Extracellular vesicles, cancer and therapeutic applications

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COST ACTION CA 17140 – NANO2CLINIC
Working group 3 workshop
Preclinical Development of Cancer Nanomedicines: State of the Art and Future Perspectives
March 24-25th 2022, Institute of Oncology Research-IOR, Bellinzona, CH

COST ACTION CA 17140
NANO2CLINIC
CANCER NANOMEDICINE - FROM THE BENCH TO THE BEDSIDE

cost
EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

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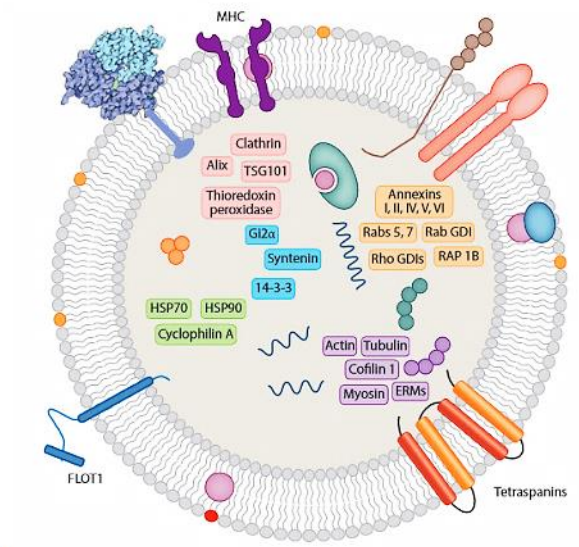
Extracellular vesicles (EVs)

- EVs are phospholipid bilayer-enclosed vesicles secreted by all cell types.
- Generated by multivesicular bodies (MVBs) or direct budding of the plasma membrane.
- Biologic function: cell-to-cell communication both in physiological and pathological conditions.
- Clinical applications of EVs:
  - Biomarkers,
  - Drug delivery vehicles.

EVs cargo



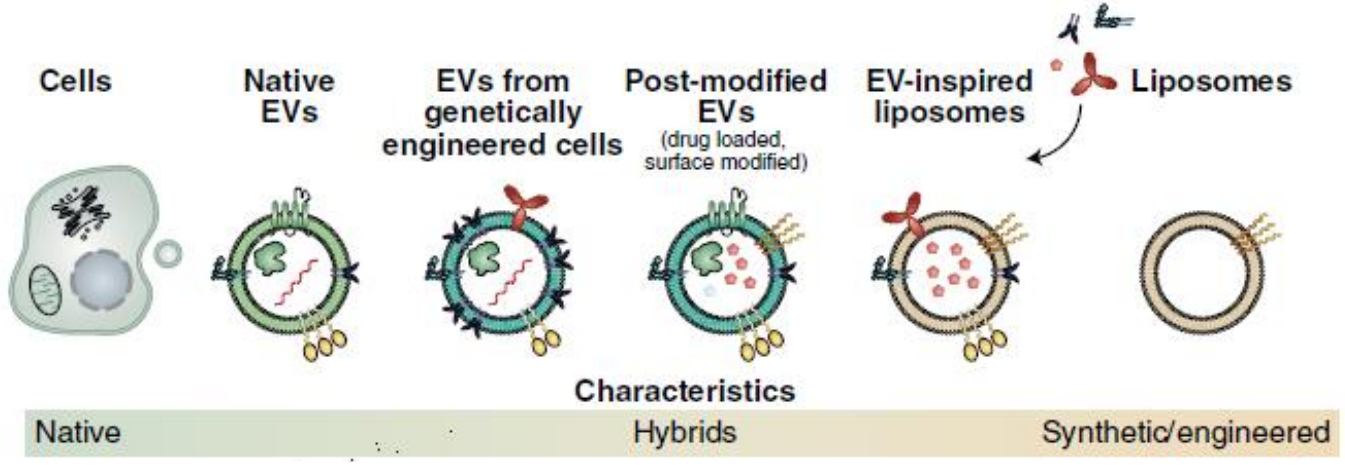
Kourembanas, 2015

DNA	Genomic and mitochondrial
RNA	mRNA, tRNA, rRNA, miRNA, small nuclear and small nucleolar RNA
Proteins	Biogenesis-related proteins, vesicular proteins and cell-type specific proteins
Lipids	Cholesterol, sphingomyelin, glycosphingolipids, phosphatidylserine
Signaling molecules	ALIX, syntenin, cofilin, annexin, RAB, cytokines

Native EVs

Advantages of natural EVs

- Cross the blood-brain barrier (BBB)
- Have long lasting effects (4-5 days) after administration
- Enter bloodstream



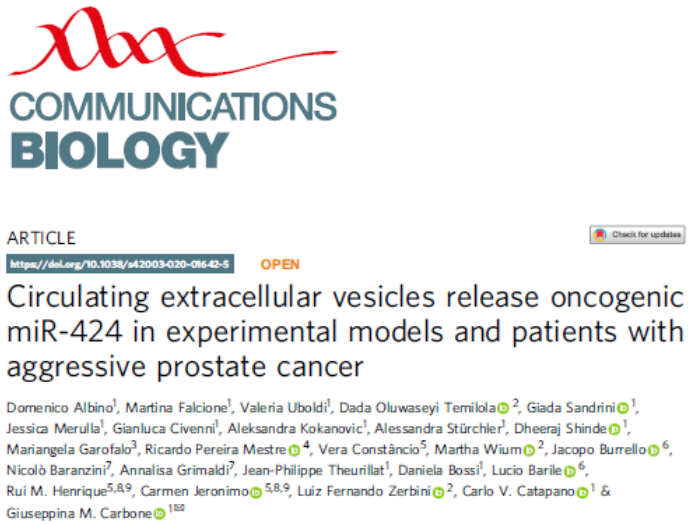
REVIEW ARTICLE
https://doi.org/10.1038/s41565-021-00931-2
nature nanotechnology
Check for updates

Extracellular vesicles as a next-generation drug delivery platform

Inge Katrin Herrmann[1,2], Matthew John Andrew Wood[3] and Gregor Fuhrmann[4,5,6]

EVs can be used as a carrier of biological and therapeutic cargoes

Examples from our research



COMMUNICATIONS BIOLOGY

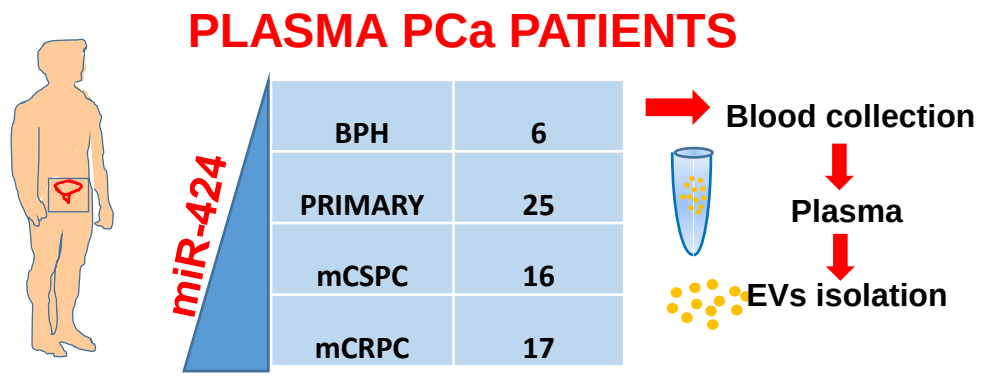
ARTICLE

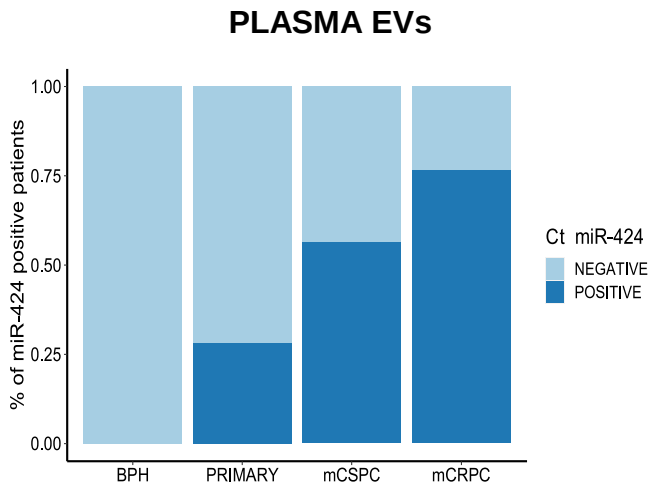
https://doi.org/10.1038/s42003-020-01642-5 OPEN

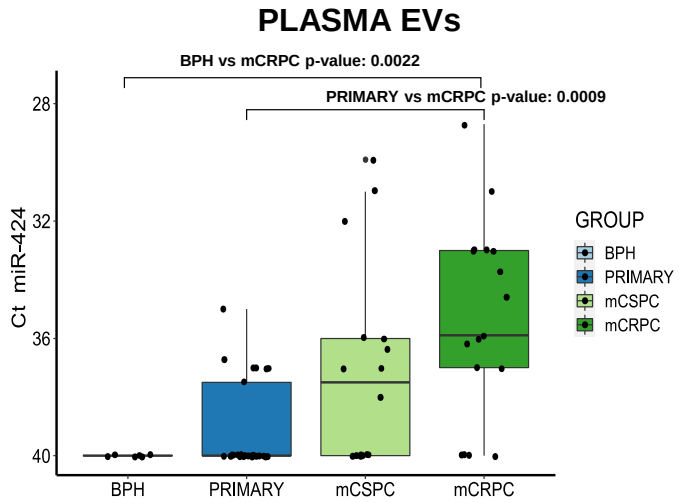
Circulating extracellular vesicles release oncogenic miR-424 in experimental models and patients with aggressive prostate cancer

Domenico Albino[1], Martina Falcione[1], Valeria Uboldi[1], Dada Oluwaseyi Temilola[2], Giada Sandrini[1], Jessica Merulla[1], Gianluca Civenni[1], Aleksandra Kokanovic[1], Alessandra Stürchler[1], Dheeraj Shinde[1], Mariangela Garofalo[3], Ricardo Pereira Mestre[4], Vera Constâncio[5], Martha Wium[2], Jacopo Burrello[6], Nicolò Baranzini[7], Annalisa Grimaldi[7], Jean-Philippe Theurillat[1], Daniela Bossi[1], Lucio Barile[6], Rui M. Henrique[5,8,9], Carmen Jeronimo[5,8,9], Luiz Fernando Zerbini[2], Carlo V. Catapano[1] & Giuseppina M. Carbone[1]✉

EVs can be isolated from plasma and their cargo evaluated







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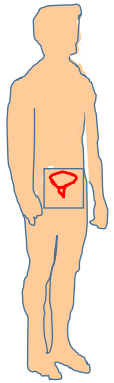
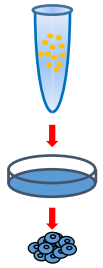
EVs are released in the circulation and impact on the phenotype of recipient cells



Patient EVs	
BPH	3
PRIMARY	5
mCSPC	5
mCRPC	4



Plasma EVs isolation

↓

miR-424 status evaluation

↓

EVs supplementation

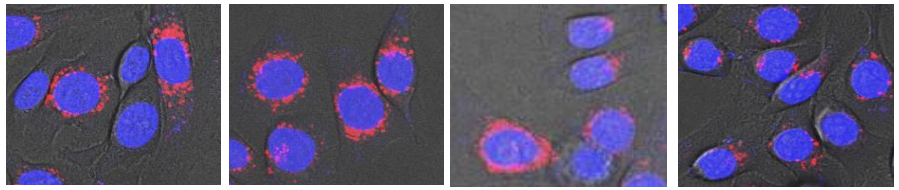
↓

Tumor-sphere assay
Relationship SFE /miR-424 status

SUPPLEMENTATION OF HUMAN PLASMA EVs TO NORMAL PROSTATE EPITHELIAL CELLS RWPE-1

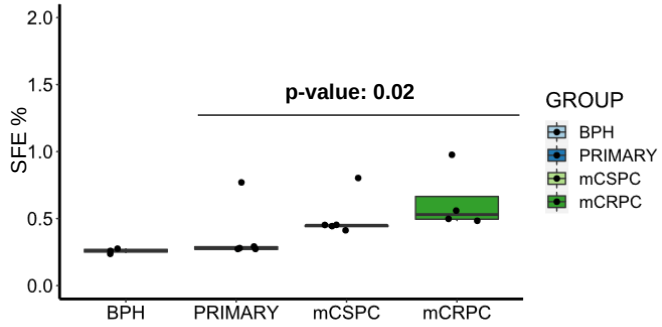
PATIENT PLASMA EVs

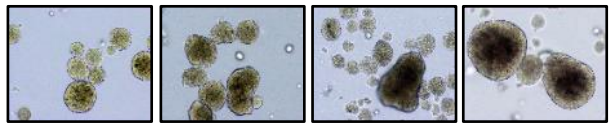
EVs-BPH EVs-PRIMARY EVs-mCSPC EVs-mCRPC



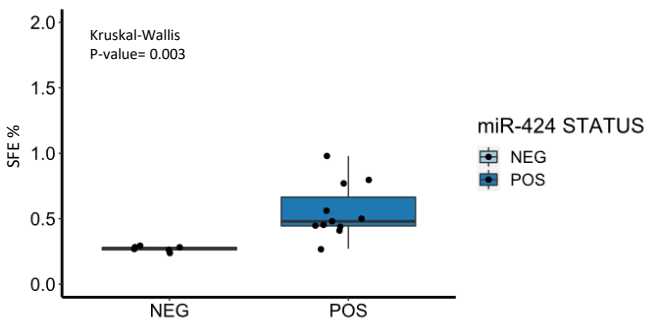
RWPE-1 RECIPIENT CELLS

SFE RWPE-1 RECIPIENT





SFE RWPE-1 RECIPIENT



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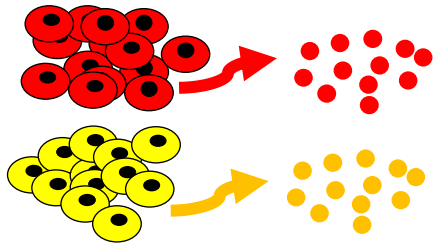
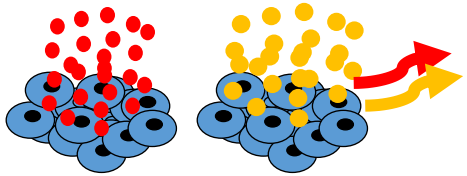
EVs from several sources significantly impact on the recipient cell phenotype

DONOR SOURCE



SUPPLEMENTATION TO RECIPIENT CELLS

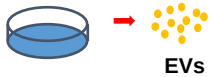


IMPACT ON RECIPIENT CELL PHENOTYPE

- CANCER STEM CELL PROPERTIES
- TUMOR INITIATION

EVs DONOR SOURCES

CELL LINES



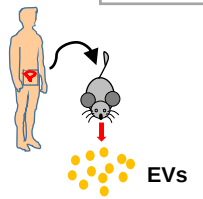
GEMM MODELS

Transgenic mice:
ERG/PTEN-KO

PDX MODELS

PDX models
EVs release

LuCaP#145.2	LuCaP#35
mCRPC	mCSPC



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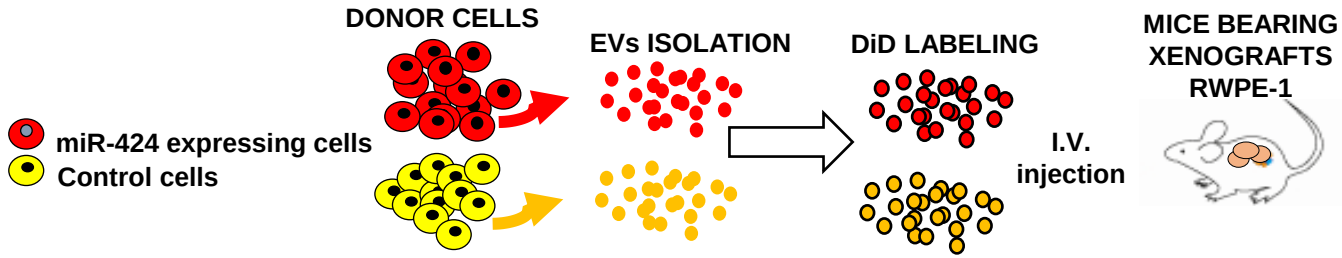
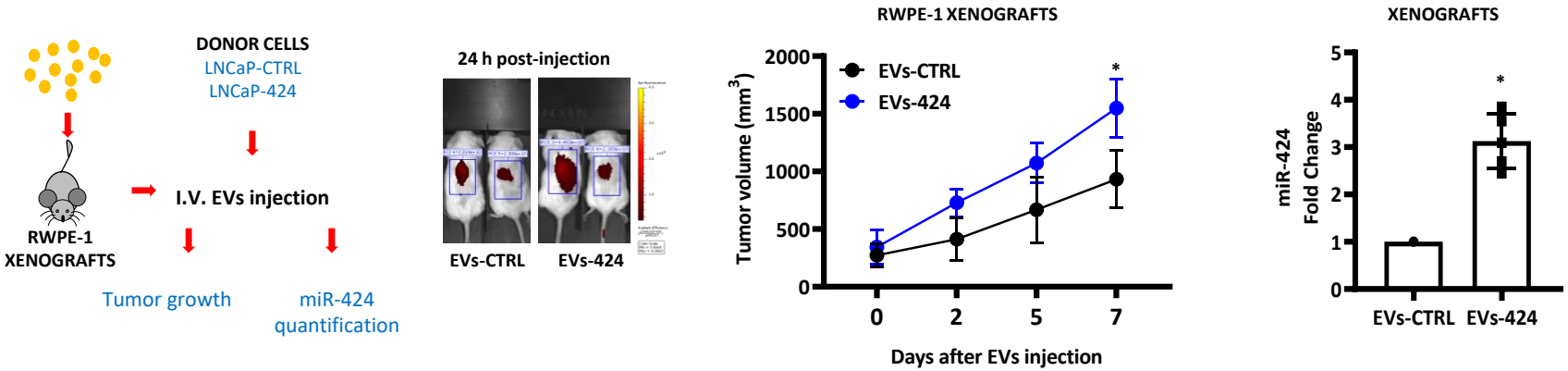
Efficient oncogenic transfer mediated by systemic delivery of EVs in mice





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Thank you!

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