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Interaction mechanisms with host of EVs derived from the opportunistic pathogen *Staphylococcus aureus*

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**11th GO-EV Network meeting with BioGenOuest labelling
19/10/2023 - Nantes**



¹INRAE, Institut Agro, STLO, Rennes, France;

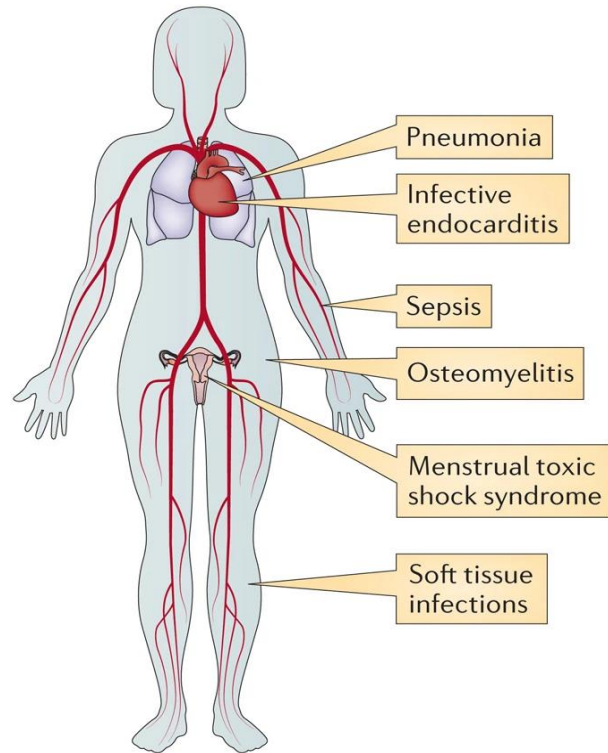
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⁴Laboratory of Cellular and Molecular Genetics, Institute of Biological Sciences, Federal University of Minas Gerais, Belo Horizonte, Brazil.

✓ *Staphylococcus aureus*

➤ Human opportunist pathogen



Diseases caused by *Staphylococcus aureus*
 Salgado-Pabón W and Schlievert P., 2014

➤ Significant impact on the veterinary medicine and food fields → Etiological agent of mastitis

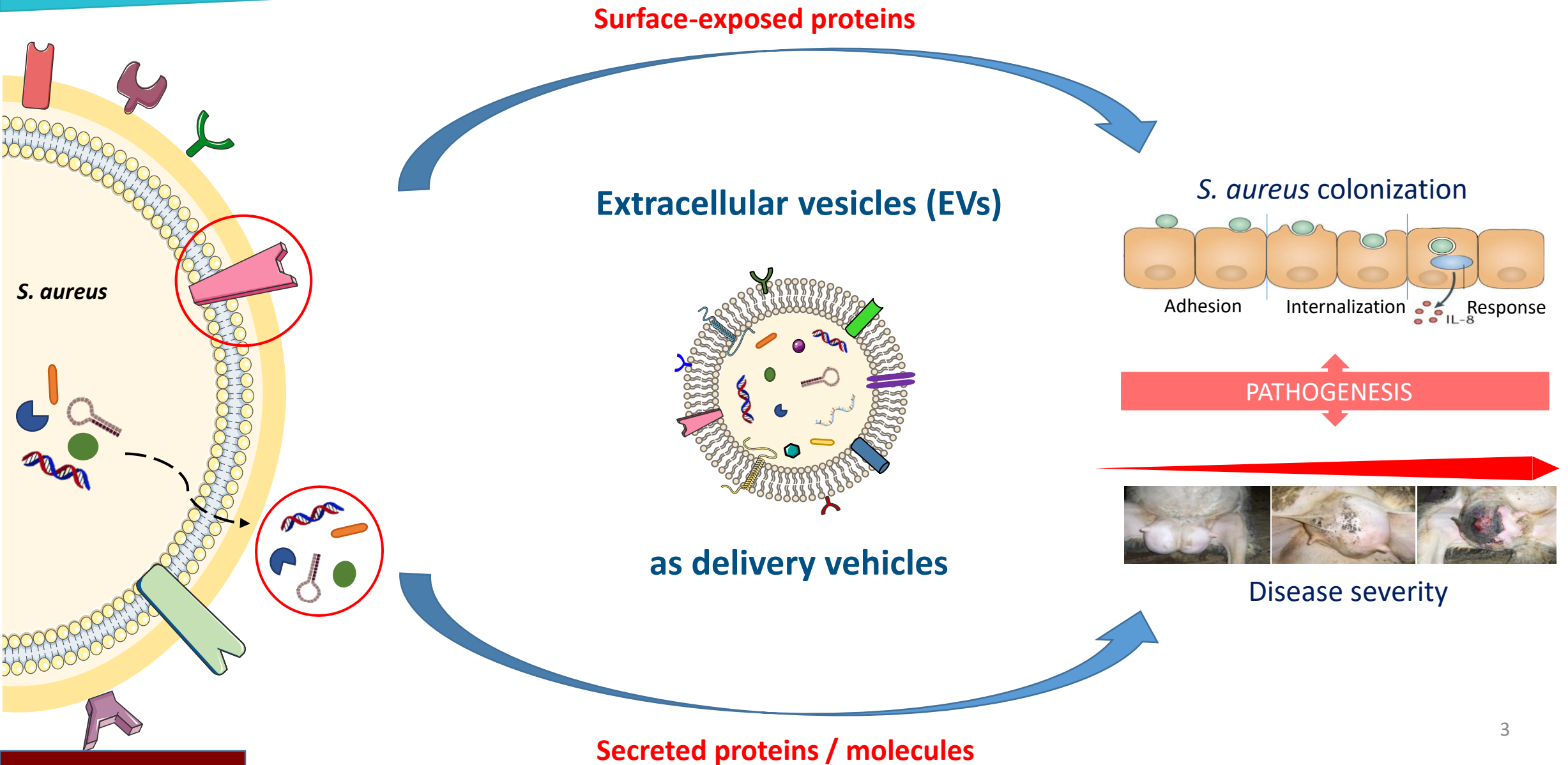


➤ The six highly virulent and antibiotic resistant bacterial pathogens

ESKAPE

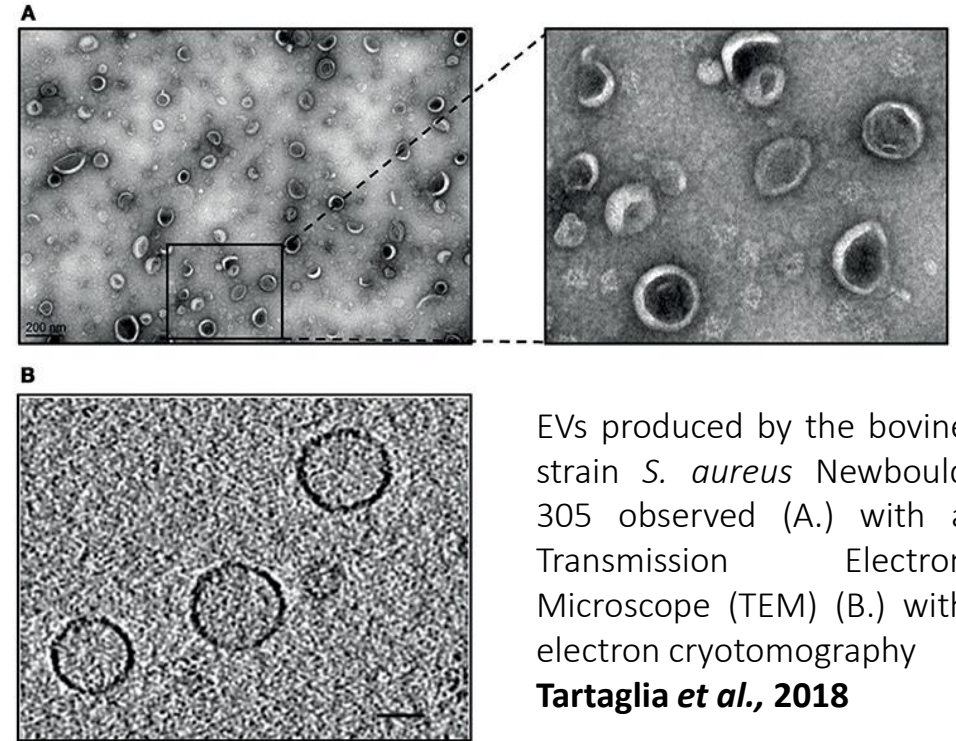


✓ *Staphylococcus aureus* virulence factors



✓ Extracellular vesicles (EVs)

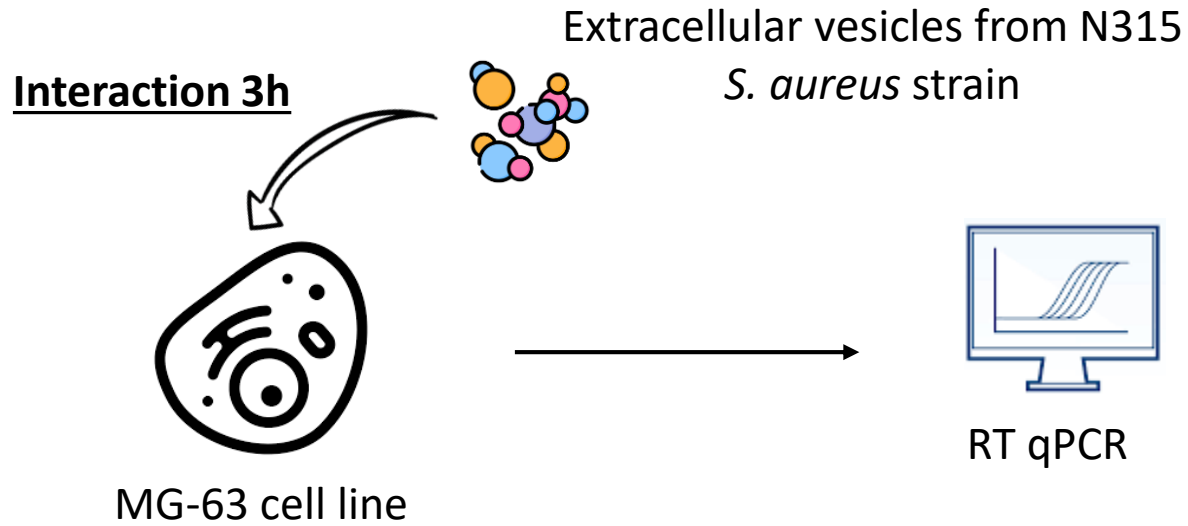
- Lipid bilayer spherical nano-sized particles (30-300 nm) which carry various molecules (eg, lipids, nucleic acids, proteins)
- Vehicles that transport and deliver molecules to local or distant cellular targets
- Imply in cell-to-cell communication and especially in host-pathogen interaction



What is the contribution of extracellular vesicles from *S. aureus* in pathogenesis ?

✓ Role of extracellular vesicles in pathogenesis

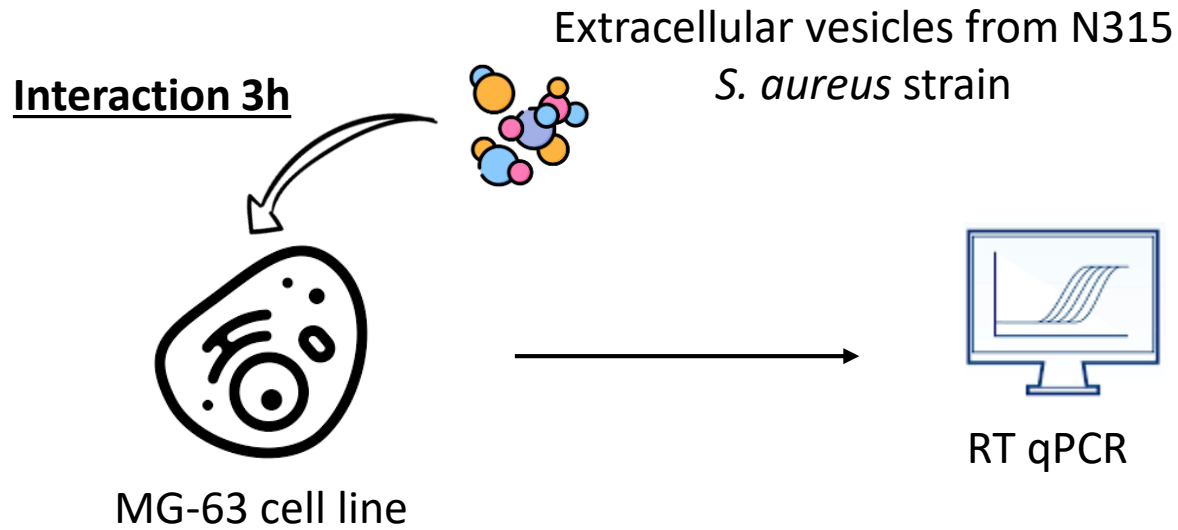
Impact of EVs on the expression of several inflammatory genes



- Human osteoblast-like non-phagocytic cell line
- Taken from patient with osteosarcoma

✓ Role of extracellular vesicles in pathogenesis

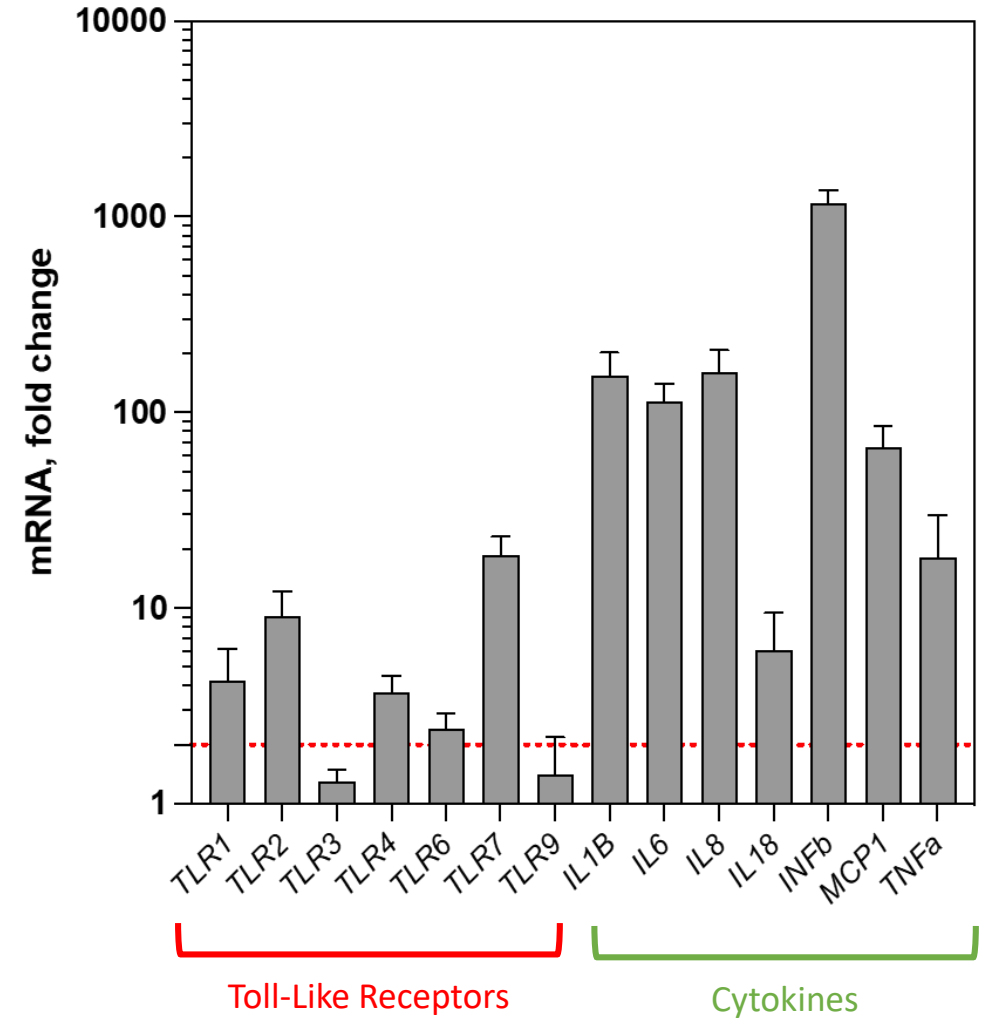
Impact of EVs on the expression of several inflammatory genes



Increased expression of genes coding for :

✓ Cytokines

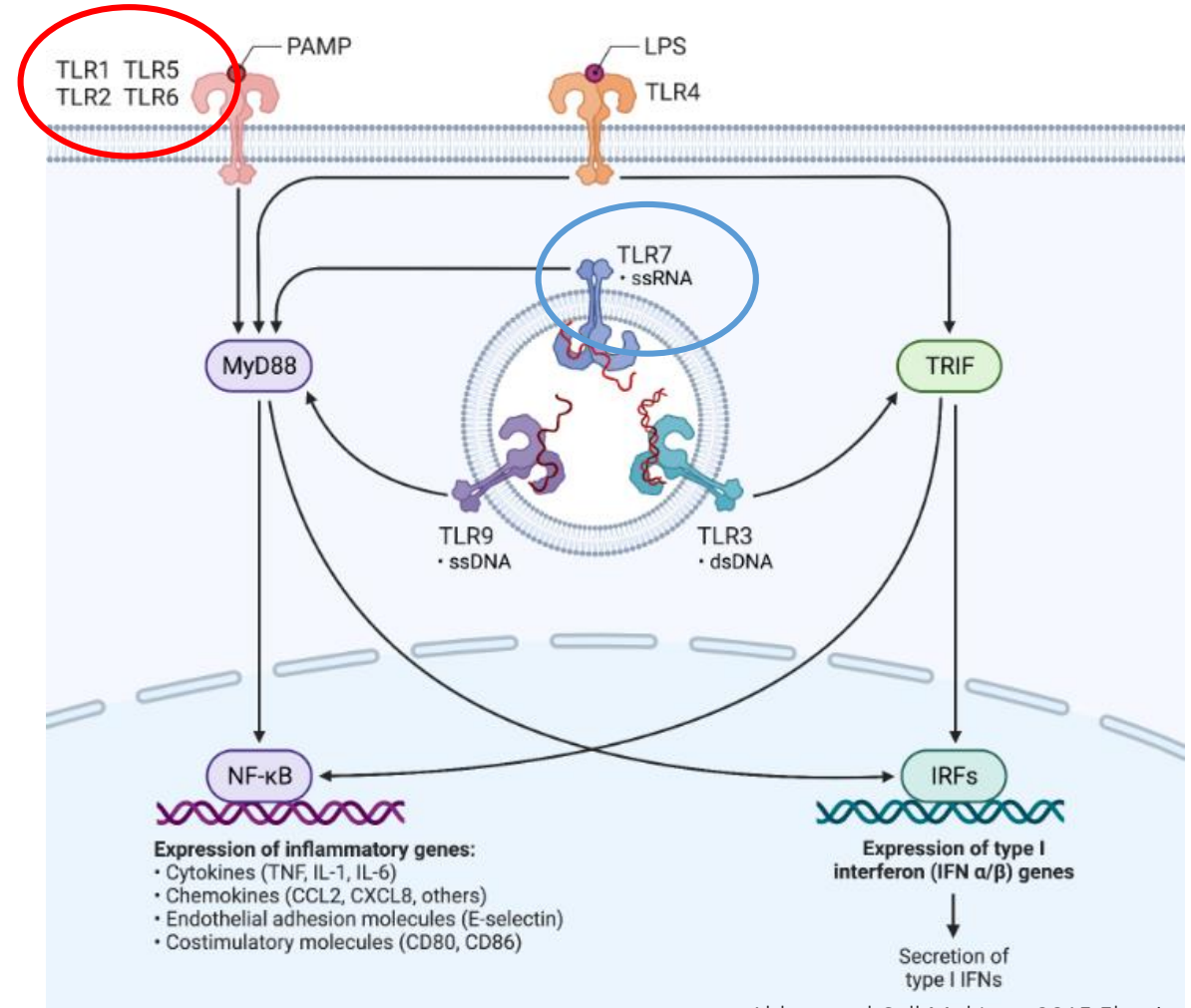
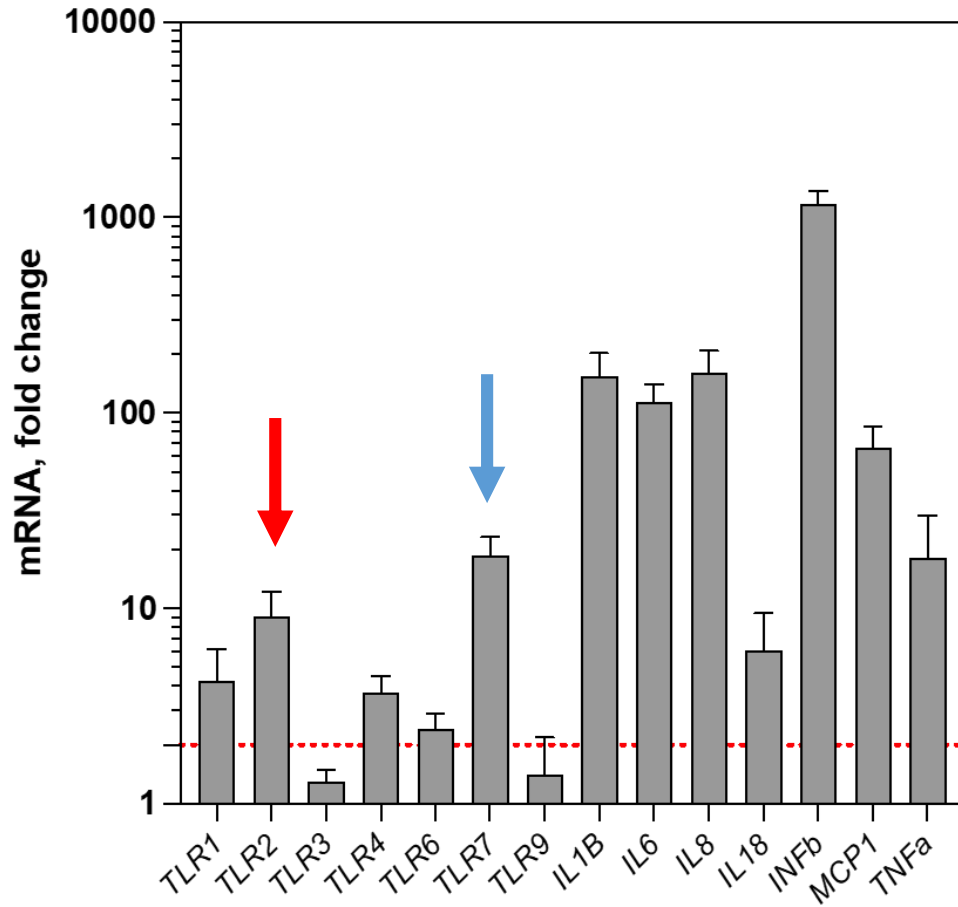
✓ Toll-Like Receptors (TLR)



→ N315-derived EVs induce the expression of various *TLR* and immune genes in MG-63 cells

✓ Role of extracellular vesicles in pathogenesis

Impact of EVs on the expression of several inflammatory genes

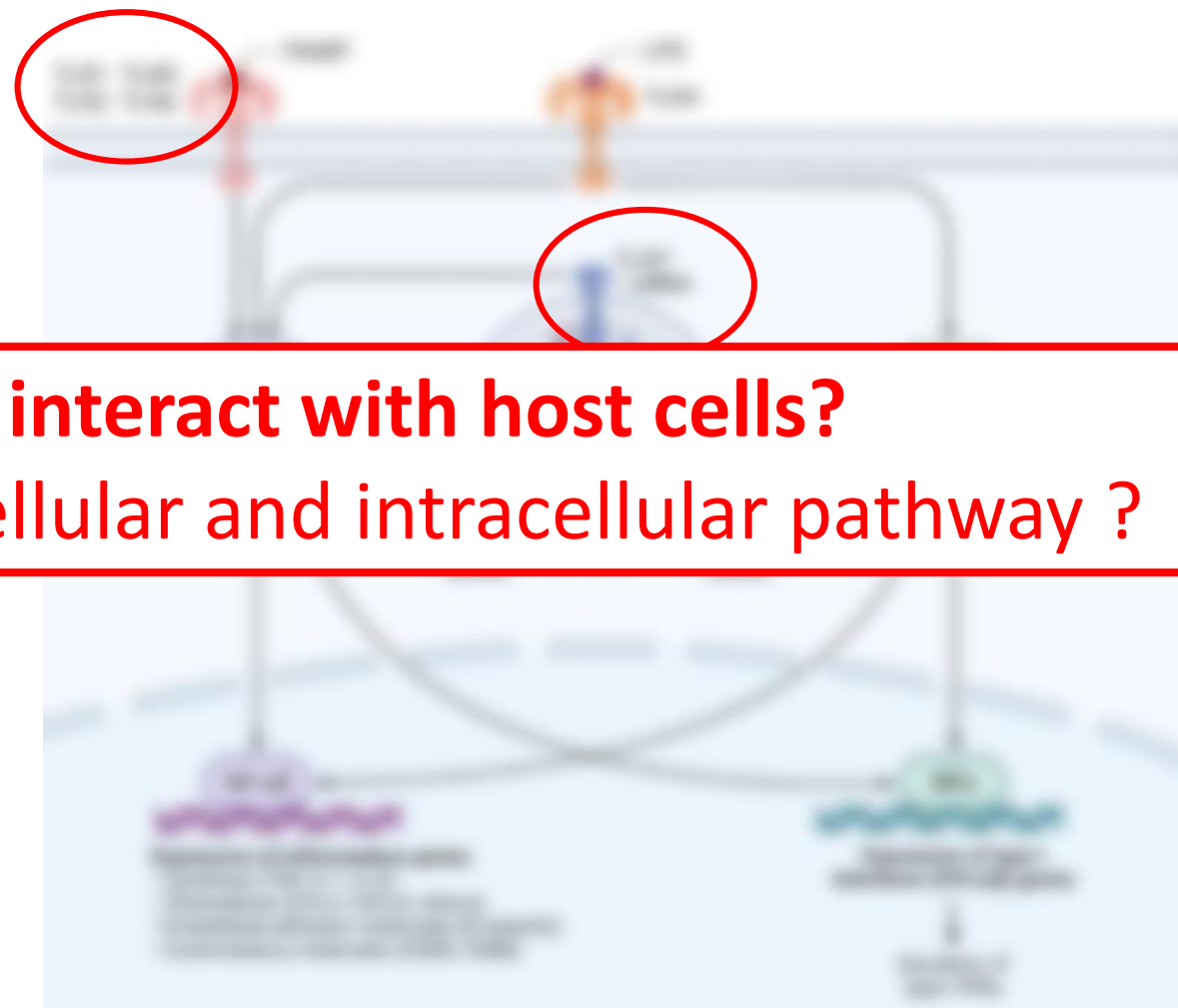
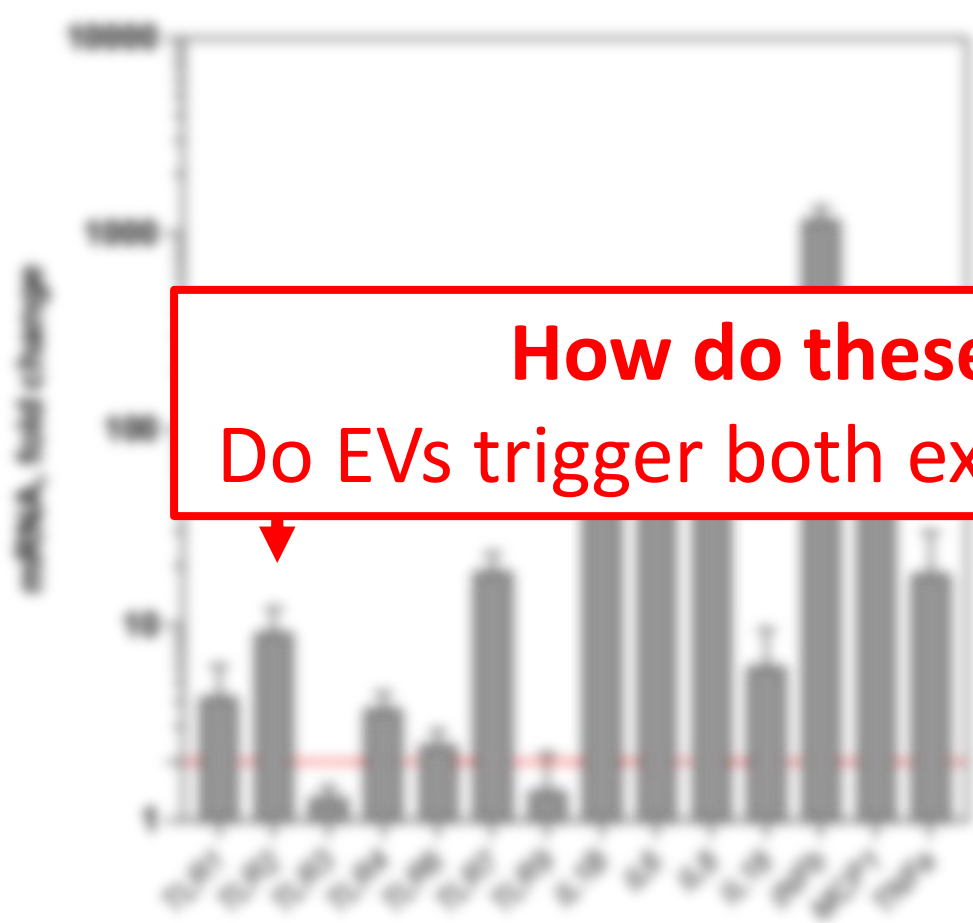


Abbas et al Cell Mol Imm 2015 Elsevier

➔ N315-derived EVs induce the expression of various *TLR* and immune genes in MG-63 cells

✓ Role of extracellular vesicles in pathogenesis

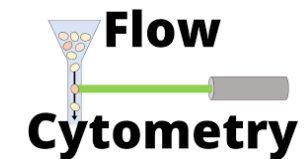
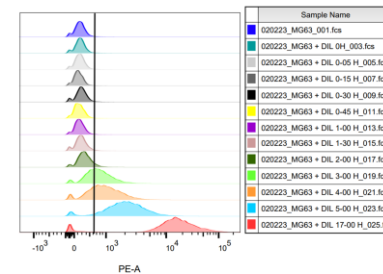
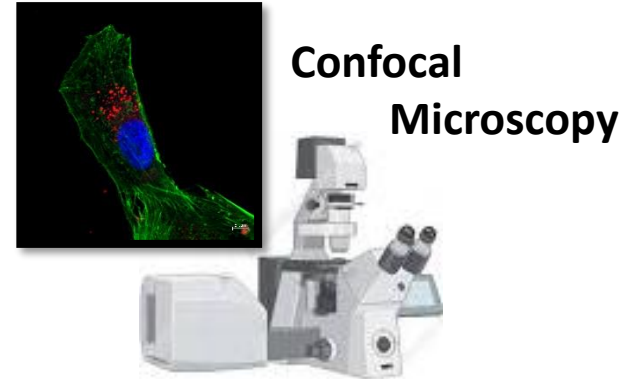
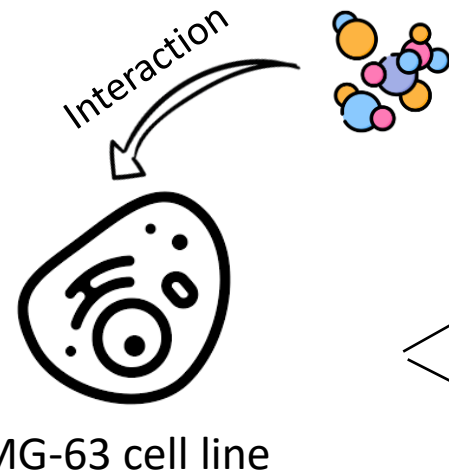
Impact of EVs on the expression of several inflammatory genes



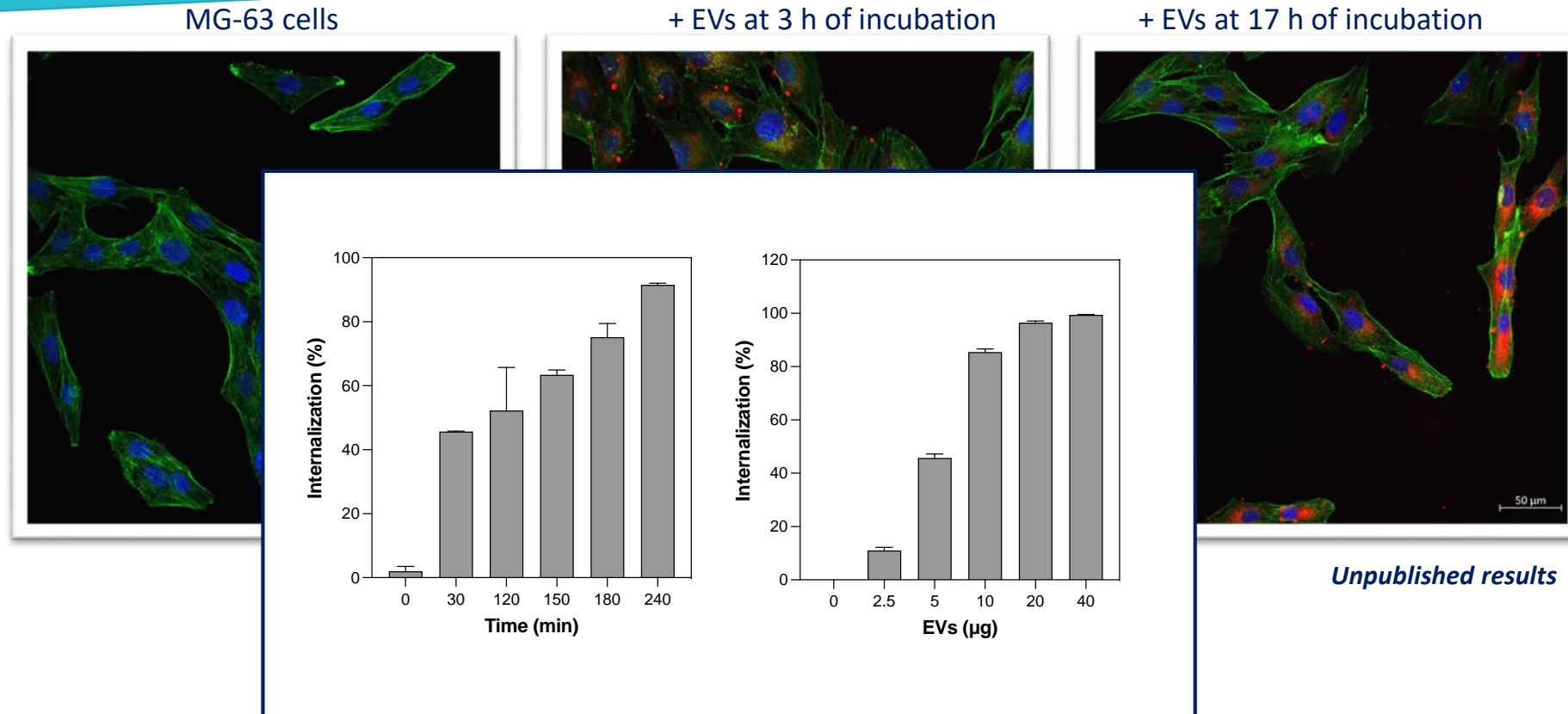
How do these EVs interact with host cells?
Do EVs trigger both extracellular and intracellular pathway ?

→ N315-derived EVs induce the expression of various *TLR* and immune genes in MG-63 cells

Dil-labelled Extracellular vesicles
from N315 strain



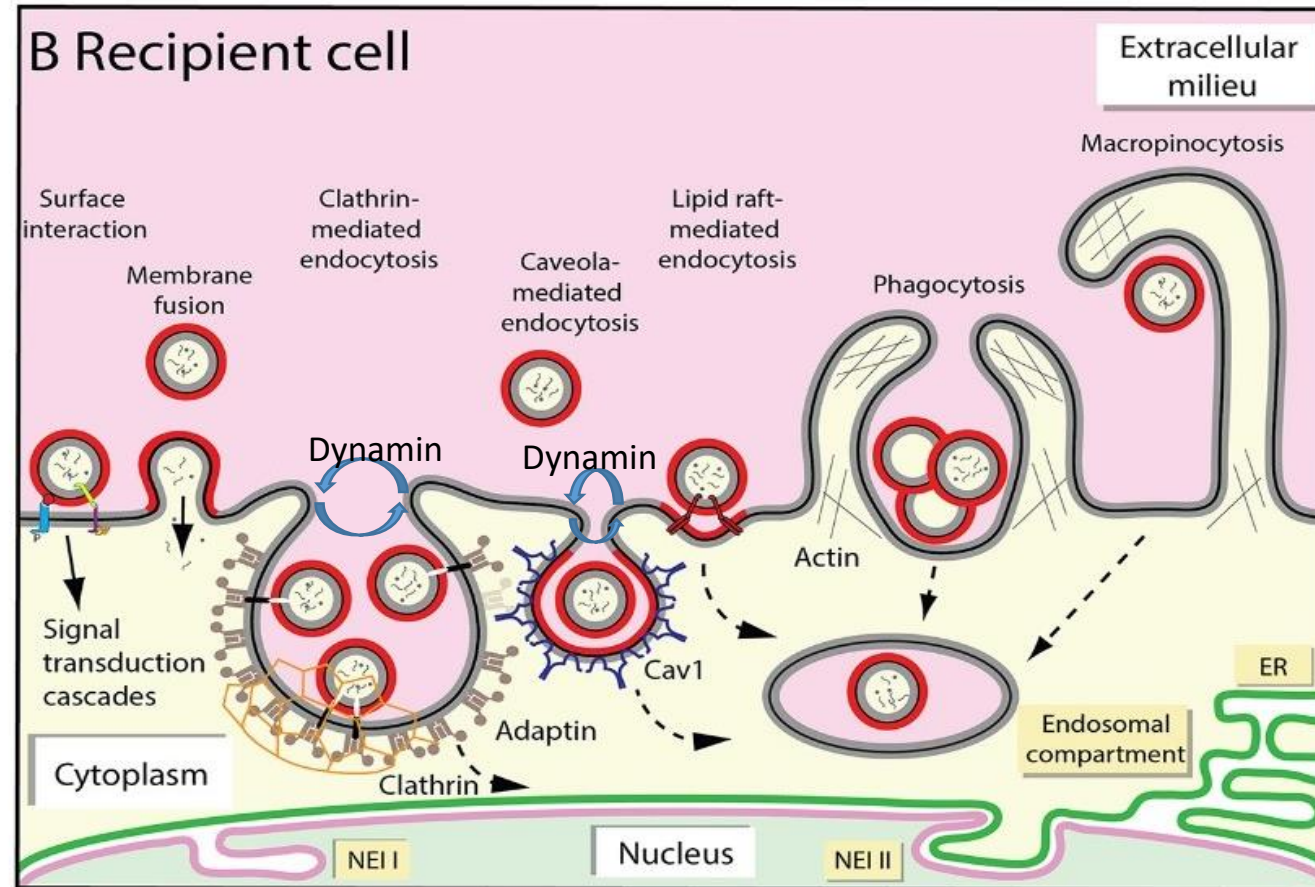
✓ Internalization of EVs by MG-63 cells



→ *S. aureus* N315-derived EVs are internalized by MG-63 cells

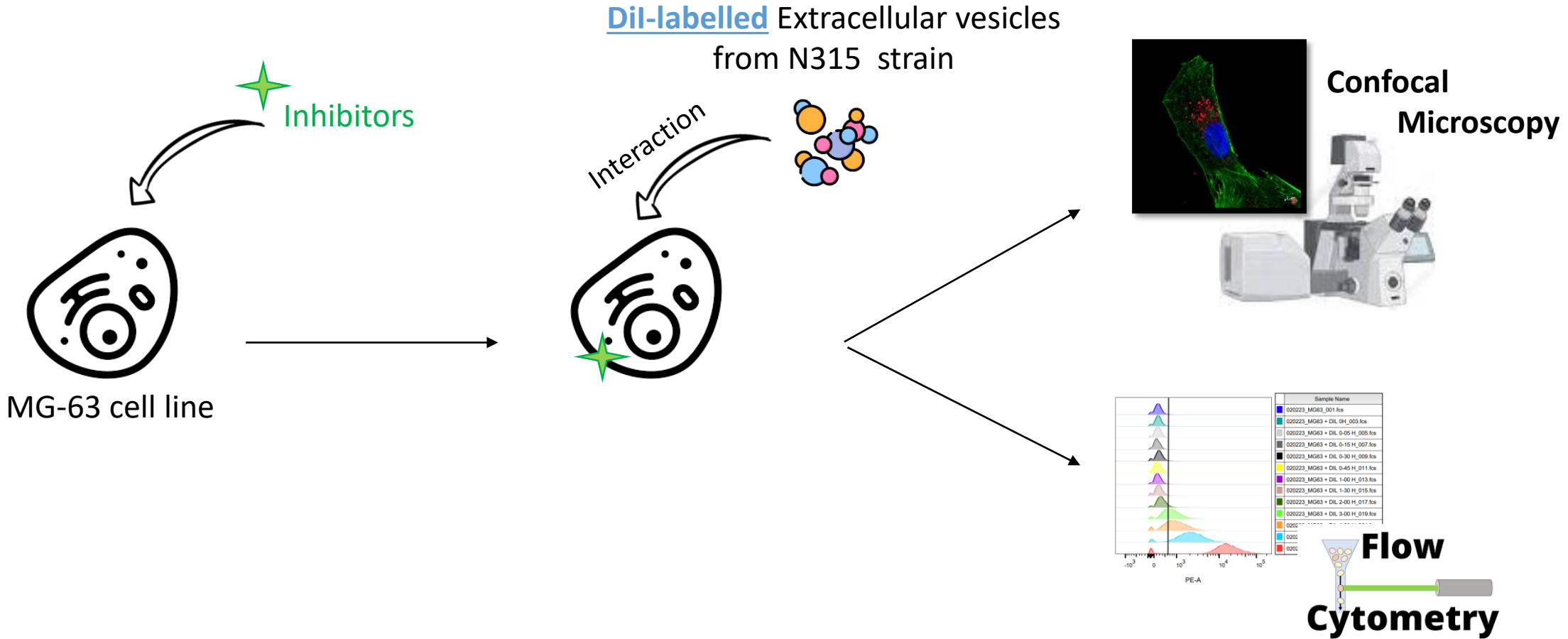
- in a dose-dependent manner
- in a time-dependent manner

✓ Internalization of EVs by MG-63 cells

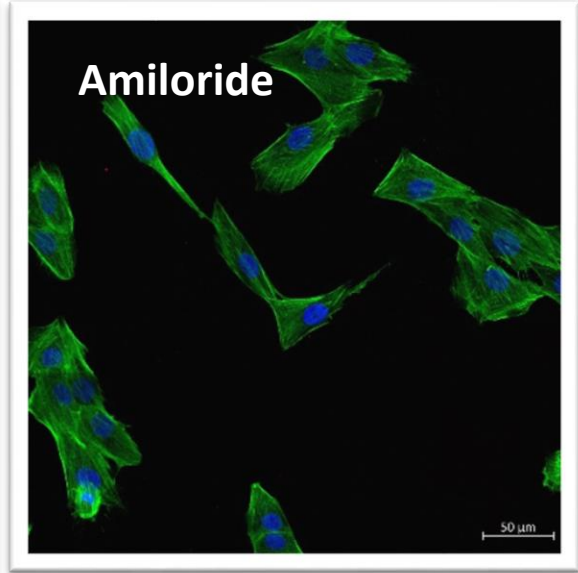
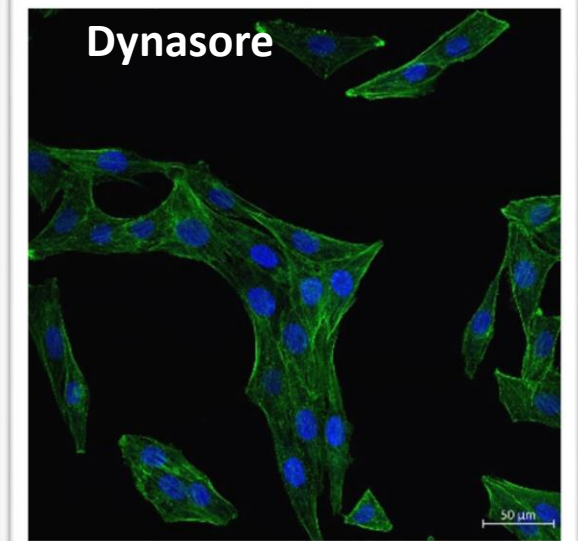
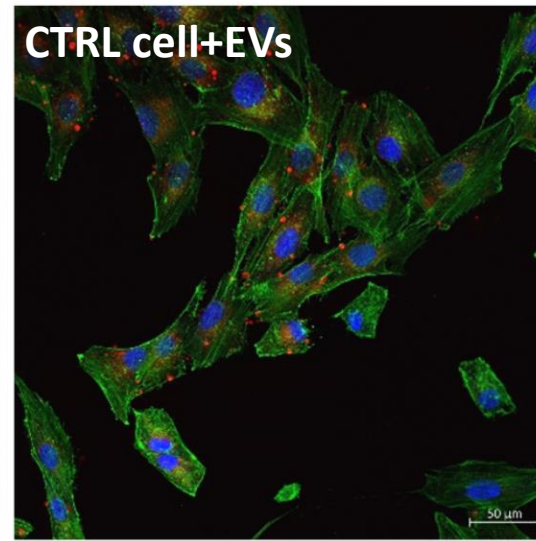
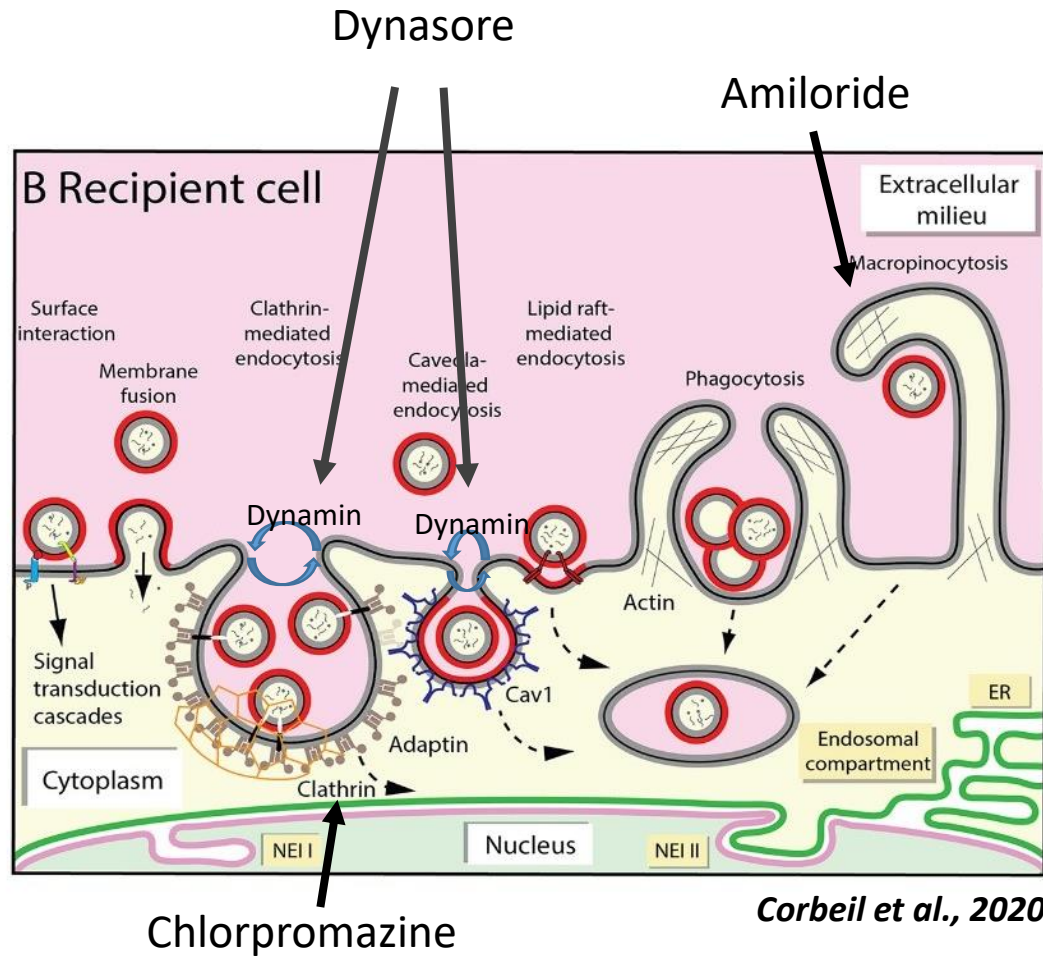


Corbeil et al., 2020

→ Several different pathways of internalization are possible



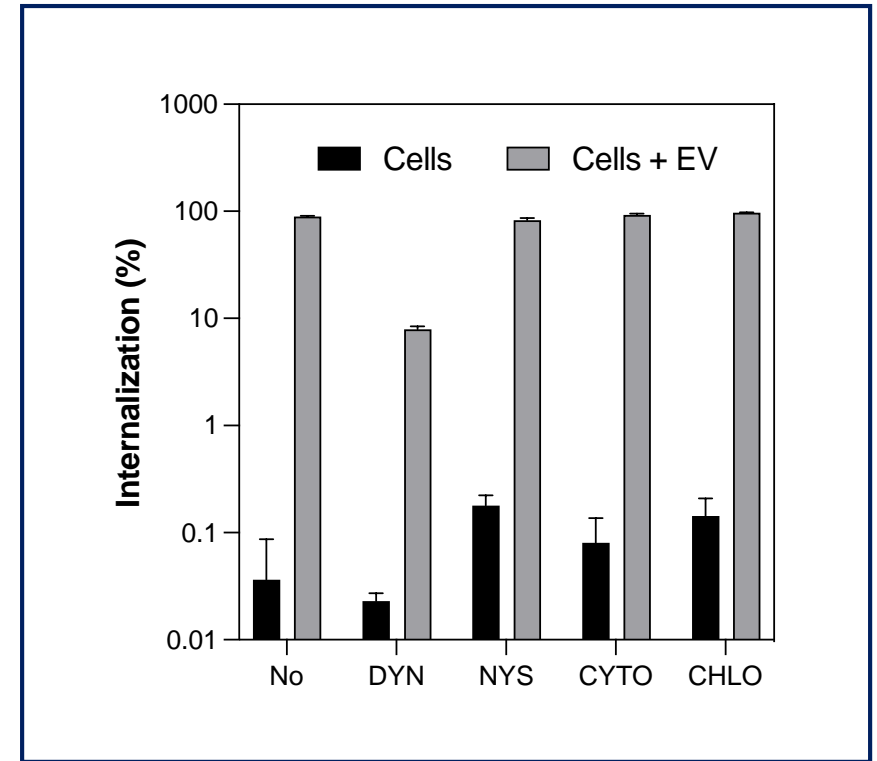
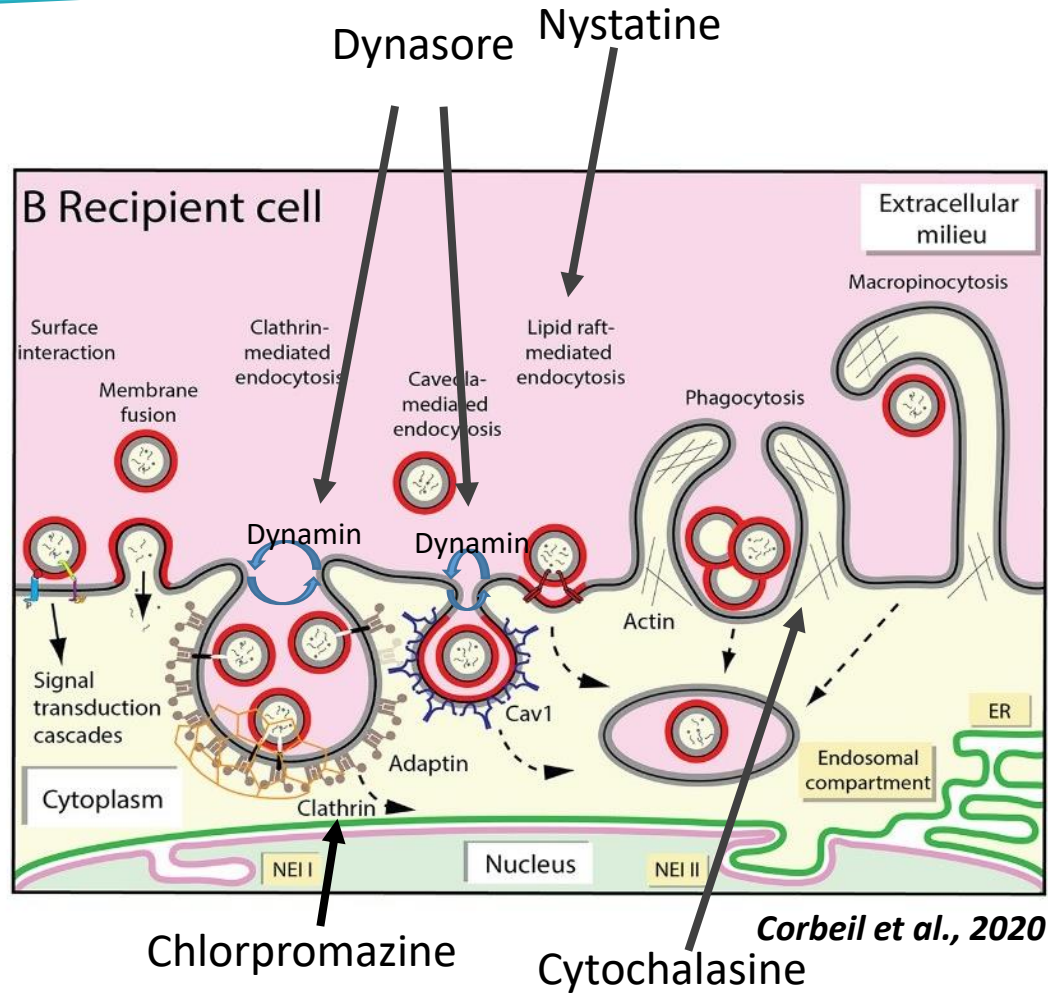
✓ Internalization of EVs by MG-63 cells



Unpublished results

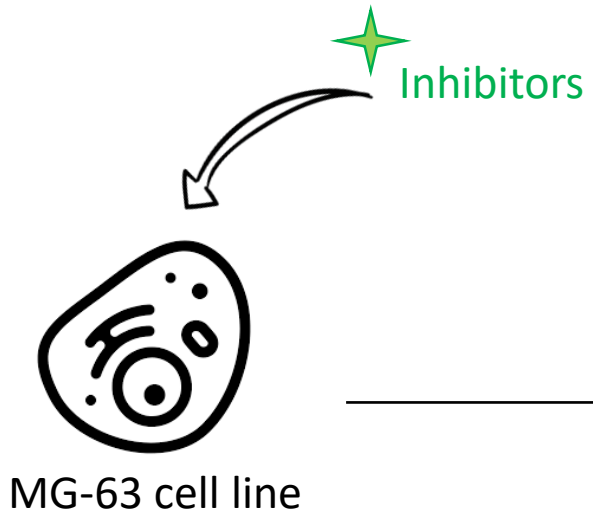
→ Internalization of N315 EVs can depend upon dynamin-mediated endocytosis and macropinocytosis

✓ Internalization of EVs by MG-63 cells

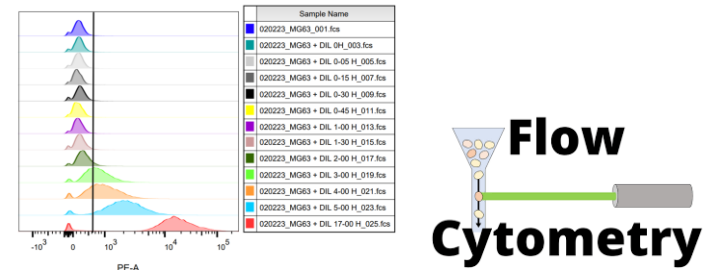
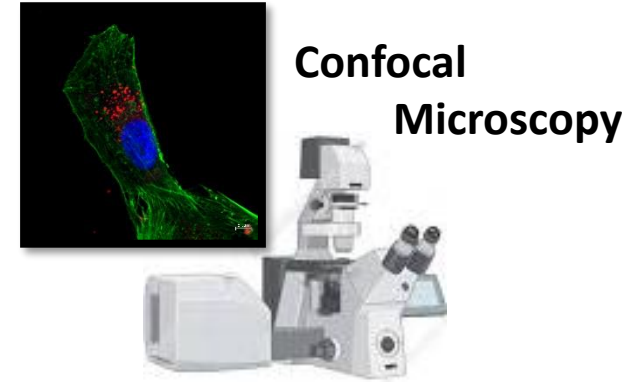
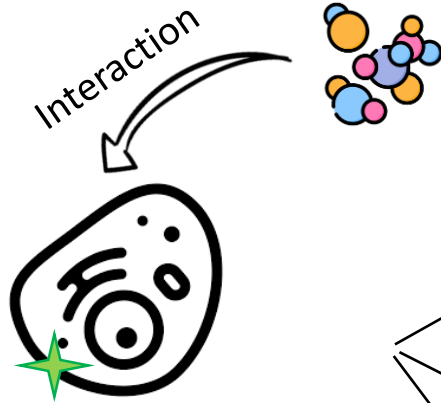


Unpublished results

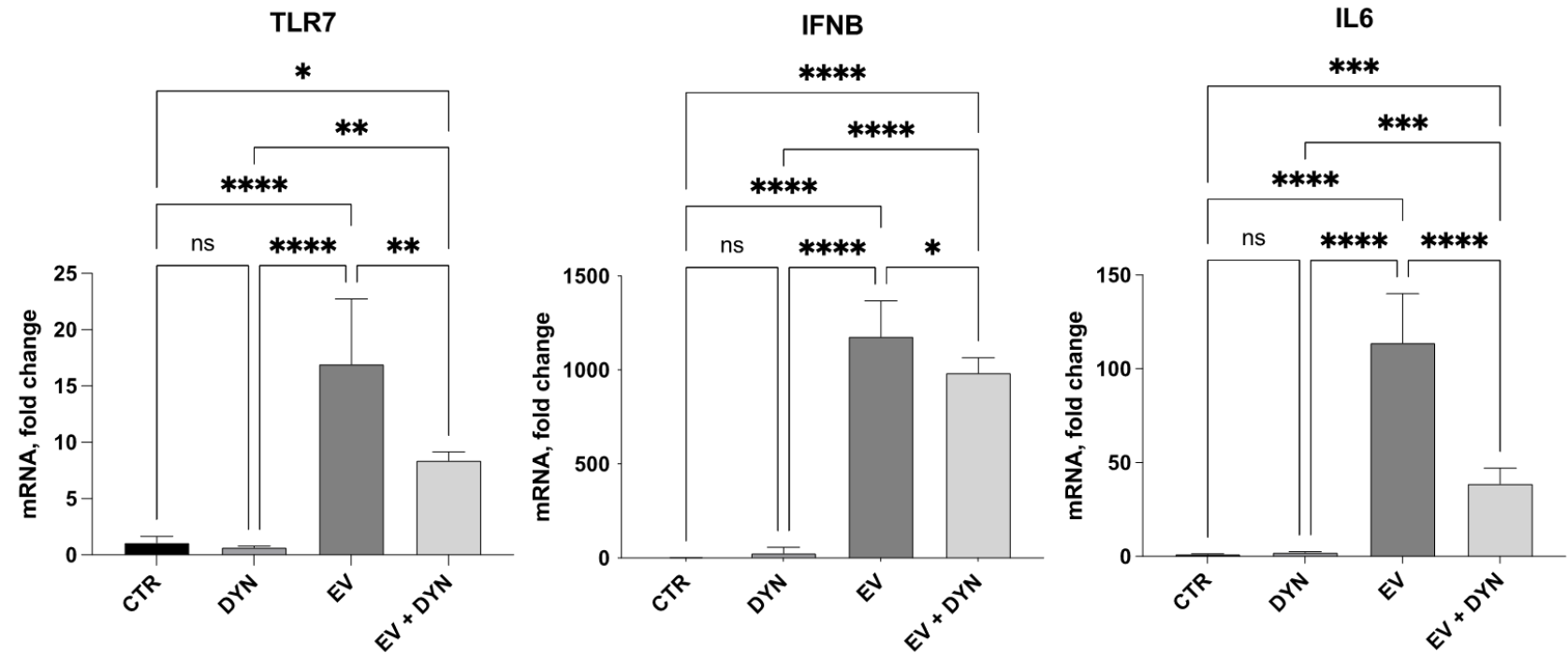
→ Internalization of N315 EVs can depend upon dynamin-mediated endocytosis and macropinocytosis



Dil-labelled Extracellular vesicles from N315 strain



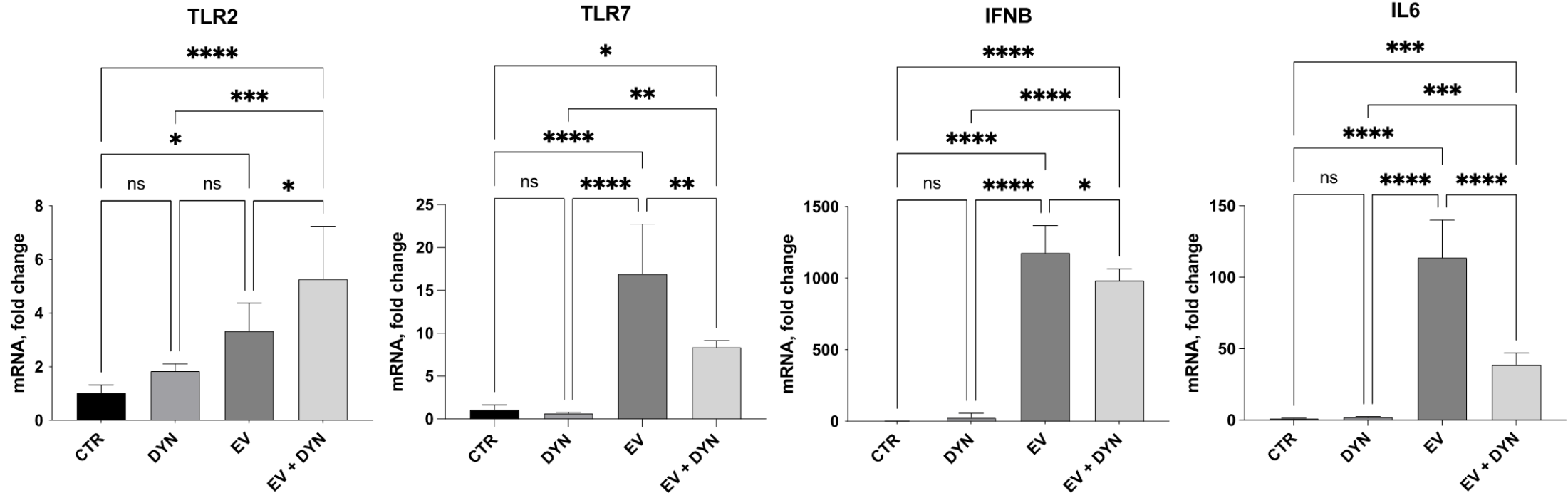
✓ Modulation of genes expression



→ The induced expression mediated by EVs of *TLR7*, *IFNβ* and *IL-6* genes is dependent on the internalization of EVs

→ Several pathways can be used by EVs to interact with host cells

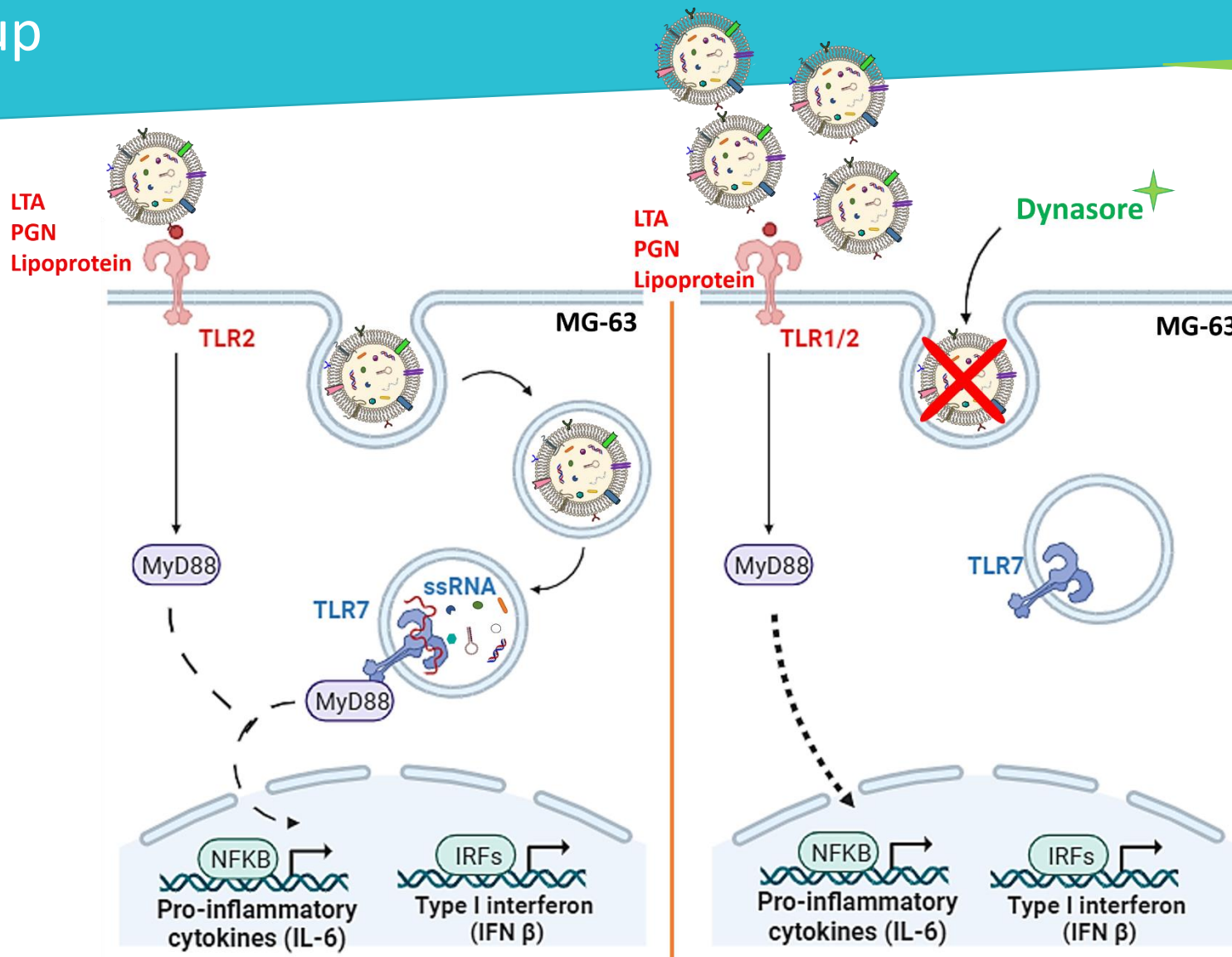
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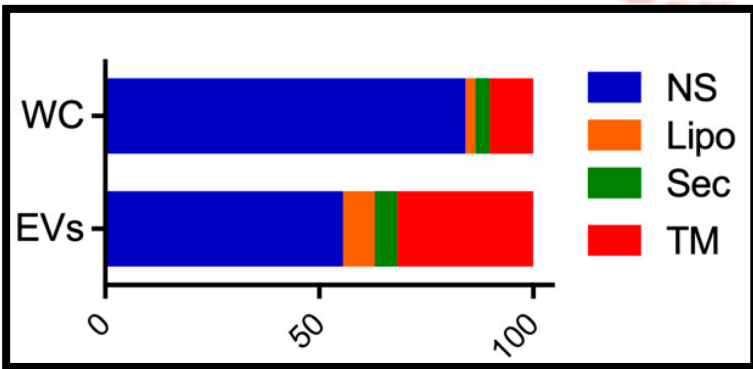
✓ To sum up



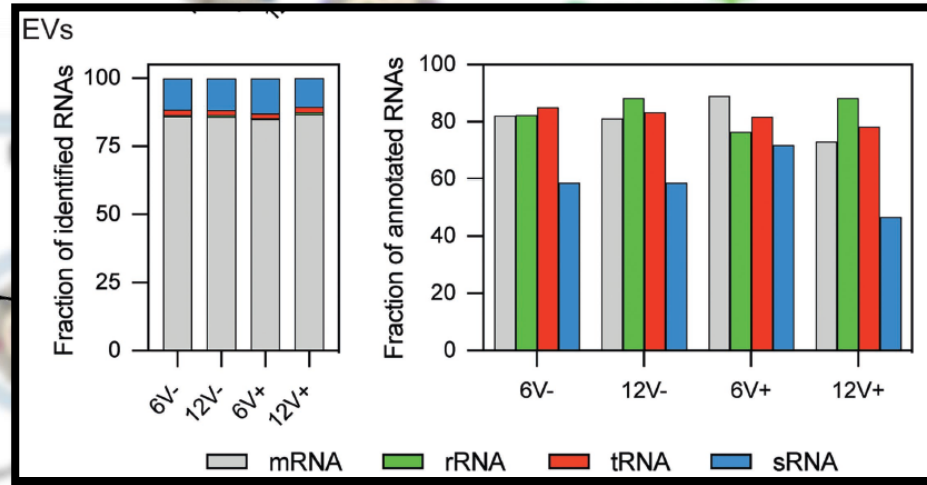
- N315-derived EVs can trigger both extracellular and intracellular signaling pathway in host cells
- Several EV components (proteins, RNA) can be involved in the interaction with host cells

✓ To sum up

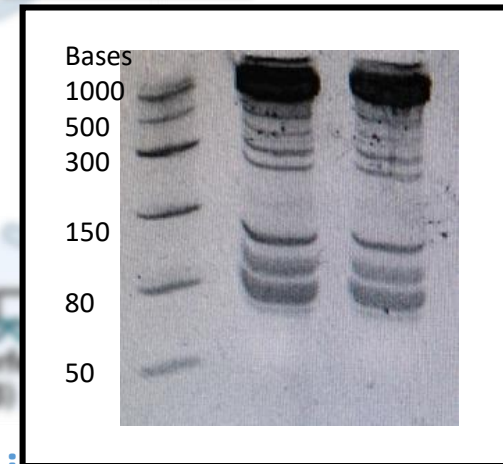
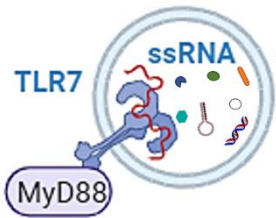
Lipoproteins



Luz and al., 2022



Luz and al., 2021



- N315-derived EVs can trigger both extracellular and intracellular signaling pathway in host cells
- Several EV components (proteins, RNA) can be involved in the interaction with host cells

Acknowledgment



Bacterial RNAs & Medicine



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