Antibody Displaying Extracellular Vesicles (Fc-EVs) for Delivery of Tumor Targeted Therapeutics

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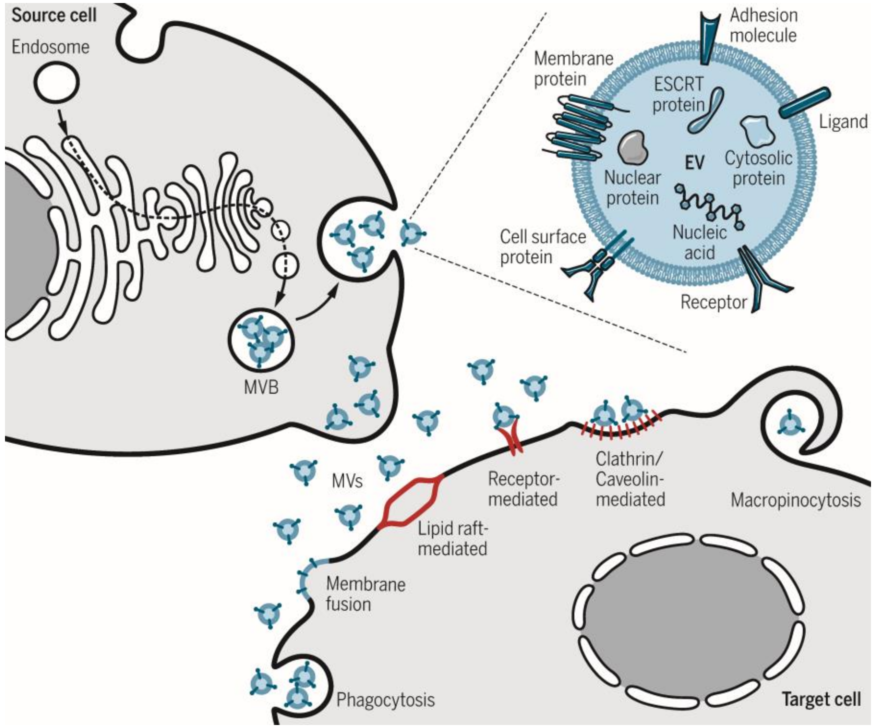
Extracellular vesicles (EVs)

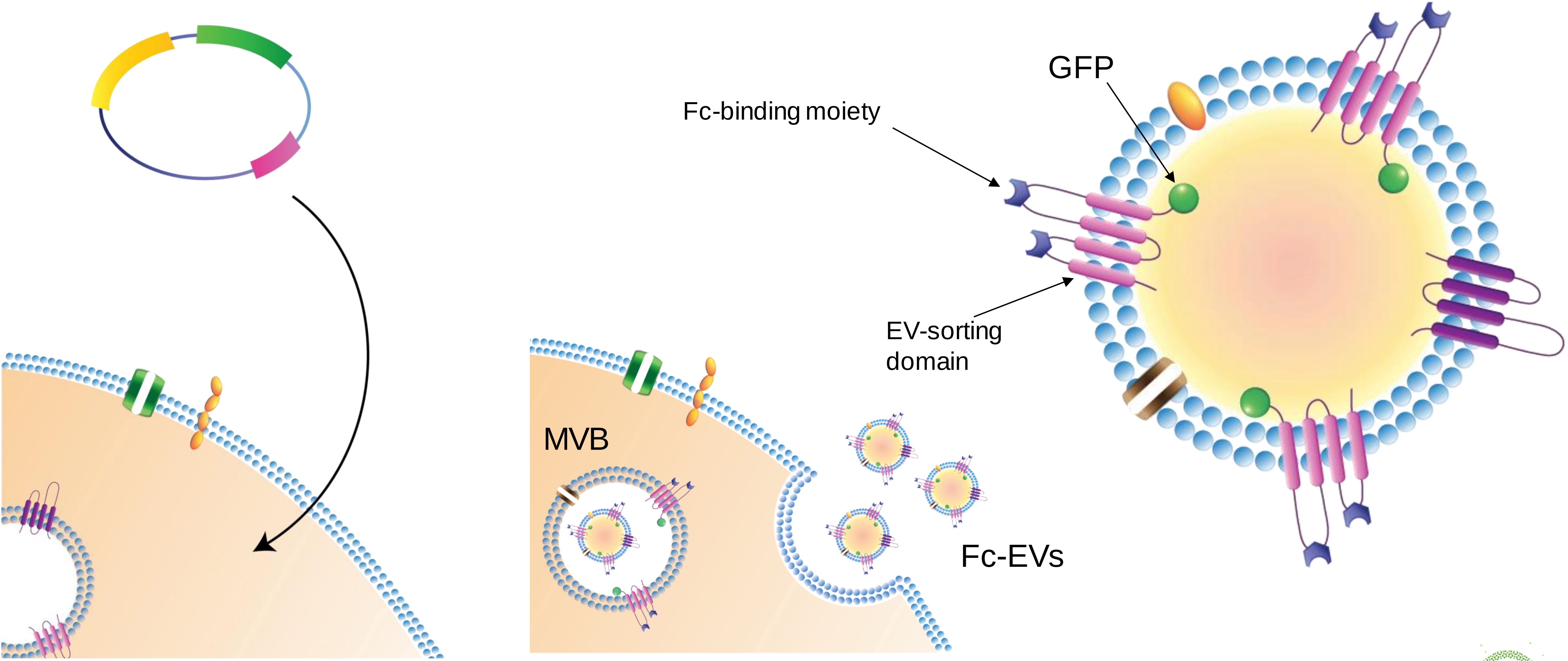


Wiklander et al, Sci Transl Med 2019

Vesicle types	Characteristics			
	Origin	Size	Markers	Contents
Exosomes	Endolysosomal pathway; intra-luminal budding of multivesicular bodies and fusion of multivesicular body with cell membrane	40–120 nm	Tetraspanins (such as TSPAN29 and TSPAN30), ESCRT components, PDCD6IP, TSG101, flotillin, MFGE8	mRNA, microRNA (miRNA) and other non-coding RNAs; cytoplasmic and membrane proteins including receptors and major histocompatibility complex (MHC) molecules
Microvesicles	Cell surface; outward budding of cell membrane	50–1,000 nm	Integrins, selectins, CD40 ligand	mRNA, miRNA, non-coding RNAs, cytoplasmic proteins and membrane proteins, including receptors
Apoptotic bodies	Cell surface; outward blebbing of apoptotic cell membrane	500–2,000 nm	Extensive amounts of phosphatidyl-serine	Nuclear fractions, cell organelles

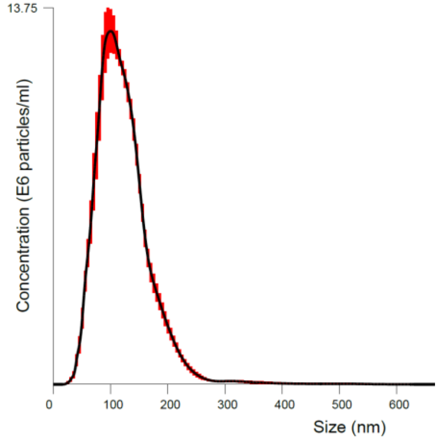
EL Andaloussi et al, Nature Reviews 2013

Fc-EVs

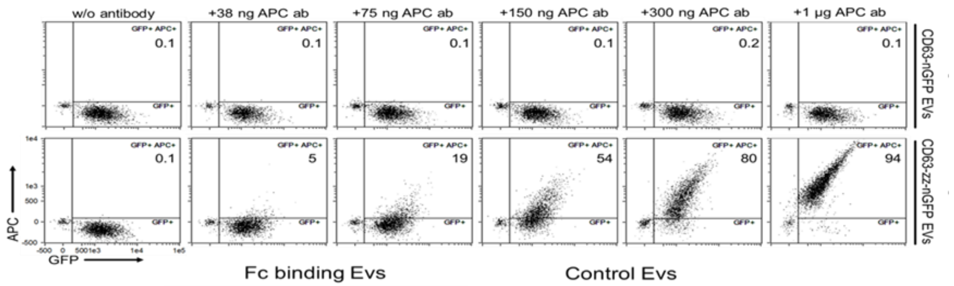


Fc-EV characterization

NTA

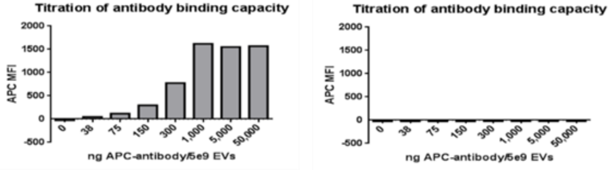


Single vesicle analysis

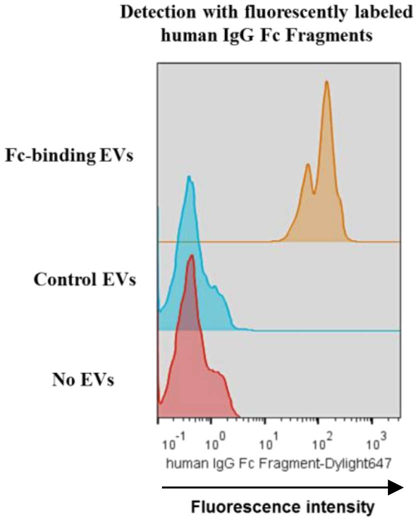


Fc binding Evs

Control Evs



MACSPlex

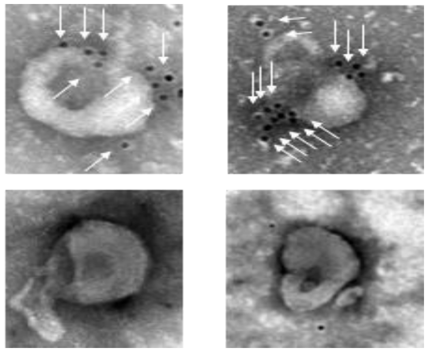


Immuno-EM

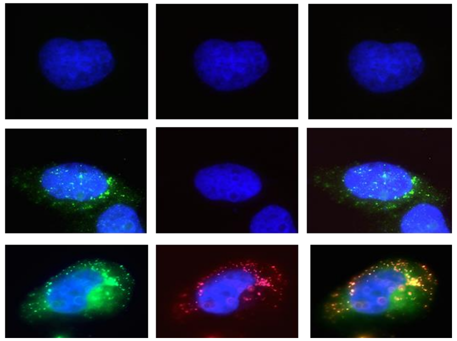
EM: EV + nanogold-Ab

Fc-binding EVs

Control EVs



Cellular uptake/association

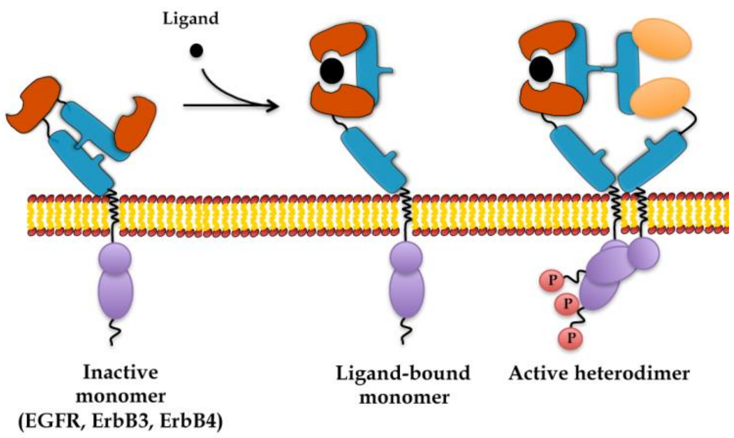


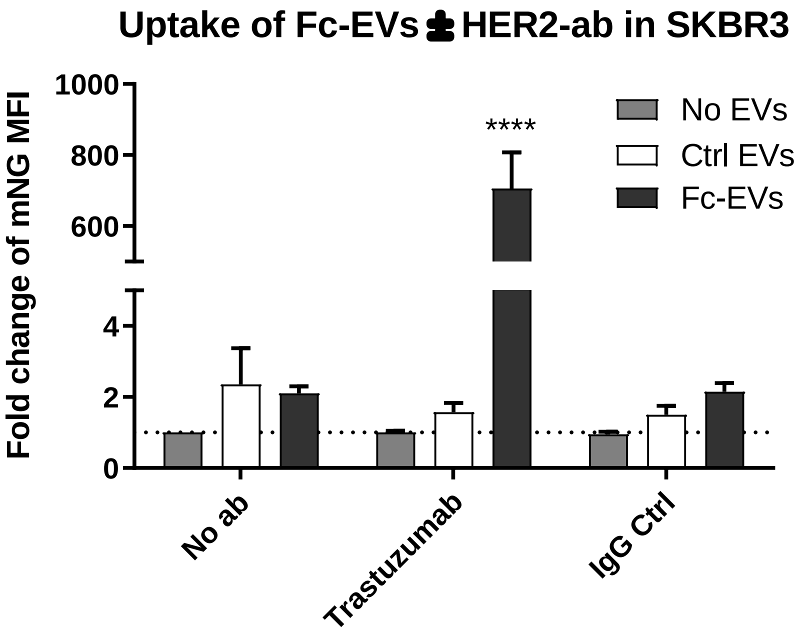
Fc-EVs targeting HER+ cancer

HER2

Human epidermal growth factor receptor 2

- Overexpressed in mainly breast cancer and gastrointestinal cancers
- Dimerization of the receptor → autophosphorylation of tyrosine residues within the cytoplasmic domain → cell proliferation





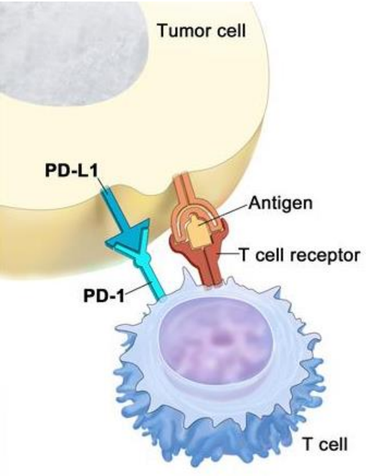
Fc-EVs targeting PDL1

PD-L1

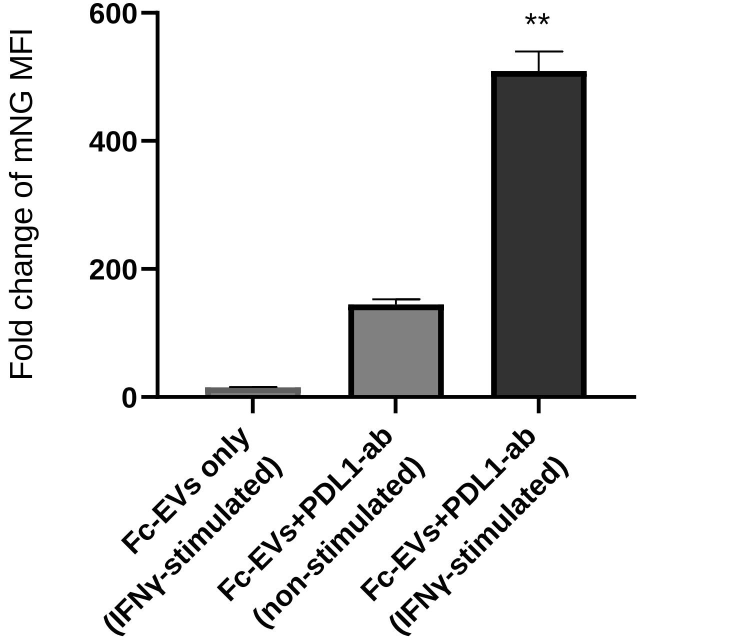
Programmed death ligand 1

Expressed on some normal cells and cancer cells.

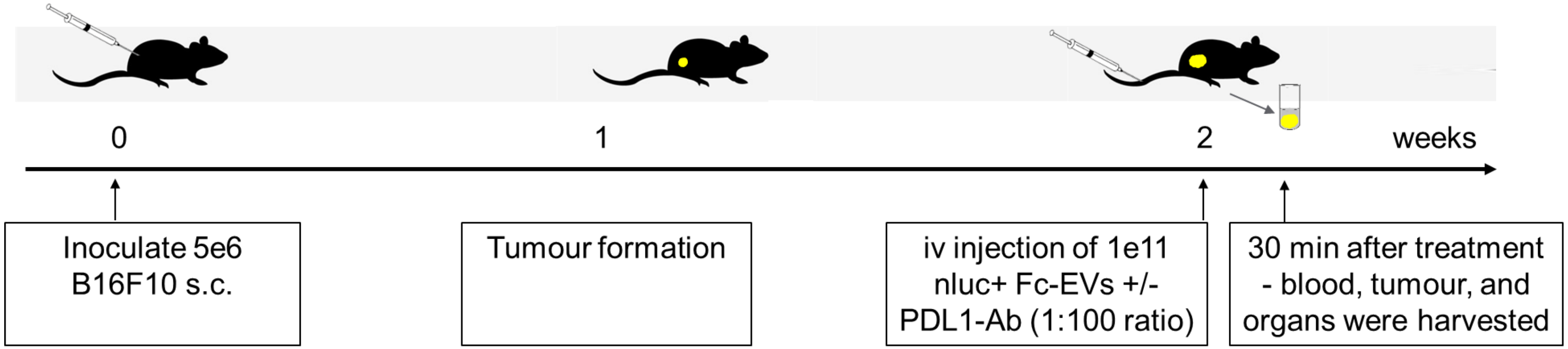
Interaction between PD-L1 and PD-1 leads to T and B cell inhibition



Uptake of Fc-EVs ± PDL1-ab in B16F10



Fc-EVs can be targeted to tumors *in vivo*



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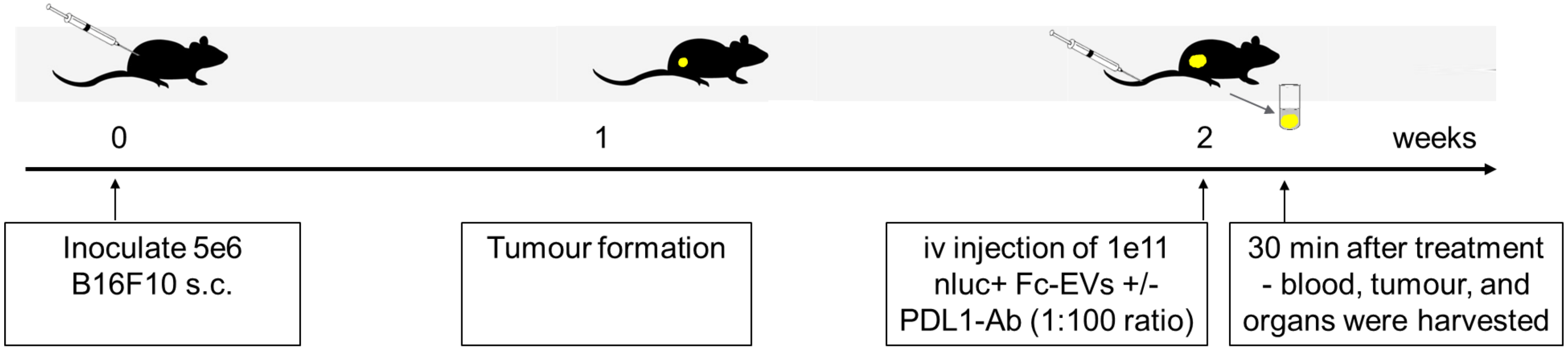

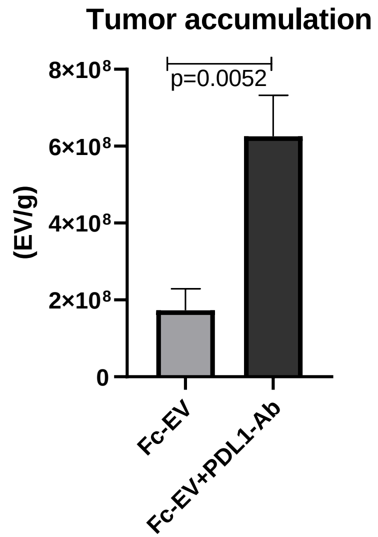

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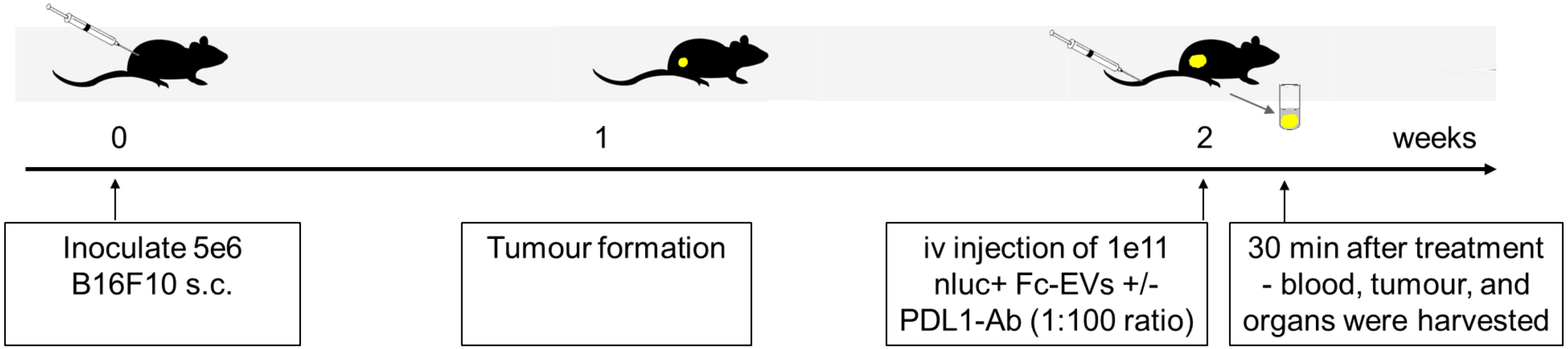
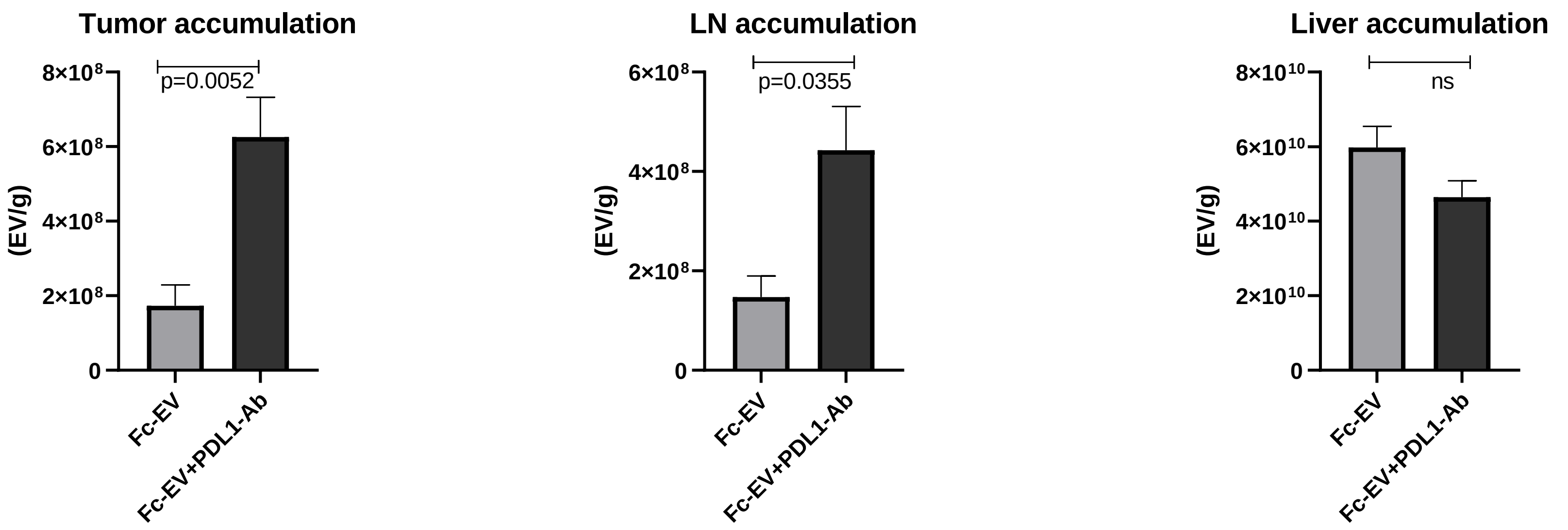
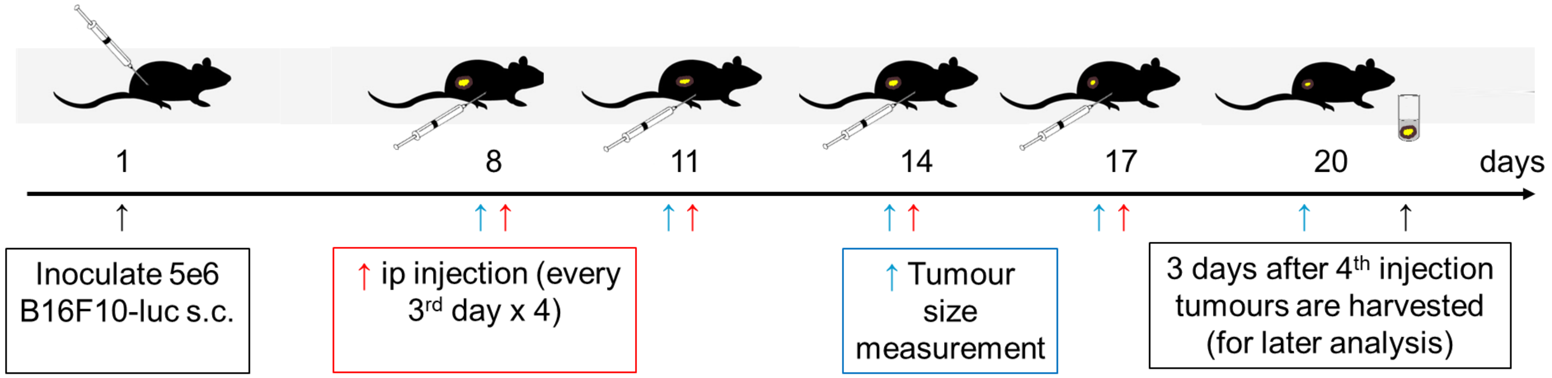




Fc-EVs loaded with doxorubicin to treat malignant melanoma



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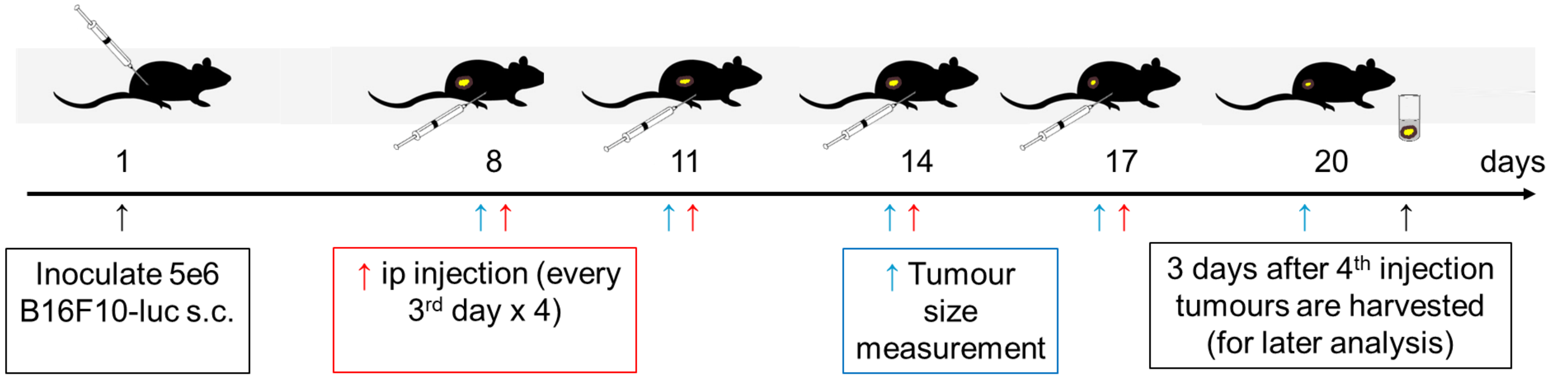

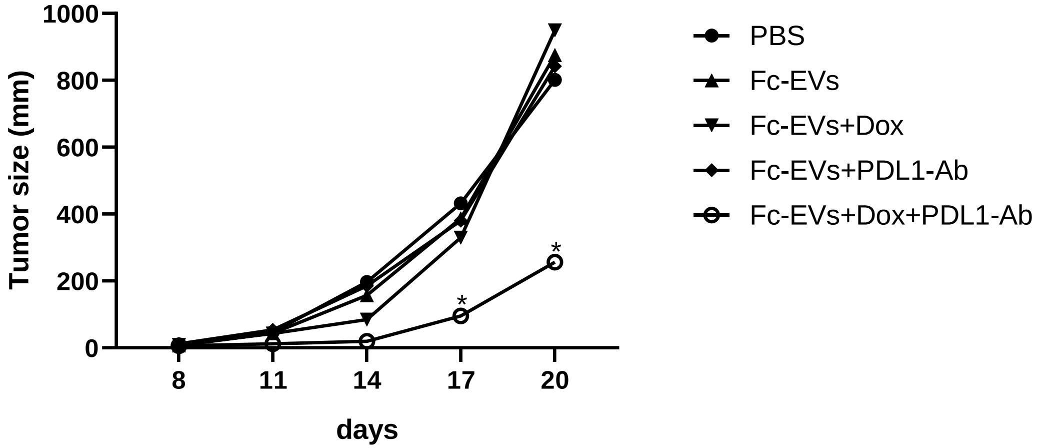

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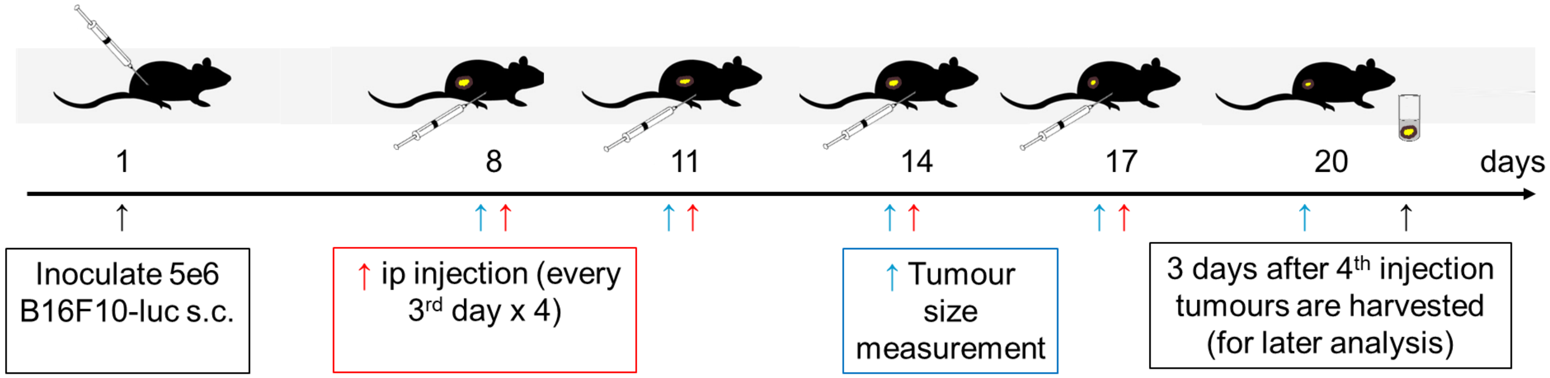

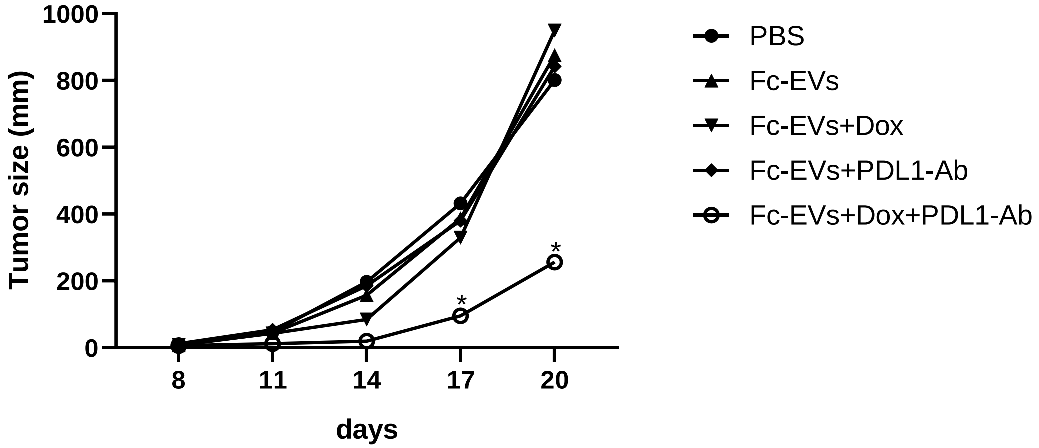

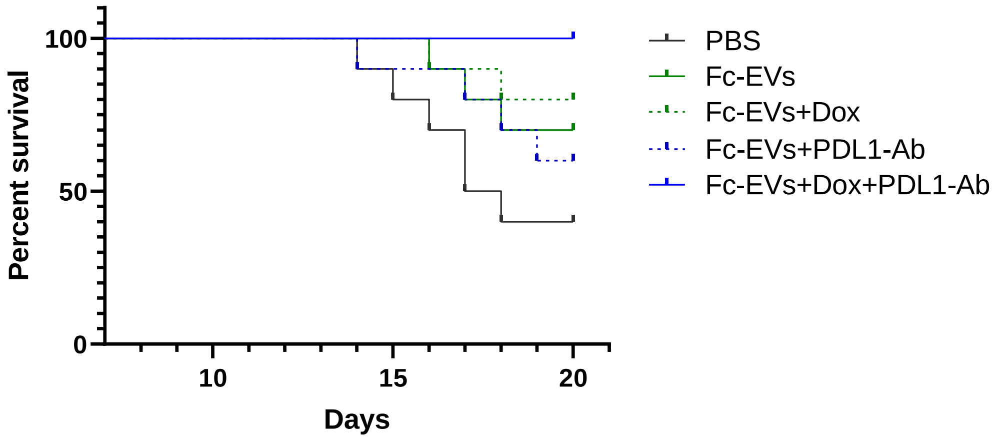

Acknowledgements

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