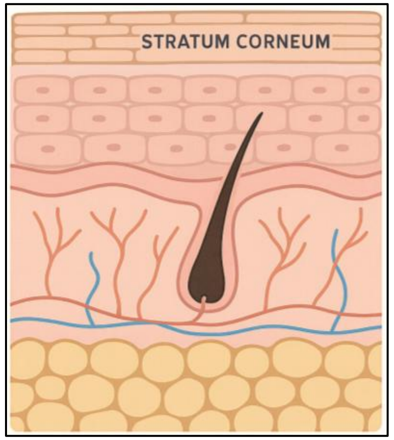
MDPI

Communication

Topical Application of Mesenchymal Stem Cell Exosomes Alleviates the Imiquimod Induced Psoriasis-Like Inflammation

Bin Zhang [1], Ruenn Chai Lai [1], Wei Kian Sim [1], Andre Boon Hwa Choo [2], Ellen Birgit Lane [3] and Sai Kiang Lim [1,4,*]






Dermatopathology in Historical Perspective

William John Munro and Munro's Abscess, and Franz Kogoj and Kogoj's Spongiform Pustule

Charles Steffen, M.D.

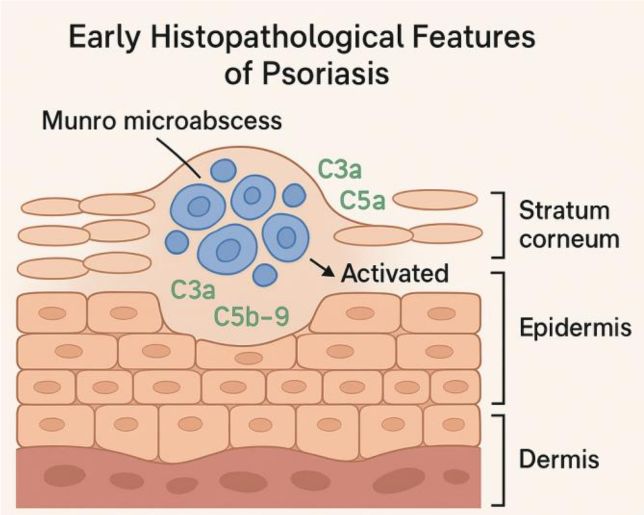

Stratum Corneum Activation of Complement Through the Antibody-independent Alternative Pathway

Tadashi Terui, M.D., Taizo Kato, M.D., and Hachiro Tagami, M.D.

CED CLINICAL AND EXPERIMENTAL DERMATOLOGY

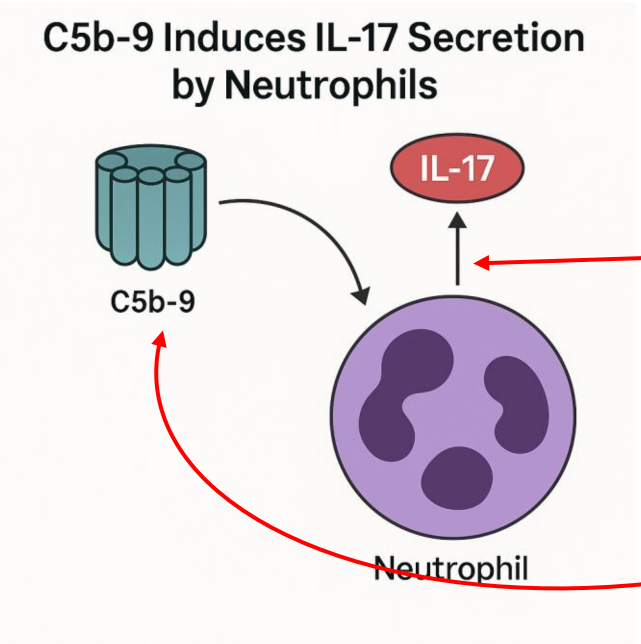
Complement activation in psoriasis

Mechanism of Action: MSC-sEV and psoriatic IL-17 secretion



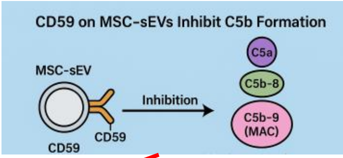
1. Munro microabscess of **neutrophils**; major source of key psoriatic inflammatory cytokine, **IL-17**
2. Activated complements, C3a, C5a and **C5b9**

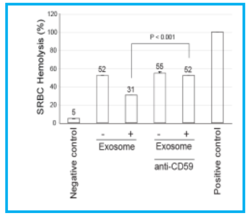
Hypothesis 1



Hypothesis 2

MSC-sEVs inhibit IL-17 secretion



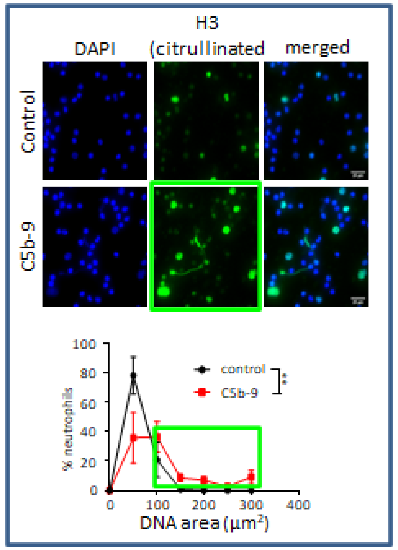


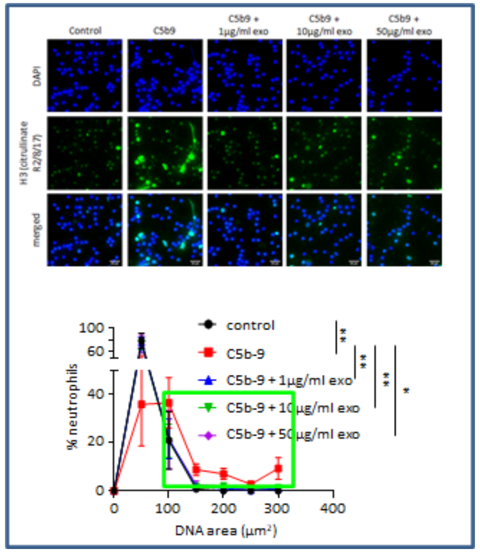
Hypothesis 3

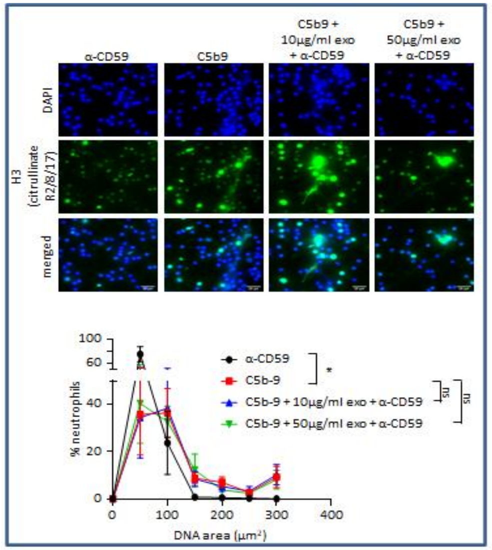
MSC-sEVs inhibit IL-17 secretion through CD59

Mechanism of Action: MSC-sEV on IL-17

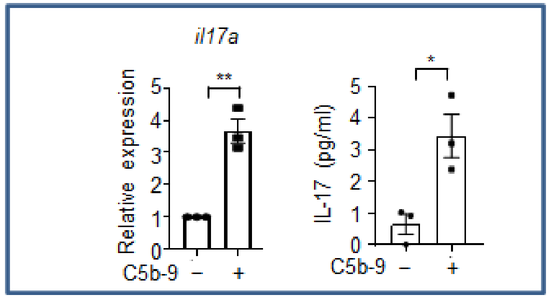
Kong Peng Lam
ASTAR SIGN



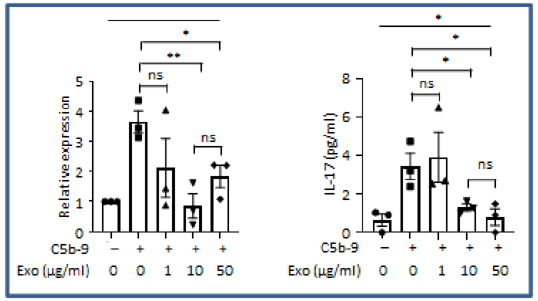




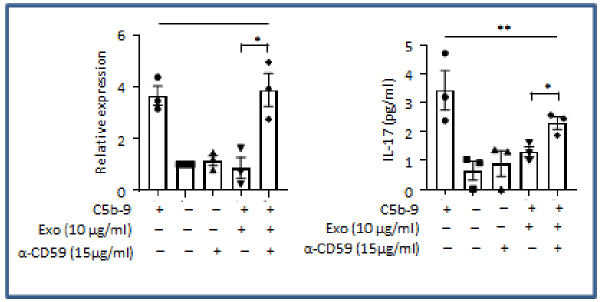
IL-17 mRNA and secretion in medium

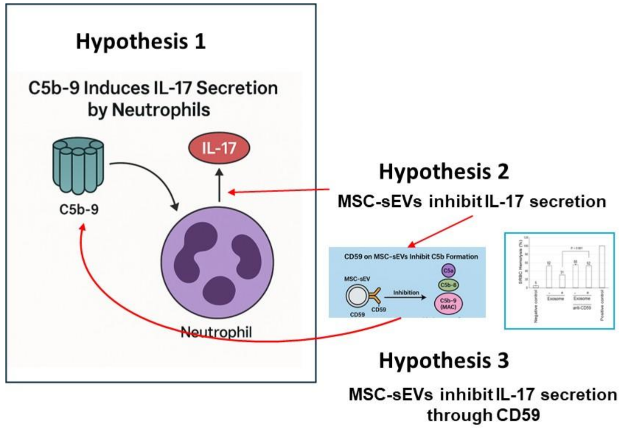


IL-17 mRNA and secretion in medium



IL-17 mRNA and secretion in medium





C5b9 + neutrophils

↑NETs; ↑IL-17

….. + MSC-sEVs

~~↑NETs; ↑IL-17~~

…. + MSC-sEVs + α CD59

↑NETs; ↑IL-17


CYTOTHERAPY

Full-length article

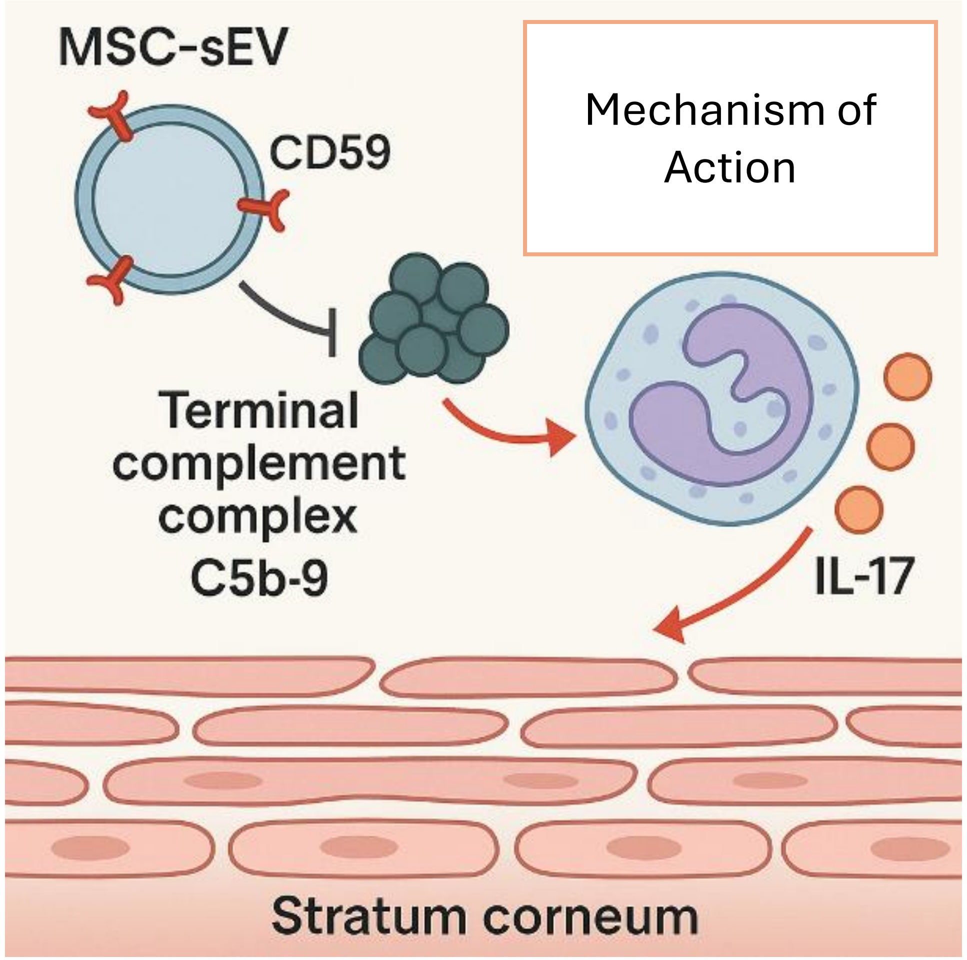
Mechanism for the attenuation of neutrophil and complement hyperactivity by MSC exosomes

Jia Tong Loh, Bin Zhang, Joey Kay Hui Teo, Ruenn Chai Lai, Andre Boon Hwa Choo, Kong-Peng Lam, Sai Kiang Lim

NUS National University of Singapore | Yong Loo Lin School of Medicine, Department of Surgery

Paracrine Therapeutics "Living well with stem cell exosomes"

MoA of MSC-sEVs in inhibiting psoriastic IL-17 secretion



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Cytotherapy 000 (2025) 1–9

Contents lists available at ScienceDirect

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CYTOTHERAPY

International Society ISCT Cell & Gene Therapy®

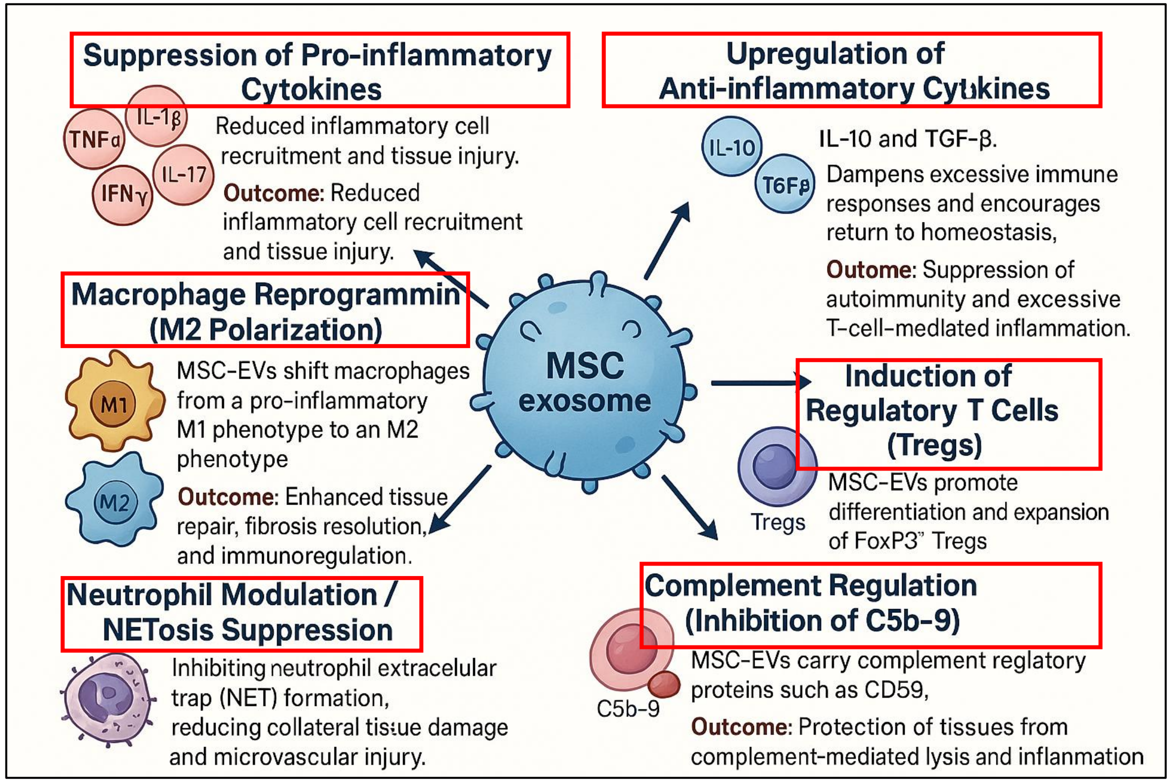
journal homepage: www.isct-cytotherapy.org

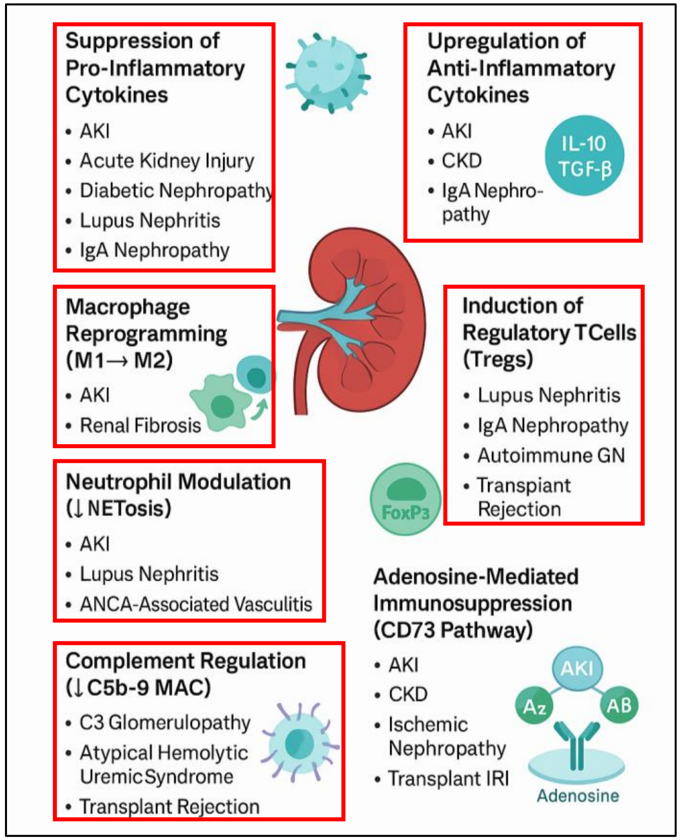
Full-length article

A phase 1, open-label study to determine safety and tolerability of the topical application of mesenchymal stem/stromal cell (MSC) exosome ointment to treat psoriasis in healthy volunteers

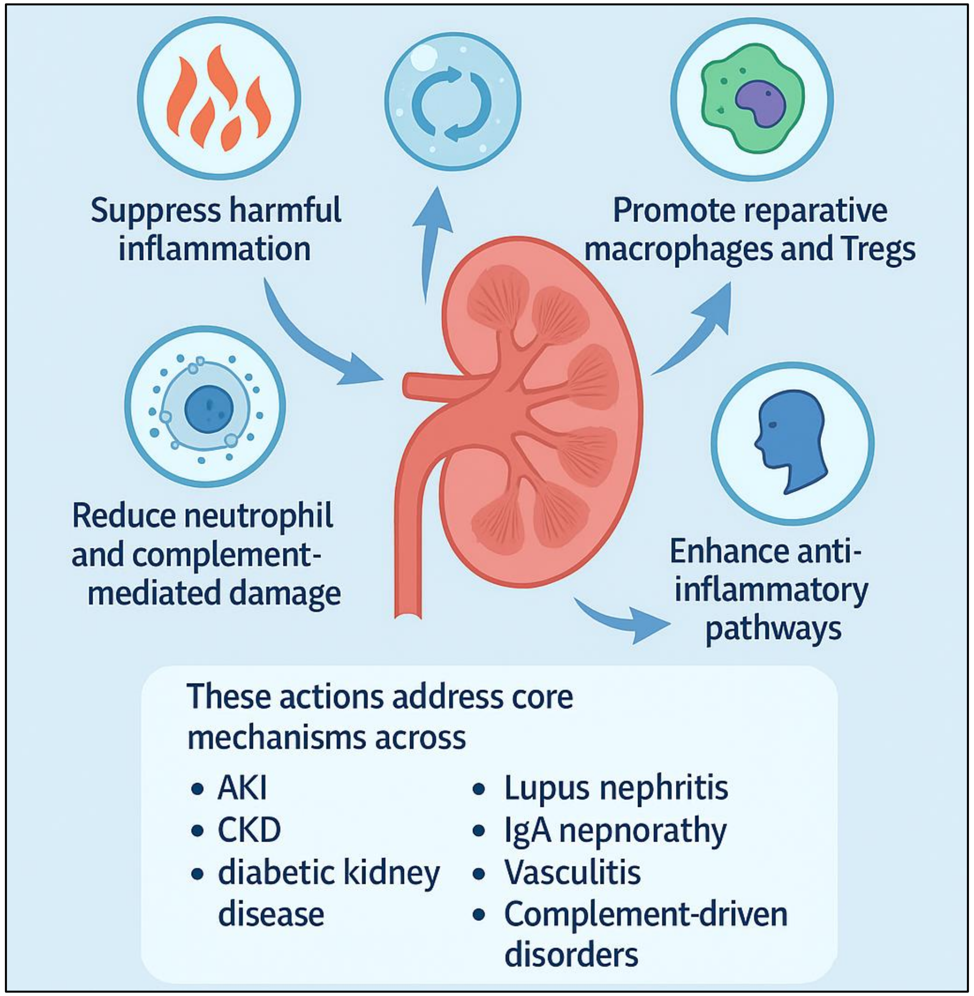
Nisha Suyien Chandran[1], Monil Nagad Bhupendrabhai[1], Thong Teck Tan[2], Bin Zhang[2], Sai Kiang Lim[2,3,*], Andre Boon Hwa Choo[4,5], Ruenn Chai Lai[2]

MSC exosomes: renal-relevant immunomodulatory activities

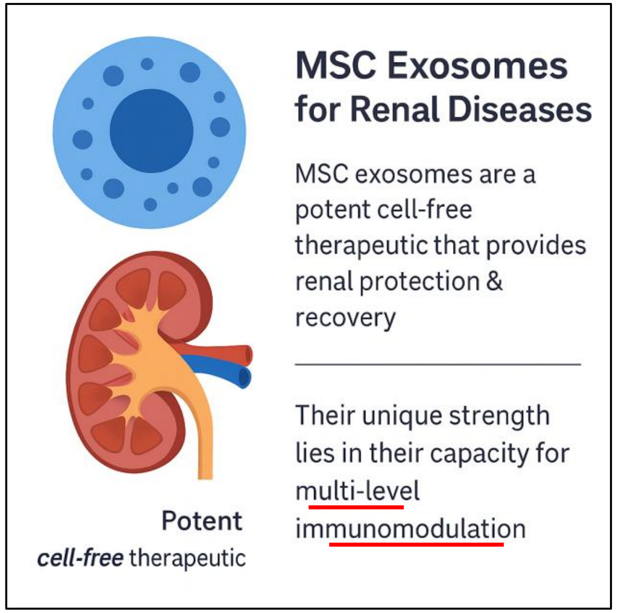




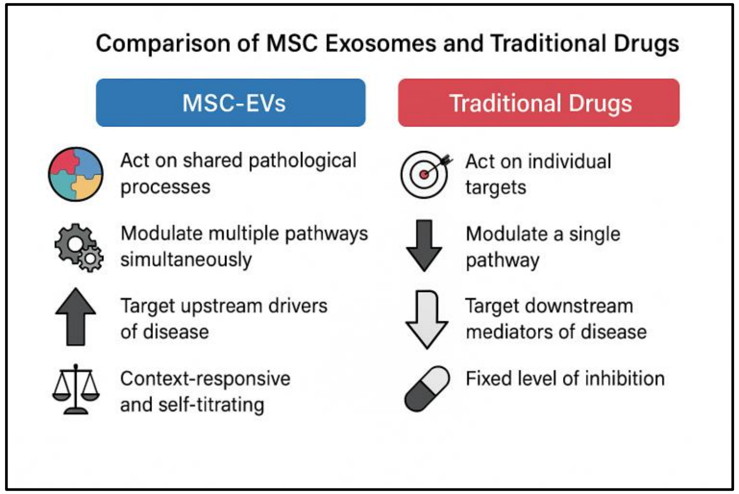
Conclusion



Suppress harmful inflammation
Promote reparative macrophages and Tregs
Reduce neutrophil and complement-mediated damage
Enhance anti-inflammatory pathways
These actions address core mechanisms across
• AKI
• CKD
• diabetic kidney disease
• Lupus nephritis
• IgA nepnorathy
• Vasculitis
• Complement-driven disorders



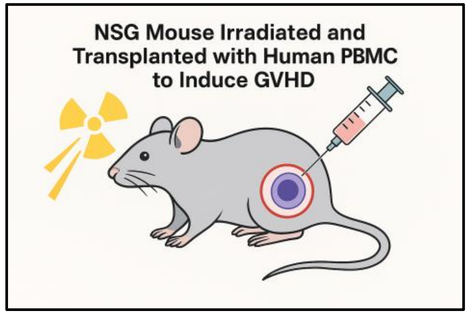
MSC Exosomes for Renal Diseases
MSC exosomes are a potent cell-free therapeutic that provides renal protection & recovery
Their unique strength lies in their capacity for multi-level immunomodulation
Potent
cell-free therapeutic



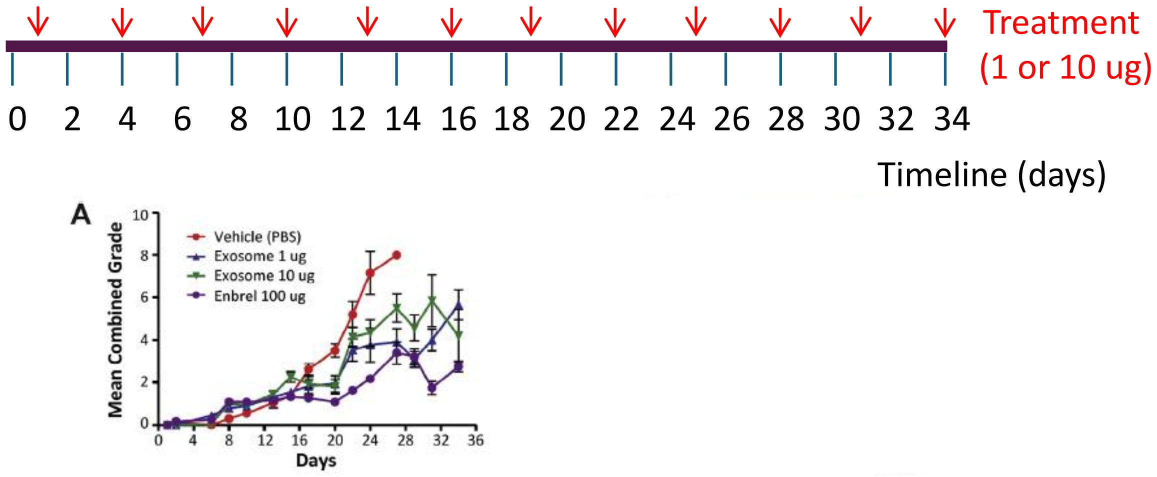
Comparison of MSC Exosomes and Traditional Drugs
MSC-EVs
Traditional Drugs
Act on shared pathological processes
Act on individual targets
Modulate multiple pathways simultaneously
Modulate a single pathway
Target upstream drivers of disease
Target downstream mediators of disease
Context-responsive and self-titrating
Fixed level of inhibition

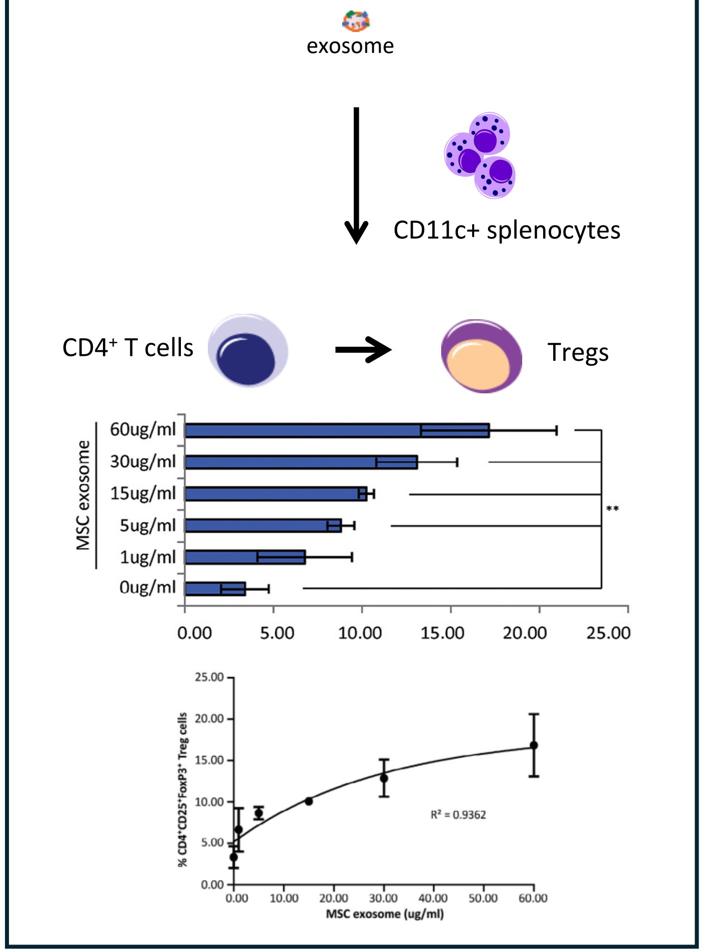

Thank You

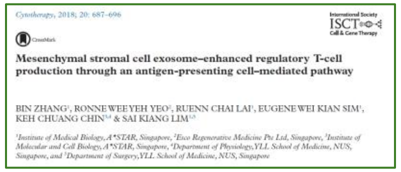
MSC exosome increase Treg in a mouse GVHD model



MSC exosomes
A) Alleviate GVHD






Cytotherapy, 2018; 20: 687–696

International Society ISCT Cell & Gene Therapy

Mesenchymal stromal cell exosome–enhanced regulatory T-cell production through an antigen-presenting cell–mediated pathway

BIN ZHANG[1], RONNE WEE YEH YEO[2], RUENN CHAI LAI[1], EUGENE WEI KIAN SIM[1], KEH CHUANG CHIN[3,4] & SAI KIANG LIM[1,5]

[1]Institute of Medical Biology, A*STAR, Singapore, [2]Esco Regenerative Medicine Pte Ltd, Singapore, [3]Institute of Molecular and Cell Biology, A*STAR, Singapore, [4]Department of Physiology, YLL School of Medicine, NUS, Singapore, and [5]Department of Surgery, YLL School of Medicine, NUS, Singapore

NUS National University of Singapore | Yong Loo Lin School of Medicine Department of Surgery

Paracrine Therapeutics "Living well with stem cell exosomes"