流式細胞儀於再生醫學的應用

Robin Hu

Associate Product Manager

BD Biosciences



More than 45 years of experience and innovation in flow cytometry

alada⁺ dab⁺ alada⁺ ninin⁺ alada⁺ |✓] alada⁺ alash⁺ tab⁺ 2016 1974 1995 2002 2007 2014 2018 2021 2023 **BD** launches **BD** First commercialized First benchtop New standard for Introduction of BD[®] First immunophenotyping BD launches next-BD expands its single-cell reagents for the UV laser: BD Cytometebr Setup and generation BD Accuri[™] C6 multiomics portfolio with FACSymphony[™] A1 Cell fluorescenceanalyzer/sorter for flow cytometry Horizon Brilliant[™] activated cell sorter four-color analysis: data quality: Tracking Beads provides Plus Flow Cytometer with BD[®] AbSeq Antibodies, Analyzer with small particle BD FACSDiva[™] (FACS) BD FACSCalibur[™] a simple solution for Ultraviolet Reagents enhanced features, driving bringing together highdetection option. Flow Cytometer Software characterizing and flow cytometry even more guality antibodies from tracking cytometer within reach the BD Pharmingen[™] --performance portfolio with FACSLyric[™] Flow Cytometer. oligonucleotides, allowing 2003 2015 researchers to perform BD launches the BD 2008 BD launches the BD single-cell multiomics FACSAria[™] Sorter. a FACSCelesta[™] Flow First seven-laser analysis. benchtop sorter with analyzer: Special Cytometer, the first BD 2021 1987 fixed alignment and 2000 order BD[®] LSR II Flow analyzer designed from the **BD** launches **BD** 2019 analyzer-like sensitivity BD introduces four-FACSymphony[™] A5 SE Cell First to offer Cvtometer ground up to fully leverage Originally launched in 2017, in color analysis with the PerCP-Cy5.5 **BD** Horizon Analyzer, a spectral-enabled, 2016 2019 BD Lvric[™] Analvzer 9 2023 🔍 BD FACStar[™] Plus Cell Brilliant[™] Reagents high-parameter flow reagents BD launches the highbecame the first clinical flow BD launches BD FACSDiscover[™] Sorter cytometer. parameter BD cytometer with 12-color S8 with BD CellView[™] Image STREET FACSymphony[™] A5 Cell capability. The system offers Technology and BD SpectralFX[™] 2000 Analvzer unparalleled standardization Technology, the first real-time BD launches BD^{*} 1985 and assay portability with imaging, spectral flow sorter with **Cvtometric Bead** First three-color and BD introduces a second novel features such as sort-capable image analysis. Array to quantify 2003 🔍 first fixed-alignment universal setup. color for the violet laser: ₫ 2015 flow cytometer:

BD launches BD OneFlow[™]

multiple proteins simultaneously on a BD FACScan[™] Flow flow cytometer

BD introduces BD Phosflow[™] Reagents, which enable activation state analysis in rare

BD Horizon[™] V500 Dye subpopulations

> 2013 BD launches the BD LSRFortessa[™] X-20 Flow Cvtometer



improving care for lymphoma and leukemia patients by ensuring standardization of testing.



2017 BD launches the BD

Rhapsody[™] System, a platform for single-cell multiomics that enables the ability to interrogate both protein and RNA in single cells simultaneously.

2019 BD launches highparameter BD FACSymphony[™] S6 Cell Sorter.

answer solution.

Launched in 2019, in

combination with the BD

true walkaway sample-to-

FACSLyric[™] Analyzer, the BD

FACSDuet[™] System is the first

2019



BD launches BD FACSDuet[™] Premium System that provides a complete walkaway workflow solution offering automatic sample transfer through physical integration with the BD



Cytometer

BD RESTRICTED

Major fields of regenerative medicine



Stem Cells





• Stem cells are undifferentiated biological cells that can differentiate into specialized cells and can divide to produce more stem cells.





Application of FCM in Stem Cell Research

- Immunophenotypic characterization of stem cells during maintenance and derivation
- Genetic manipulation
- Stem cell enrichment by FACS sorting
- Cell replacement therapies (animal models)



Immunophenotyping

- Immunophenotyping is a cellular analysis method for the identification of biomarkers and their expression/co-expression profiles using directly- or indirectly-fluorochrome conjugated antibodies and an analyzer such as a flow cytometer or imaging system.
- The identification of biomarkers using immunophenotyping methods facilitates the characterization of a cell type, its identification, and its isolation.
- Identification of cell subpopulations:
 - Cells suitable for transplantation
 - Tumor initiating cells



Immunophenotyping

- Isolation of pure cell populations for downstream assays
- - Arrays/sequencing
- - In vitro disease models
- - Biochemistry
- - Transplantation
- Development of **quality control assays** for cell preparations:
- - Assessing purity
- - Identification of contaminants



Biomarkers are Crucial for Stem Cell Analysis and Isolation







S BD

Embryonic Stem Cells

• ESCs are pluripotent stem cells derived from the inner cell mass of a blastocyst. ES cells give rise during development to all derivatives of three primary germ layers: ectoderm, endoderm and mesoderm.



ESCs and iPSCs markers and products

Embryonic Ste	em Cells
Embryonic Stem Ce	ll Markers
Alkaline Phosphatase	Nanog (Human)
CD9	Nanog (Mouse)
CD15 (SSEA-1, Lewis X)	Nucleostemin
CD24	Oct3/4
CD29 (Integrin β 1)	Oct3/4A
CD30	Podocalyxin
CD49f (Integrin α 6)	Podocalyxin Associated
CD133 (AC133, Prominin-1)	Keratin Sulfate
CD194 (CCR4)	PRC2 (Suz12)
CD324 (E-Cadherin)	Rex-1
CD326 (EpCAM)	Ronin
CD338 (ABCG2)	SFRP2
c-Myc	Smad2/3
Cripto	Sox2
DPPA4	SSEA-3
DPPA5 (ESG1)	SSEA-4
FGF-4	SSEA-5
FoxD3	STAT3
Frizzled-5	STAT3 (pS727)
GCNF (NR6A1)	STAT3 (pY705)
GCTM-2	STAT3-interacting protein 1
GDF-3	TRA-1-60 Antigen
Hsp27	TRA-1-81 Antigen
Lefty-A	UTF-1
Lin-28	Zic3
Induced Pluripoten	cy Markers
c-Myc	Nanog
KLF4	Oct3/4
Lin-28	Sox2

Cat.No	Description	Component
560461	BD Stemflow [™] Human Pluripotent Stem Cell Sorting And Analysis Kit	SSEA-1, SSEA-3, TRA-1-81
560477	BD Stemflow [™] Human And Mouse Pluripotent Stem Cell Analysis Kit	Oct3/4, SSEA-1, SSEA-4
560589	BD Stemflow [™] Human Pluripotent Stem Cell Transcription Factor Analysis Kit	Nanog, Oct3/4, Sox2
560585	BD Stemflow [™] Mouse Pluripotent Stem Cell Transcription Factor Analysis Kit	Nanog, Oct3/4, Sox2
563398	BD Pharmingen [™] PE Mouse anti-Human Lin-28	
563753	BD Pharmingen [™] Alexa Fluor® 647 Mouse Anti-Human SSEA-5	
562740	BD Horizon [™] BV421 Mouse Anti-Human CD338	

BD Stemflow[™] Pluripotent Stem Cell Kits



	Species	Antibodies	Cell Surface Analysis	Intracellular Analysis	Sorting	Drop-ins	GFP
Human Pluripotent Stem Cell Sorting and Analysis Kit (Cat. No. 560461)	Hu	SSEA-1 FITC SSEA-3 PE Tra-1-81 Alexa Fluor® 647	1		*	*	
Human and Mouse Pluripotent Stem Cell Analysis Kit (Cat. No. 560477)	Hu/Ms	SSEA-1 PE Oct3/4 PerCP-Cy™5.5 SSEA-4 Alexa Fluor® 647	*	*		*	~
Human Pluripotent Stem Cell Transcription Factor Analysis Kit (Cat. No. 560589)	Hu	hNanog PE Oct3/4 PerCP-Cy™5.5 Sox2 Alexa Fluor® 647		1		*	~
Mouse Pluripotent Stem Cell Transcription Factor Analysis Kit (Cat. No. 560585)	Ms	mNanog PE Oct3/4 PerCP-Cy™5.5 Sox2 Alexa Fluor® 647		1		~	~

· All pluripotent stem cell kits contain BD™ CompBead Plus compensation particles

Isotype controls

Intracellular analysis kits contain fix and perm buffers

50 tests

🍪 BD

H9 cell sorting using Human Pluripotent Stem Cell Sorting and Analysis Kit





Gating strategy for Cat.No 560461 on BD FACSAria II

H9 cells cultured 4 days post-sorted, using BD FACSAria II, 25PSI, 100 micron nozzle



BD

Neural Stem Cells

NSCs are self-renewing, multipotent cells that generate the main phenotype of the nervous system. NSCs primarily differentiate into neurons, astrocytes and oligodendrocytes.



NSCs markers and products

Neural Stem Cell N	larkers
A2B5	CD349 (
BMI-1	Ki-67
CD15 (SSEA-1, Lewis X)	MSI1 (N
CD15s (Sialyl Lewis x)	MSI2 (N
CD24	Nanog (
CD29 (Integrin β1)	Nestin
CD49f (Integrin α 6)	Noggin
CD54 (ICAM-1)	Notch1
CD81 (TAPA-1)	Pax-6
CD95 (Fas/APO-1)	Promini
CD133 (AC133, Prominin-1)	PSA-NC
CD146 (MCAM, MUC18)	Sox1
CD184 (CXCR4)	Sox2
CD271 (p75, NGFR/NTR)	Vimenti
CD338 (ABCG2)	

CD349 (Frizzled-9) Ki-67 MSI1 (Musashi-1) MSI2 (Musashi-2) Nanog (Mouse) Nestin Noggin Notch1 Pax-6 Prominin-2 **PSA-NCAM** Sox1 Sox2 Vimentin

Cat.No	Description	Component		
562271	BD Stemflow [™] Human Neural Cell Sorting Kit	CD24, CD271, CD44, CD15, CD184		
561526	BD Stemflow [™] Human Neural Lineage Analysis Kit	Sox2, GFAP, Doublecortin, Nestin, Ki-67, Sox1, CD44		
560393	BD Pharmingen [™] Alexa Fluor [®] 647 Mouse Anti-Nestin			
564685	BD Horizon [™] BB515 Mouse Anti-Human CD54			
562337	BD Pharmingen [™] PE Mouse Anti-Human Vin	nentin		

BD Stemflow[™] Neural Stem Cell Kits



	Antibodies	Cell Surface Analysis	Intracellular Analysis	Sorting	Drop-ins	GFP
Human Neural Lineage Analysis Kit (Cat. No. 561526) 25 tests	CD44 FITC Ki-67 Alexa Fluor® 488 Doublecortin PE Sox1 PerCP-Cy™5.5 Sox2 PerCP-Cy™5.5 GFAP Alexa Fluor® 647 Nestin Alexa Fluor® 647		*		~	
Human Neural Cell Sorting Kit (Cat. No. 562271) 20 tests	CD24 PE CD271 PerCP-Cy™5.5 CD44 PerCP-Cy™5.5 CD15 PE-Cy7 CD184 APC	*		*	*	•

Neural Cell population identified using Human Neural Lineage Analysis Kit

Cat.No	Specificity	Clone	Molecule	Population identified
	CD44	G44-26	H-CAM	Glial cells, astrocytes, astrocyte precursors
561526	Ki-67	B56	Nuclear proliferation marker	All proliferating cell types
BD Stemflow [™] Human Neural	Doublecortin	30/Doublecortin	Neuron filament	Immature post-mitotic neurons
	Sox2	030-678	Transcription Factor	Glial cells, embryonic and neural stem cells
Lineage Analysis Kit	Sox1	N23-844	Transcription Factor	Glial cells and neural stem cells
	GFAP	1B4	Filament	Astrocytes
	Nestin	25/Nestin	Filament	Glial cells, astrocytes, embryonic and neural stem cells

Sorting NSC from differentiating hESC using same antibodies in NSC Sorting Kit





Plos ONE, March 2011, Vol 6, Issue 3, e17540



Four color intracellular staining of CD184⁺CD271⁻CD44⁻ CD24⁺ NSC at 3th passage post-sorted



Proliferation assay with post-sorted NSCs



Mesenchymal Stem Cells

MSCs are multipotent stromal cells that can differentiate into a variety of cell types, including: osteoblasts (bone cells), chondrocytes (cartilage cells), myocytes (muscle cells) and adipocytes (fat cells).



MSC Definition



Cytotherapy (2006) Vol. 8, No. 4, 315-317



POSITION PAPER Minimal criteria for defining multipotent mesenchymal stromal cells. The International Society for Cellular Therapy position statement

M Dominici¹, K Le Blanc², I Mueller³, I Slaper-Cortenbach⁴, FC Marini⁵, DS Krause⁶, RJ Deans⁷, A Keating⁸, DJ Prockop⁹ and EM Horwitz¹⁰

- MSCs must be plastic adherent
- MSCs must express CD73, CD105 and CD90 and lack expression of CD45, CD34, CD14, CD11b, CD79a and CD19
- MSCs must differentiate into osteoblasts, adipocytes and chondrocytes in vitro

MSCs markers

Mesenchymal Ster	n Cell Markers (Bone Ma	arrow)		Mesenchymal Sten	n Cell Markers (Fat)
Negative Markers		Positive Markers		Negative Markers	
CD11a (Integrin αL chain) CD11b (Integrin αM chain) CD14 CD19 CD31 (PECAM1)	CD34 (Mucosialin, gp 105-120) CD45 (Leukocyte Common Antigen, Ly-5) CD79a HLA-DR	CD10 CD13 CD14 CD15 (SSEA-1, Lewis X) CD29 (Integrin β1) CD44 (Pgp-1, H-CAM) CD49d (Integrin α4)	CD117 (SCF R, c-kit) CD120a (TNF Receptor Type I) CD120b (TNF Receptor Type II) CD146 CD166 CD166 (ALCAM) CD271 (p75, NGFR/NTR)	CD11b (Integrin αM chain) CD14 CD19 CD45 (Leukocyte Common Antigen, Ly-5) <u>Positive Markers</u>	CD79a CD117 (SCF R, c-kit) HLA-DR
		CD49e (Integrin α5) CD51 (Integrin αV) CD54 (ICAM-1) CD56 (NCAM) CD71 (Transferrin Receptor) CD73 (Ecto-5'-nucleotidase) CD90 (Thy-1) CD105 (Endoglin) CD106 (VCAM-1)	Flk-1 (KDR, VEGF-R2, Ly-73) GD2 Ly-6A/E (Sca-1) Nucleostemin SSEA-4 STRO-1 TAZ Vimentin	CD9 CD10 CD13 CD29 (Integrin β 1) CD44 CD49d (Integrin α 4) CD49e (Integrin α 5) CD54 (ICAM-1) CD55 CD59	CD73 (Ecto-5'-nucleotidase) CD90 (Thy-1) CD105 (Endoglin) CD106 (VCAM-1) CD146 (MCAM, MUC18) CD166 (ALCAM) Fibronectin HLA I Vimentin

MSCs products

Cat.No	Description	Component
562245	BD Stemflow [™] Human MSC Analysis Kit	CD90, CD44, CD73, CD105
562530	BD Stemflow [™] PE Human Mesenchymal Stem Cell Lineage Antibody Cocktail, with Isotype Control	CD34, CD11b, CD19, CD45, HLA- DR
562496	BD Stemflow [™] Human Definitive and Pancreatic Endoderm Analysis Kit	Pax-6, PDX-1, FoxA2, Sox2, Sox17, Nanog

	Antibodies	Cell Surface Analysis	Intracellular Analysis	Sorting	Drop-ins	GFP
Human MSC Analysis Kit (Cat. No. 562245) 50 tests	MSC Positive Cocktail: CD105 PerCP- Cy5.5/CD73 APC/CD90 FITC + CD44PE MSC Negative Cocktail: CD45/CD34/CD11b/CD19/HLA-DR PE	4			*	

MSCs surface marker expression using Human MSC Analysis Kit



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-10²-10³10²

102

PE hMSC Negative Cocktail CD45/CD34/CD11b/CD19/HLA-DR PE

104



BD

Hematopoietic Stem Cells

HSCs are multipotent, selfrenewing progenitor cells that develop from mesodermal hamangioblast cells. All differentiated blood cells from the lymphoid and myeloid lineages arise from HSCs. HSCs can be found in adult bone marrow, peripheral blood and umbilical cord blood.



HSC phenotyping



HSCs markers

Hematopoietic Stem Cell Markers

Negative Markers

CD2	CD24
CD3	CD33
CD4	CD36
CD7	CD38
CD8	CD45 (Leukocyte Common
CD10	Antigen, Ly-5)
CD11b	CD45R (B220)
CD13	CD48
CD14	CD56 (NCAM)
CD15 (SSEA-1, Lewis X)	CD97
CD15s (Sialyl Lewis x)	CD114 (G-CSF Receptor)
CD16	CD138 (Syndecan-1)
CD19	CD235a
CD20	GATA3

Positive Markers

BMI-1 CaM Kinase IV CD31 (PECAM1) CD34 (Mucosialin, gp 105-120) CD40f (Integrin α6 chain) CD44 CD59 CD90 (Thy-1) CD90.1 (Thy-1.1) CD105 (Endoglin) CD106 (VCAM-1) CD117 (SCF R, c-kit) CD133 (AC133, Prominin-1) CD164 CD184 (CXCR4) CD201 (EPCR) CD202b (TIE2) CD202b (TIE2) (pY992) CD202b (TIE2) (pY1102) CD325 (N-Cadherin)

CDw93 (C1qRp) CDw338 (ABCG2) DAZL Flk-1 (KDR, VEGF-R2, Ly-73) F0X01 G-CSF Gfi-1 HOXB4 Jak2 Lmo2 Ly-6A/E (Sca-1) MRP1 NF-YA Notch1 P-glycoprotein Runx1 (CBFA2) Sox7 Tal (SCL) WASP (Wiskott-Aldrich Syndrome Protein)

HSCs products

Cat.No	Description	Component
560492	BD Stemflow [™] Mouse Hematopoietic Stem Cell Isolation Kit	CD34, c-Kit, Sca-1, Lineage cocktail, Fc block, 7-AAD
562722	BD Pharmingen [™] Human Lineage Cocktail 4 (lin 4)	CD2, CD3, CD4, CD7, CD8, CD10, CD11b, CD14, CD19, CD20, CD56, CD235a

	Antibodies	Cell Surface Analysis	Intracellular Analysis	Sorting	Drop-ins	GFP
Mouse HSC Isolation Kit (Cat. No. 560492) 100 tests (10 sorts of the bone marrow pooled from 10 mice)	CD177 (c-Kit) PE CD34 FITC Sca-1 PE-Cy7 Lineage cocktail APC	*		*	*	

Sorting mHSCs from BM using Mouse HSC Isolation Kit



н G Lin/c-Kit*/Sca-1* (KLS) Tube: pre sort BM Population %Parent %Total #Events All Events - Sunt **#* 100.0 P1 539.289 90.0 90.0 P7 93.2 P2 502.685 83.9 2 97.7 82.0 491,074 487,311 99.2 81.4 0 77,910 13.0 16.0 1,827 2.3 0.3 10 105 -🖾 P7 129 7.1 0.0 CD34 FITC

Gating strategy for sorting KSL/CD34^{-/dim} cells using BD Stemflow[™] Mouse Hematopoietic Stem Cell Isolation Kit

LT-HSCs phenotyping



Frozen human cord blood mononuclear cells were enriched using BD IMag human lineage cell depletion set(Cat.No. 560030), stained with antibodies, 7-AAD and **BD** Pharmingen Human Lineage Cocktail 4 Kit (Cat.No. 562722), and acquired and analyzed on BD LSRFortessa flow cytometer.



How to identify surface marker signatures of Stem Cells and their derivatives outside hematopoiesis?

> Enythrocyte (Red Blood Cell

BD Lyoplate Screening Panels

• Comprehensive system available for efficient profiling of hundreds of murine and human cell surface makers by flow cytometry





Cat.No.	Description	Contents	Size
560747	BD Lyoplate Human Cell Surface Marker Screening Panel	242 markers	5 tests
562208	BD Lyoplate Mouse Cell Surface Marker Screening Panel	176 markers	5 tests

hESC and NSC surface marker screening using Lyoplate





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Hit verification

Hits from

hESCs and NSCs surface marker screening using BD Lyoplate Human Cell Surface Marker Screening Panel (Cat.No. 560747), and potential positive candidates were verified using flow cytometry and bioimaging. Data acquired and analyzed on BD LSR II with HTS. *Plos ONE*, March 2011, Vol 6, Issue 3, e17540

Other things should be considered in Stem Cell analysis and sorting



Using IMag enrichment before stem cell soring increases purity and reduces time of sorting



560030 BD IMag[™] Human Lineage Cell Depletion Set -DM CD3, CD14, CD16, CD19, CD41a, CD56, CD235a

Sec. BD

Using Accutase for Stem Cell detachment

Accutase is a cell detachment solution comprised of collagenolytic and proteolytic emzymes and does not contain mammalian or bacterial derived products. Accutase is a replacement for trypsin solution and performs well when detaching cells for the analysis of many cell surface markers using flow cytometry and for cell sorting.



H9 human ES cells were detached with Accutase Cell Detachment Solution and then stained with pluripotency markers on BD LSR II flow cytometer.

Cat.No.	Description
561527	BD [™] Accutase [™] Cell Detachment Solution

Cell Derivatives

Exosomes



Exosome function and role

- The mRNA, microRNA, and other substances contained in exosomes play an important role in cell-to-cell interactions and are related to cancer cell metastasis.
- exosomes isolated from platelets can enhance the tissue invasion ability of the A549 (human lung cancer) cell line.
- Exosomes can be used as drug or mRNA carriers to treat diseases.
- The size of exosomes is about 40-150 nm, and their heterogeneity and low refractive index make them difficult to detect with traditional flow cytometry.



Zhang et al., 2015

BD Flow cytometers in the field of exosome research







BD FACSLyric[™] Analyzer

FACSymphony A1[™] Analyzer

FACSDiscover[™] S8 Cell Sorter + Image

Advantages of Flow Cytometry in Exosome Analysis

• Particle analysis

 Small particle detectors can rapidly detect thousands of single cells or particles per second, quickly obtaining single particle information



- Multicolor fluorescence labeling
- Using multicolor antibodies or membrane protein dyes to simultaneously analyze exosome purity (CD9/CD63/CD81) and exosomes from different sources



- Immune monitor or cytology after the action of exosomes
- Changes in immune cell morphology, cytokines, and cell activation and apoptosis influenced by exosomes



FACSLyric small particle detection



Mixture of all size

Using blue laser (488 nm) FSC and SSC, particles of 130 nm can be analyzed. Testing of the FACSLyric has shown that it can distinguish particles of 130 nm. This expands the analysis to microvesicles (EV), exosomes, bacteria, viruses, etc. Since small particles can be analyzed using blue laser FSC and SSC, there is no need to sacrifice a violet laser channel for VSSC.

EV/LNP related Research

IF: 17.694



ARTICLE

https://doi.org/10.1038/s41467-019-12275-6 OPEN

Linkage between endosomal escape of LNP-mRNA and loading into EVs for transport to other cells

Marco Maugeri ¹, Muhammad Nawaz ¹, Alexandros Papadimitriou¹, Annelie Angerfors ², Alessandro Camponeschi¹, Manli Na¹, Mikko Hölttä³, Pia Skantze², Svante Johansson², Martina Sundqvist ³ Johnny Lindquist³, Tomas Kjellman², Inga-Lill Mårtensson¹, Tao Jin ¹, Per Sunnerhagen ⁴, Sofia Östman⁵ Lennart Lindfors² & Hadi Valadi ¹

IF: 17.521



RESEARCH ARTICLE

www.advancedscience.com

Lipid Nanoparticles Deliver the Therapeutic VEGFA mRNA In Vitro and In Vivo and Transform Extracellular Vesicles for Their Functional Extensions

Muhammad Nawaz, Sepideh Heydarkhan-Hagvall, Benyapa Tangruksa, Hernán González-King Garibotti, Yujia Jing, Marco Maugeri, Franziska Kohl, Leif Hultin, Azadeh Reyahi, Alessandro Camponeschi, Bengt Kull, Jonas Christoffersson, Ola Grimsholm, Karin Jennbacken, Martina Sundqvist, John Wiseman, Abdel Wahad Bidar, Lennart Lindfors, Jane Synnergren, and Hadi Valadi*

Characterization of endo-EVs derived from LNP-treated cells







- LNPs are novel carriers for delivering mRNA with great potential for disease treatment.
- MC3-LNPs were used to deliver modified human erythropoietin mRNA.
- To confirm whether EVs carrying LNP-mRNA are taken up by endocytosis, CD9+CD63 EVs were analyzed using FACSLyric to observe mRNA expression.
- EVs can protect exogenous mRNA during the delivery process in vivo, thereby producing human proteins in mice, which can be detected in plasma and most organs

BD

- Marco Maugeri et al., Linkage between endosomal escape of LNP-mRNA and loading into EVs for transport to other cells
- Nature Communications. 2019. (IF: 17.694)

Thank you

