XIX CONGRESSO NAZIONALE SIES 2026

Significato patogenico dei marcatori circolanti: il ruolo delle vescicole extracellulari

Lucia Catani

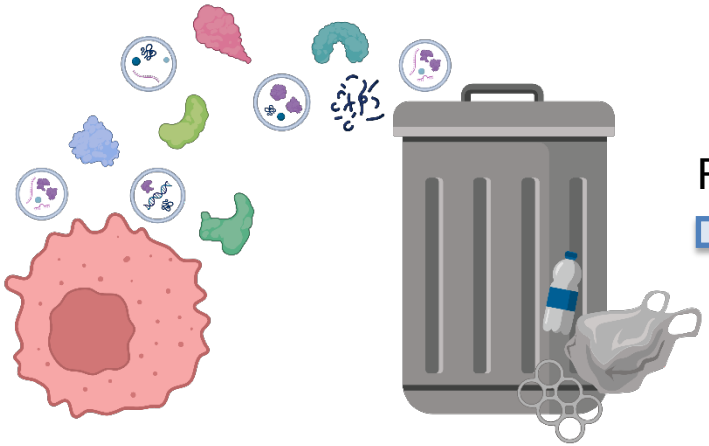
Firenze | 4-6 marzo 2026
Palazzo degli Affari

Disclosures of Lucia Catani

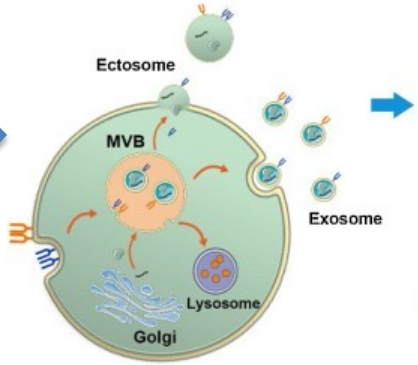
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Nessuna							

Extracellular vesicles

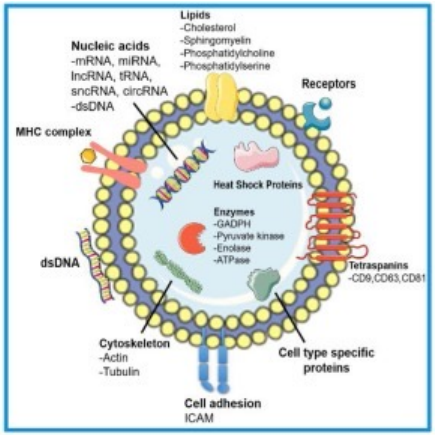
Then: 1980s view



Paradigm shift



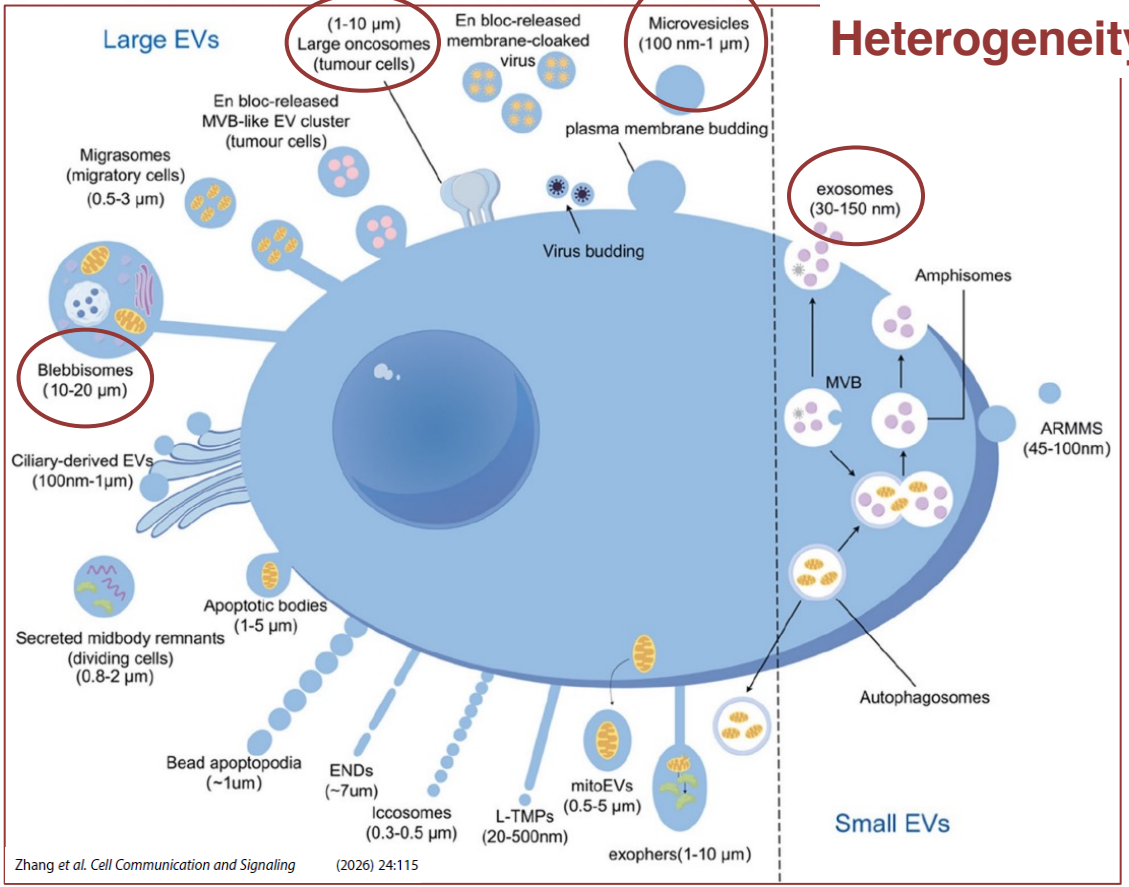
Now: 2020s view



Old view: simple garbage bags
Function: excision of unwanted components

New view: intercellular communication
Function: educate, pave, evade

Heterogeneity of extracellular vesicles (EVs)



Zhang *et al. Cell Communication and Signaling* (2026) 24:115

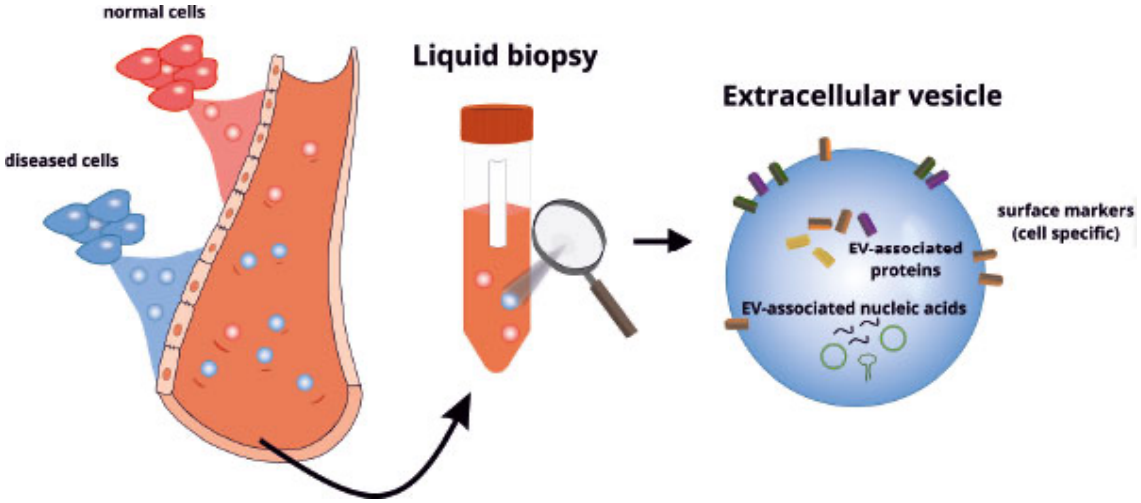
POSITION PAPER

Minimal information for studies of extracellular vesicles (MISEV2023): From basic to advanced approaches

J Extracell Vesicles. 2024;13:e12404.

https://doi.org/10.1002/jev2.12404

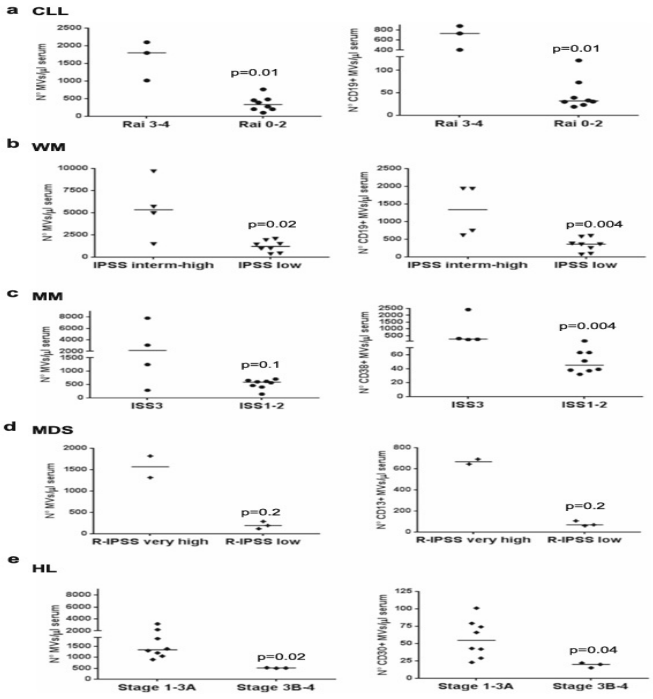
Extracellular vesicles as diagnostic and prognostic biomarkers



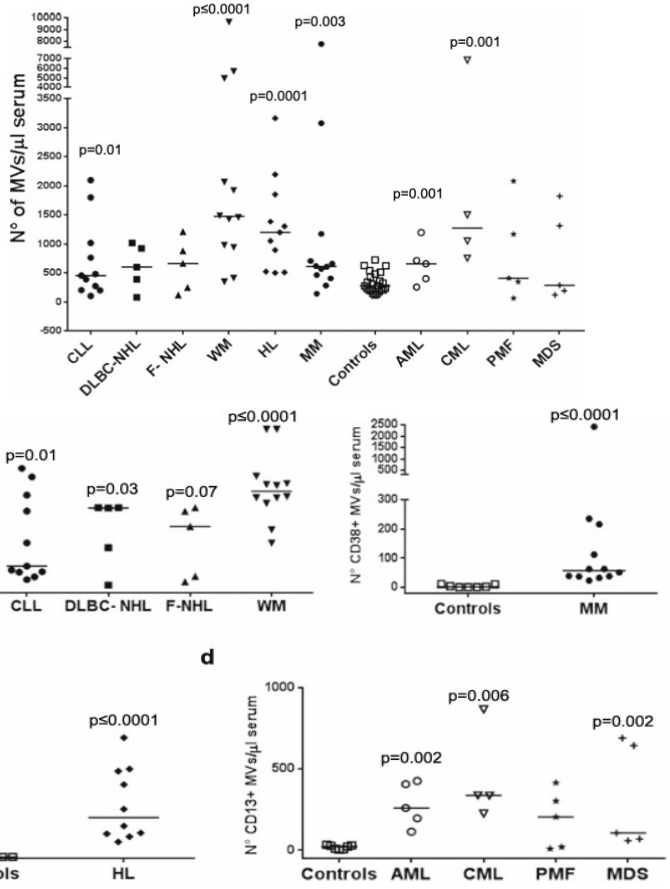
Harshman SW et al. J Proteomics 2016; Provencio M et al. Oncotarget 2017; Manier S et al. Blood 2017; Kang K-W et al. Anticancer Res 2018; Barone M et al. Br J Haematol 2019; Laurenzana I et al. Int J Nanomedicine 2021; Zhu S et al. Sci Rep 2022; Ferreira BV et al. Front Oncol 2022

❑ High serum levels of extracellular vesicles expressing malignancy-related markers in blood cancers

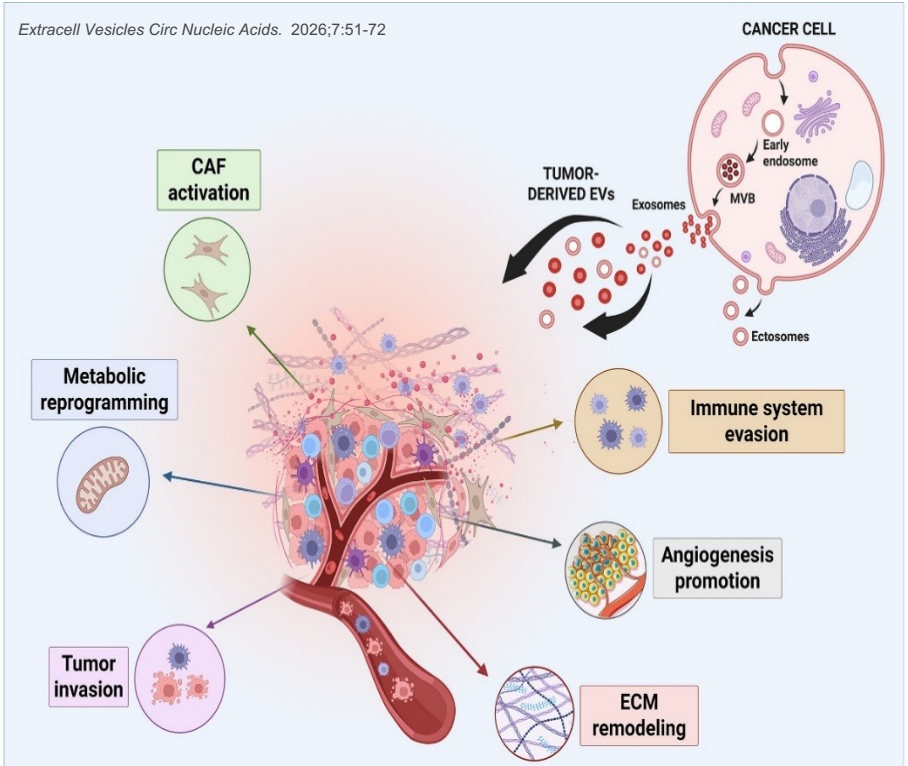
Association with EV amount and clinical features



Malignancy-related phenotype



Caivano A et al., Tumor Biology 2015

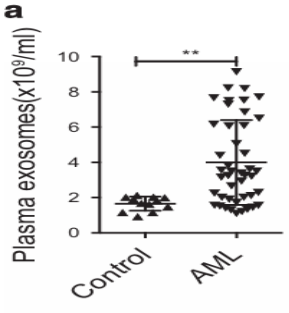


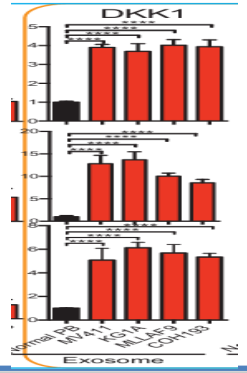
Tumor-derived extracellular vesicles *in vitro* and *in vivo* function

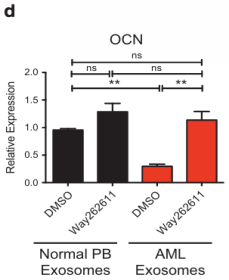
- **Microenvironment remodelling**
- **Metabolic reprogramming**
- **Immune evasion**

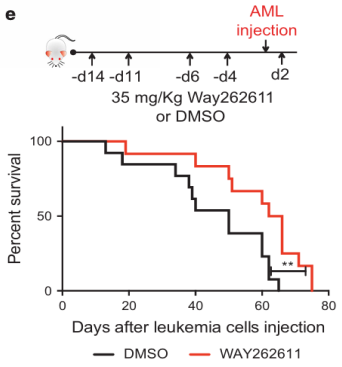
Corrado C. et al. Cancer Letters 2014; Paggetti J et al. Blood 2015; Wang J et al. J Pathology 2016; Kumar B et al. Leukemia 2018; Van Niel G. et al. Nat Rev Mol Cell Biol 2018; Chen T. et al. Life Sci 2019; Gargiulo E. et al., Cells 2019; Raimondo S et al. Cancers 2020; Laurenzana I et al. Front. Med 2021; Trino S., et al. Front Oncol 2022; Giannandrea D et al. Haematologica 2022

❑ Acute myeloid leukemia transforms the bone marrow niche into a leukemia-permissive microenvironment through exosome secretion

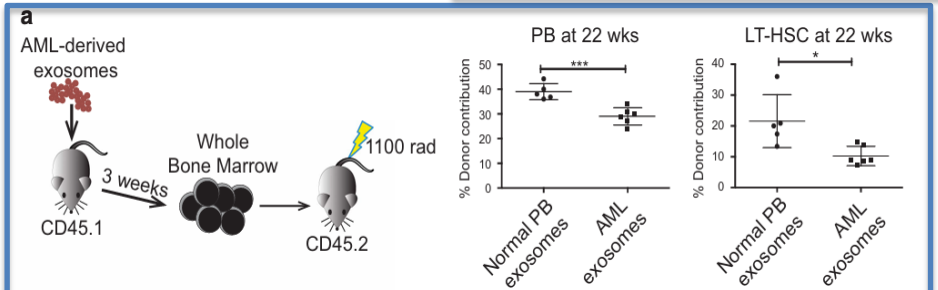




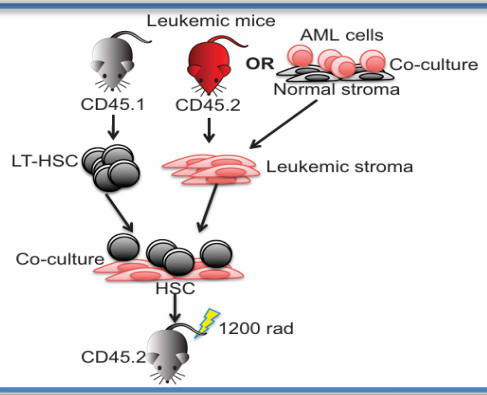


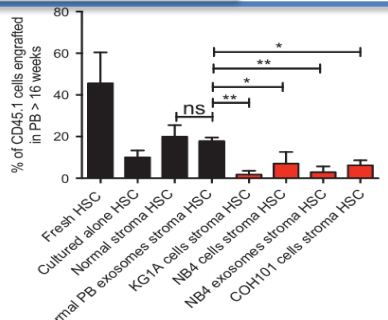


Treatment with a DKK1 inhibitor delays AML progression and prolongs survival in AML-engrafted mice



AML derived exosomes reduce hemopoietic stem cell activities

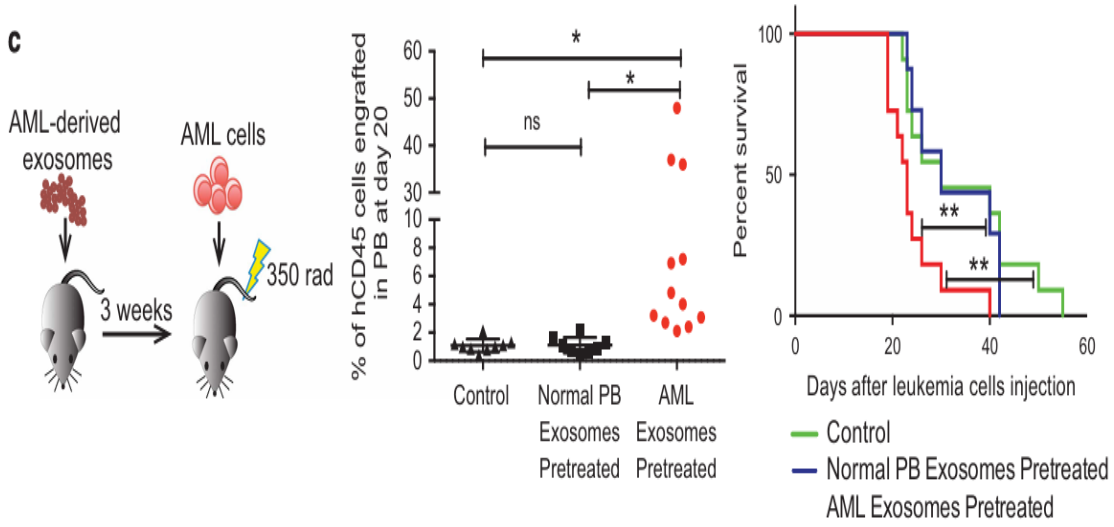




AML-derived exosomes limit ability of stroma to support normal HSCs

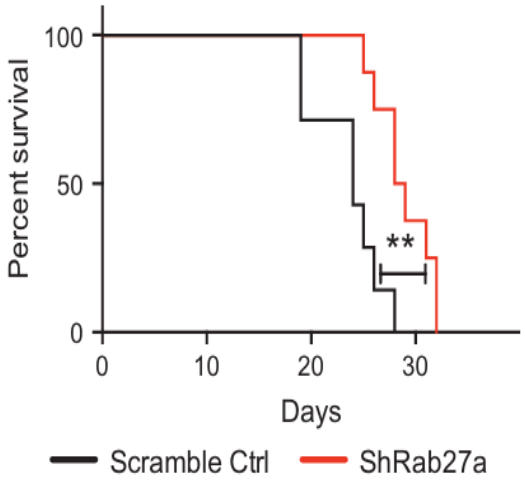
Kumar B et al. Leukemia 2018

AML-derived exosomes accelerate AML progression



AML-derived exosomes are important for transforming the composition and function of the BM niche

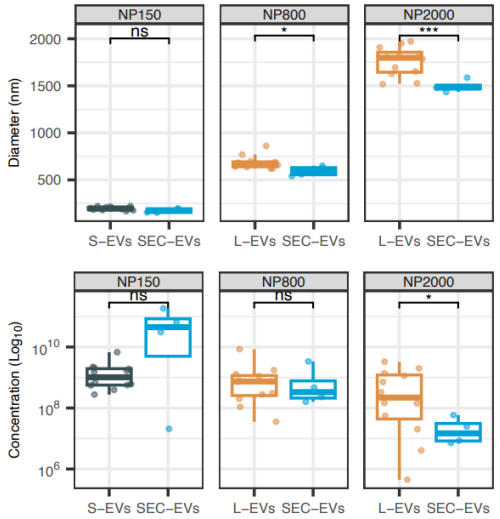
Disruption of exosome production delays AML progression



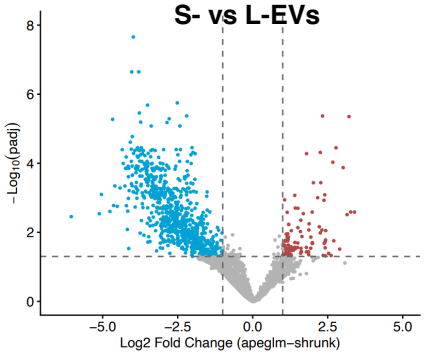
Kumar B et al. Leukemia 2018

❑ Circulating Small and Large Extracellular Vesicles of Diffuse Large B-Cell Lymphoma Originate from Different Cell Types of the Tumor Microenvironment

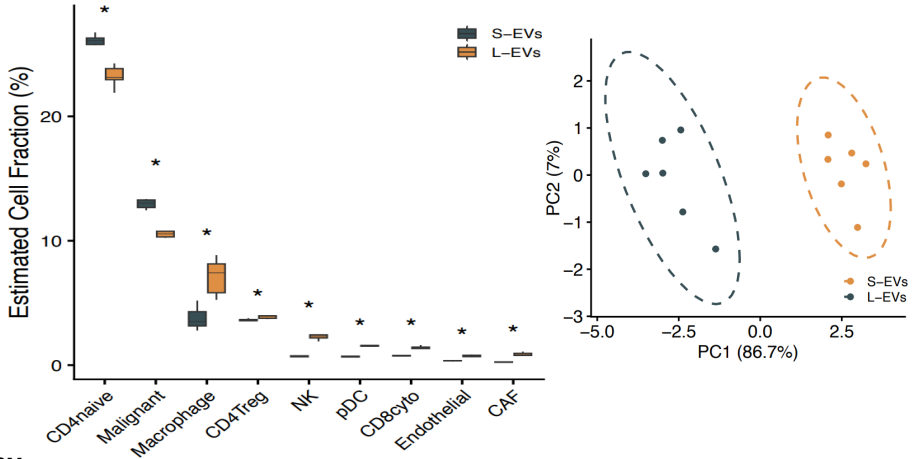
TRPS analysis



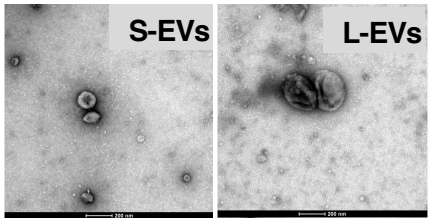
mRNA sequencing

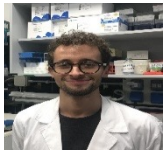


Transcriptomic deconvolution analysis



Transmission Electron Microscopy



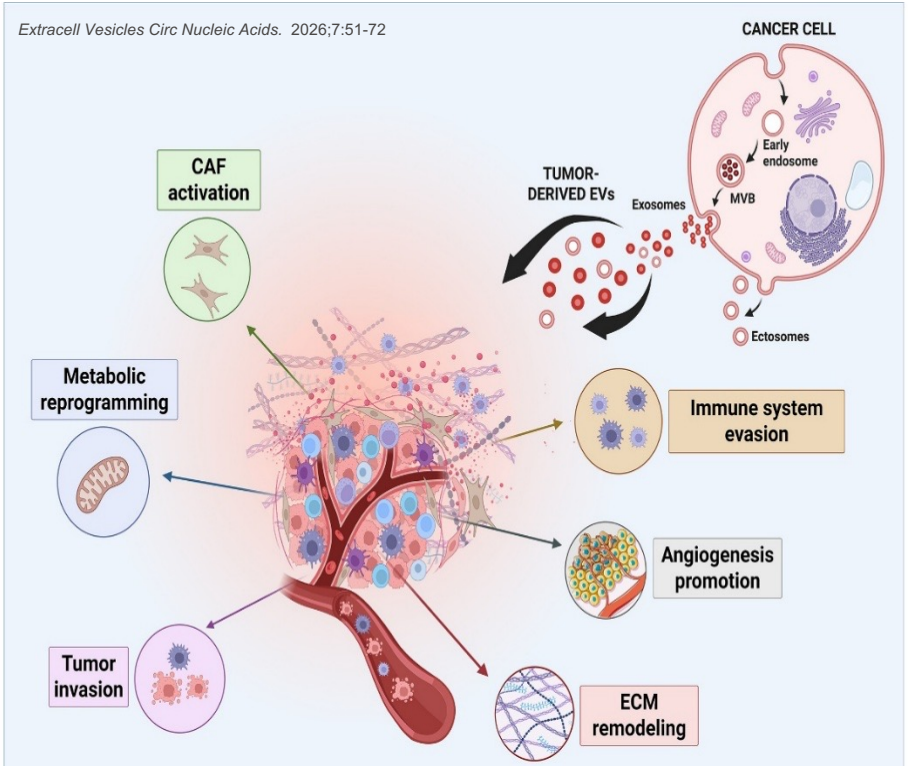


Filippo Maltoni

S-EVs Small extracellular vesicles
L-EVs Large extracellular vesicles

S-EVs are predominantly of malignant B cell origin, whereas L-EVs derive from cellular components of the tumor microenvironment (macrophages, NK cells, dendritic cells, fibroblasts)

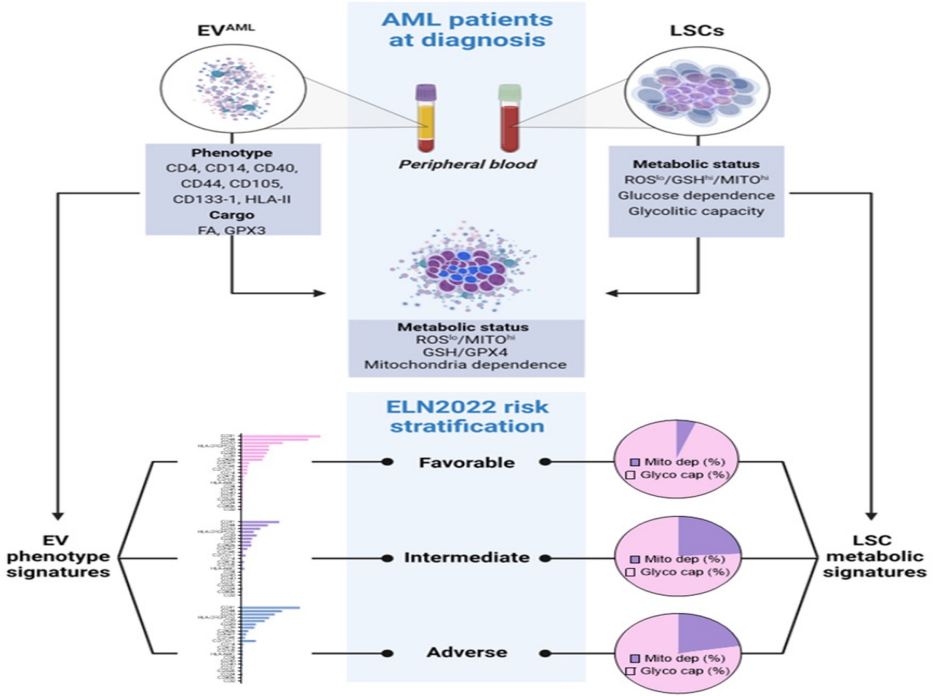
(Maltoni, Wang et al. Journal of Extracellular Vesicles accepted for publication)



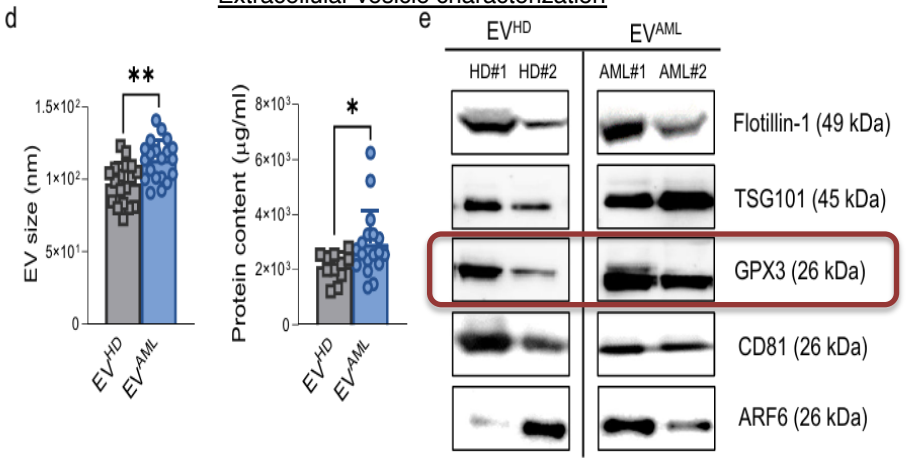
Tumor-derived extracellular vesicles *in vitro* and *in vivo* function

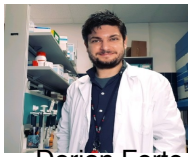
- Microenvironment remodelling
- **Metabolic reprogramming**
- Immune evasion

❑ Parallel Single-cell Metabolic Analysis and Extracellular Vesicle Profiling Reveal Vulnerabilities with Prognostic Significance in AML



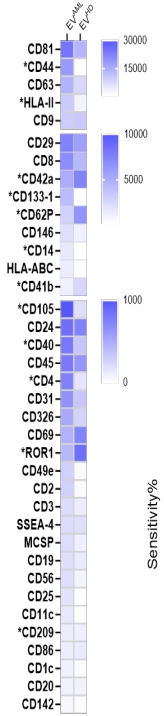
Extracellular vesicle characterization





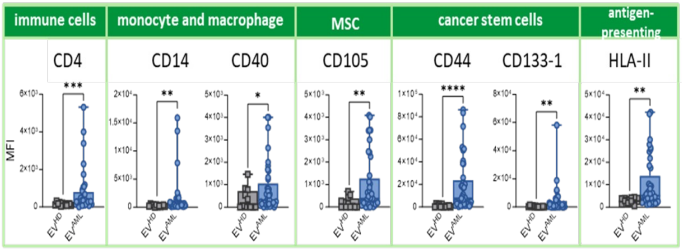
Dorian Forte

Multiplex protein analysis on EVAML reveals prognostic significance

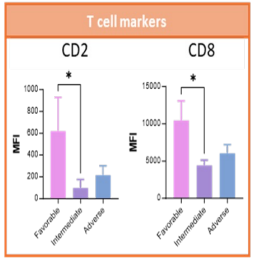


- Bead-based multiplex EV analysis by flow cytometry

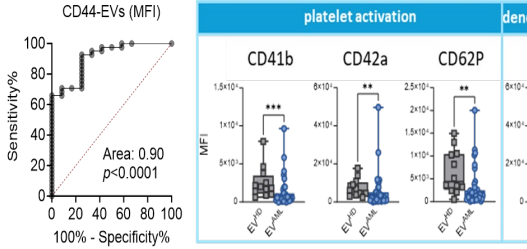
▶ Up-regulated in EV^{AML} vs EV^{HD}

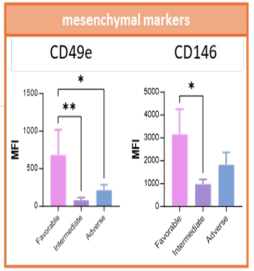


▶ EV^{AML} stratified by ELN2022 risk

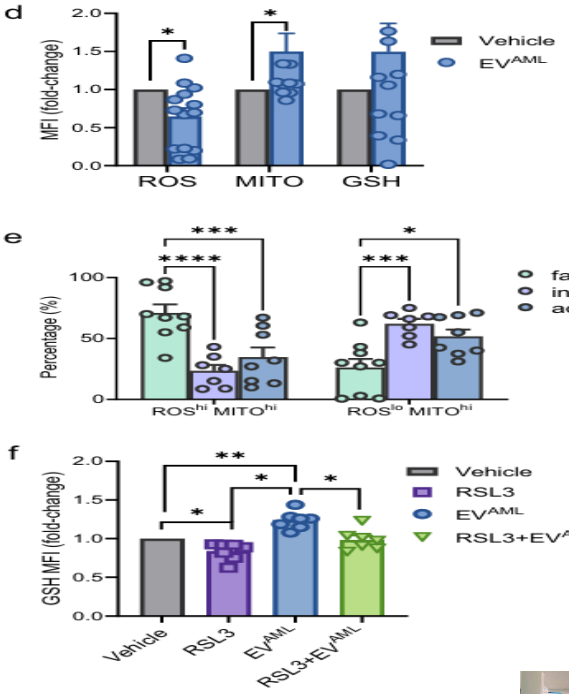


▶ Down-regulated in EV^{AML} vs EV^{HD}

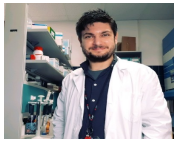




N=41 AML vs 12 HD



Extracellular vesicles enhance mitochondrial functionality and dependence on CD34+ AML cells via the glutathione/GPX4 axis

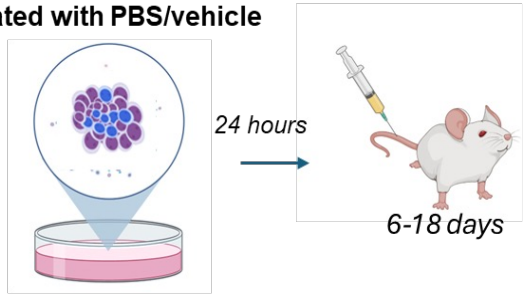


Dorian Forte

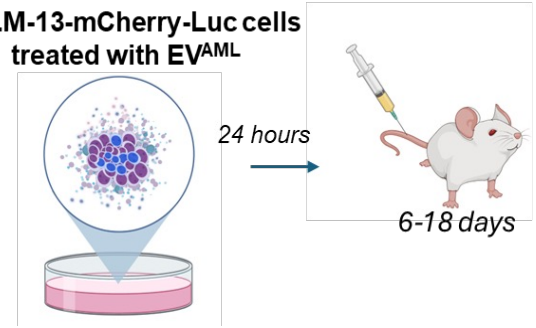
Extracellular vesicles from adverse-risk patients enhance leukemia cell engraftment *in vivo*

- *Leukemia xenograft assay*

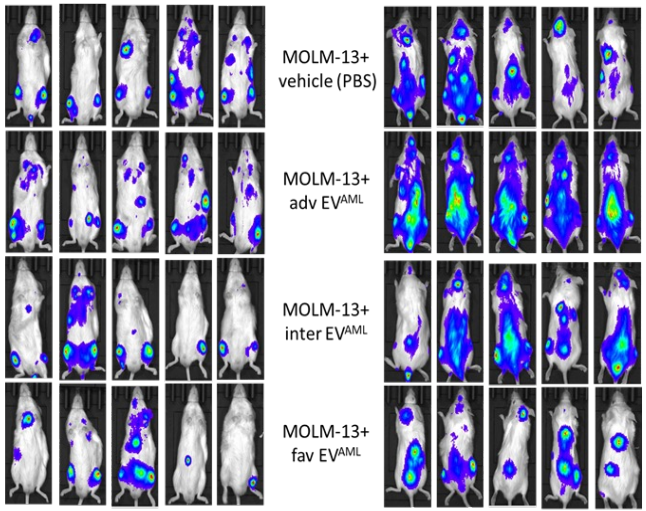
MOLM13-mCherry-Luc cells treated with PBS/vehicle

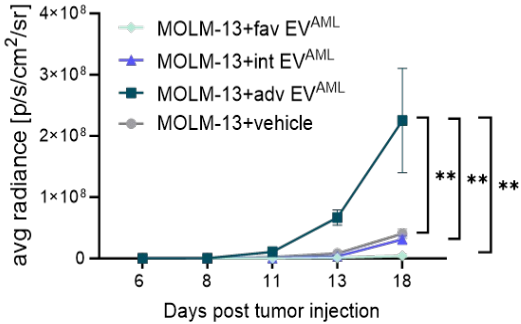


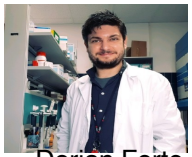
MOLM-13-mCherry-Luc cells treated with EV^{AML}



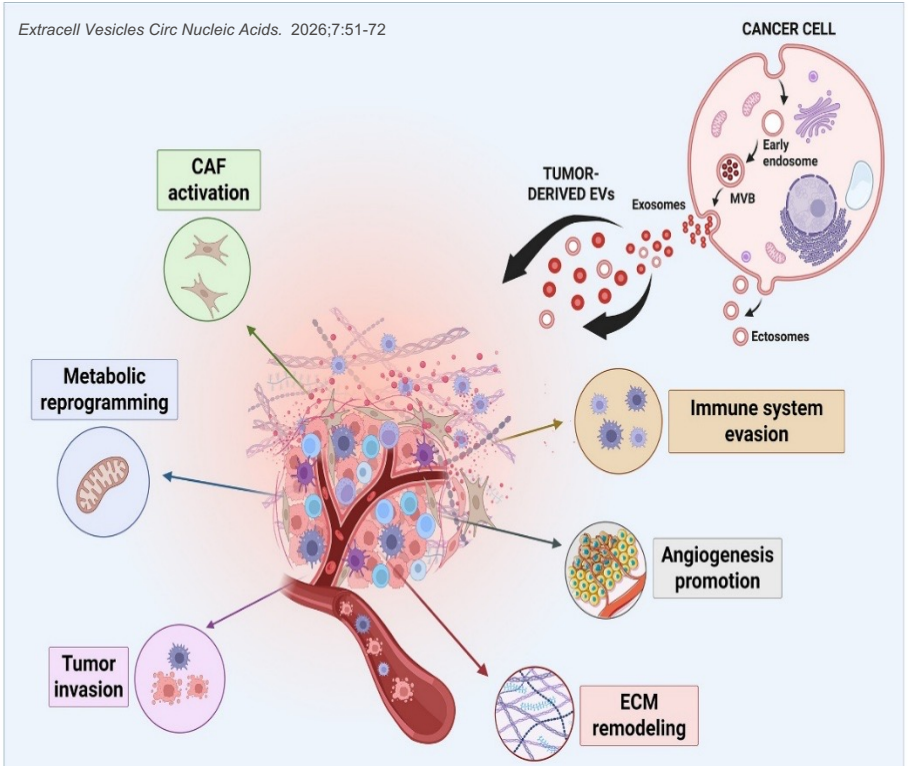
- *Bioluminescence imaging*







Dorian Forte



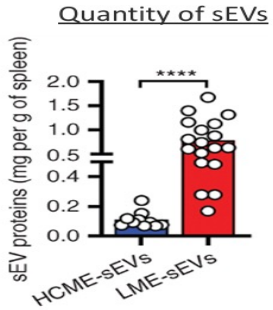
Tumor-derived extracellular vesicles *in vitro* and *in vivo* function

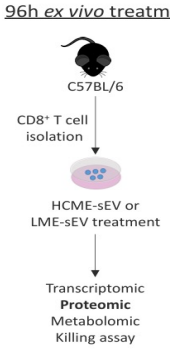
- Microenvironment remodelling
- Metabolic reprogramming
- **Immune evasion**

Wang J et al. Oncotarget 2015; Smallwood DT. Et al. Blood 2016; Jafarzadeh N et al. J Cell Physiol 2019; Bottcher M et al. Cells 2022; Lopes R et al. Front Immunol 2022; Gargiulo E et al. Blood Cancer Discov 2022

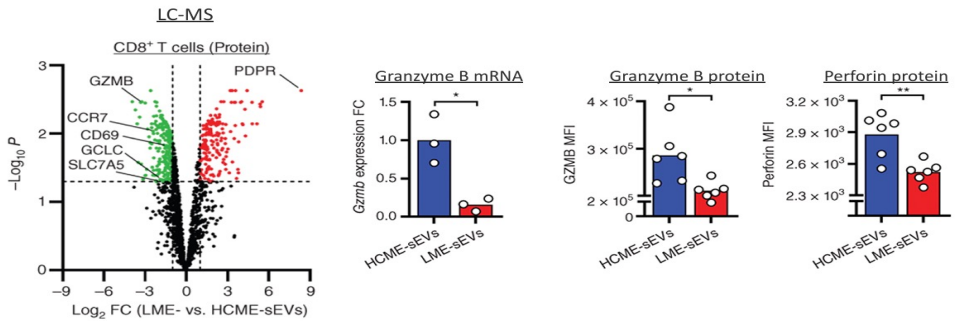
❑ Extracellular vesicles promote an immunosuppressive and CLL supportive microenvironment

sEVs Are Enriched in the Leukemia Microenvironment

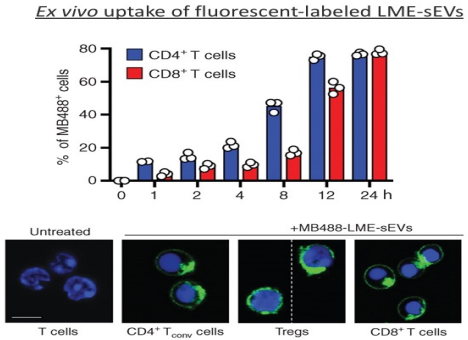




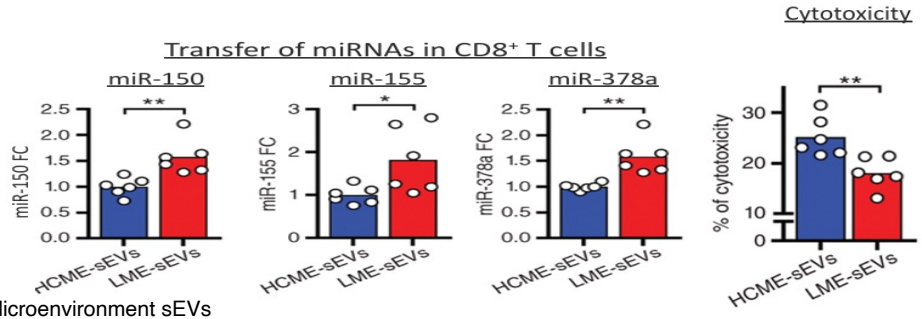
LME-sEVs Alter CD8+ T cell Immune Functionality ex vivo



LME-sEVs Enter Different T-cell Subsets in the Spleen



LME-sEVs Alter CD8+ T cell Immune Functionality by miRNAs Transfer

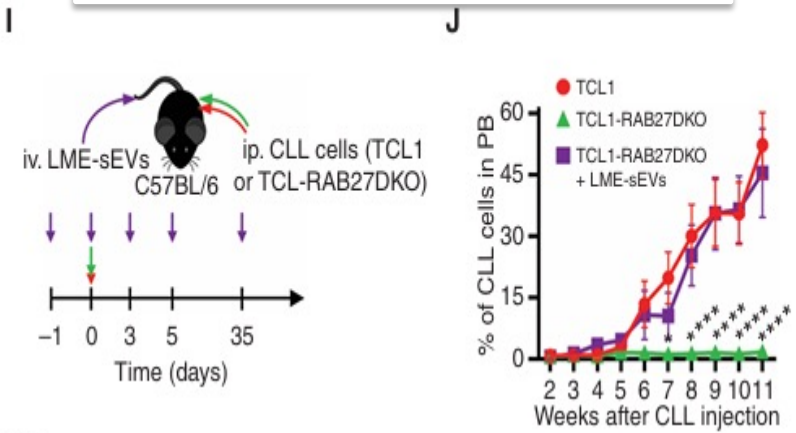


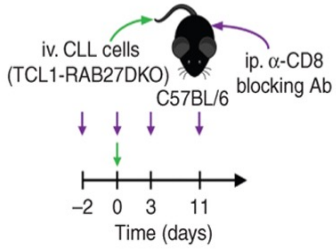
LME-sEVs – Leukemia Microenvironment sEVs
HCME-sEVs – Healthy Control Microenvironment sEVs

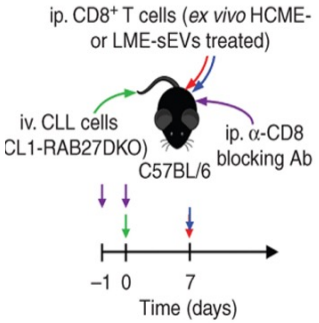
Gargiulo et al. Blood Cancer Discovery 2023

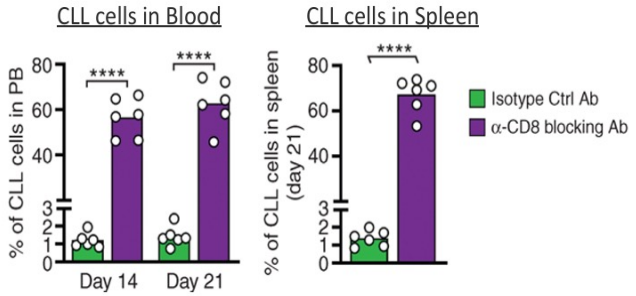
sEVs Are Crucial for CLL Development *in vivo by impairing the antitumor immune response*

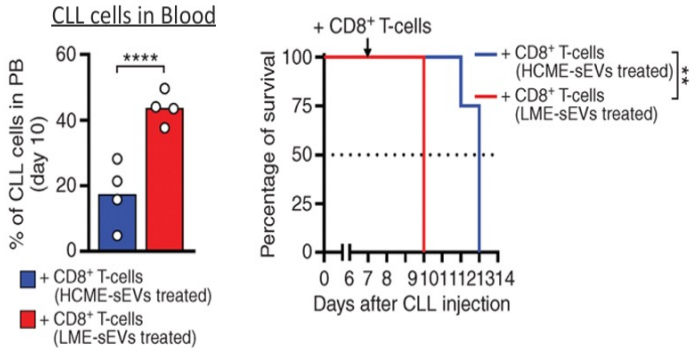
Impact of LME-sEVs on CLL development







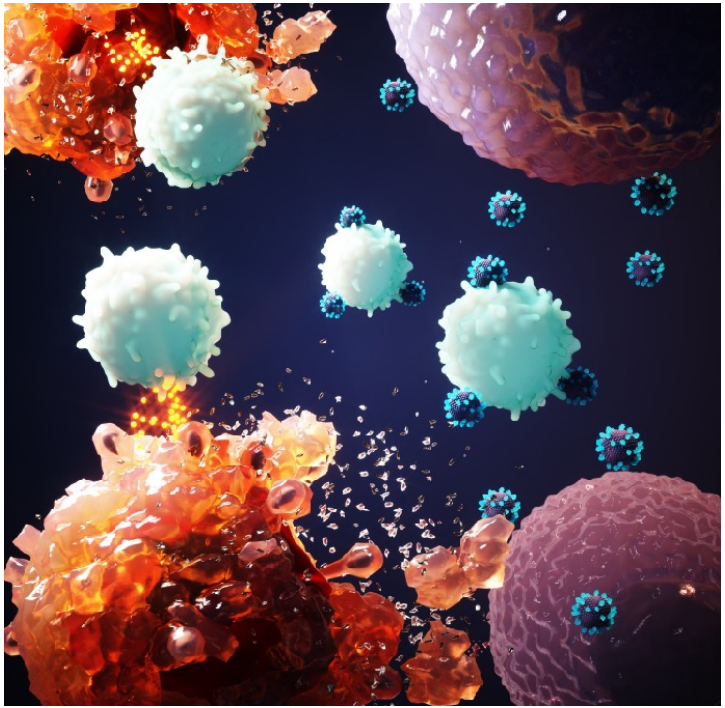




LME-sEVs – Leukemia Microenvironment sEVs
HCME-sEVs – Healthy Control Microenvironment sEVs

Gargiulo et al. Blood Cancer Discovery 2023

Highlights



- Extracellular vesicles are source of information on blood cancer biology with the potential as **diagnostic and prognostic biomarkers** to guide the management of patients with hematological malignancies
- Extracellular vesicles are able to interact with the **tumor microenvironment** and non-malignant cells to **"educate"** the microenvironment and promote malignancy

§No blood-based biomarker is yet approved for blood cancer screening or diagnosis

§Extracellular vesicles show strong diagnostic and prognostic promise but need large-scale validation

§Extracellular vesicles can be engineered and have clinical utility as next generation drug delivery platforms for therapeutics

§Technological advances and improved integration of omics may enable early tumor detection in the future

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