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Julia Papail, Ligia Prado, Nathalie Daniel, Daniele Vassaux, Yann Le Gouar, Nadia Berkova, Julien Jardin, Svetlana Chabelskaia, Yves Le Loir, Vasco Azevedo, et al.

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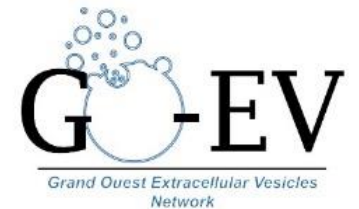


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# Interaction mechanisms with host of EVs derived from the opportunistic pathogen *Staphylococcus aureus*

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



<sup>1</sup>INRAE, Institut Agro, STLO, Rennes, France;

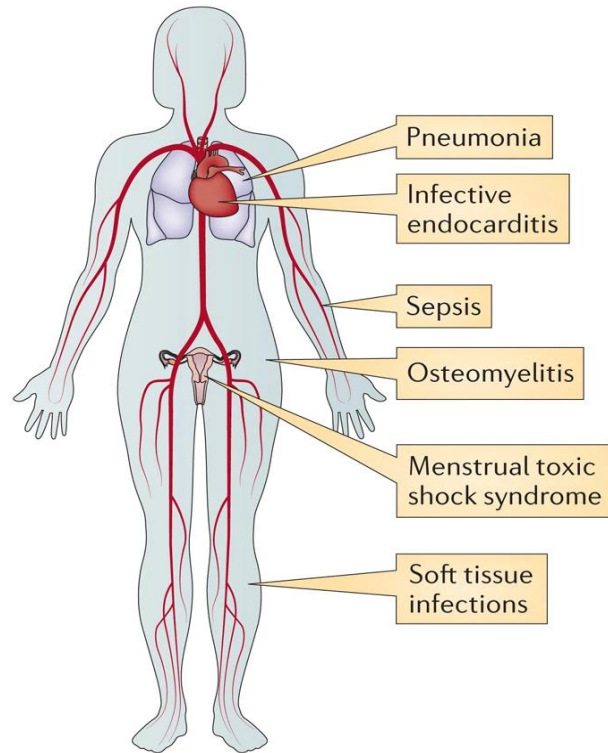
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<sup>3</sup>Université de Rennes, INSERM U1230, BRM, Rennes, France;

<sup>4</sup>Laboratory 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

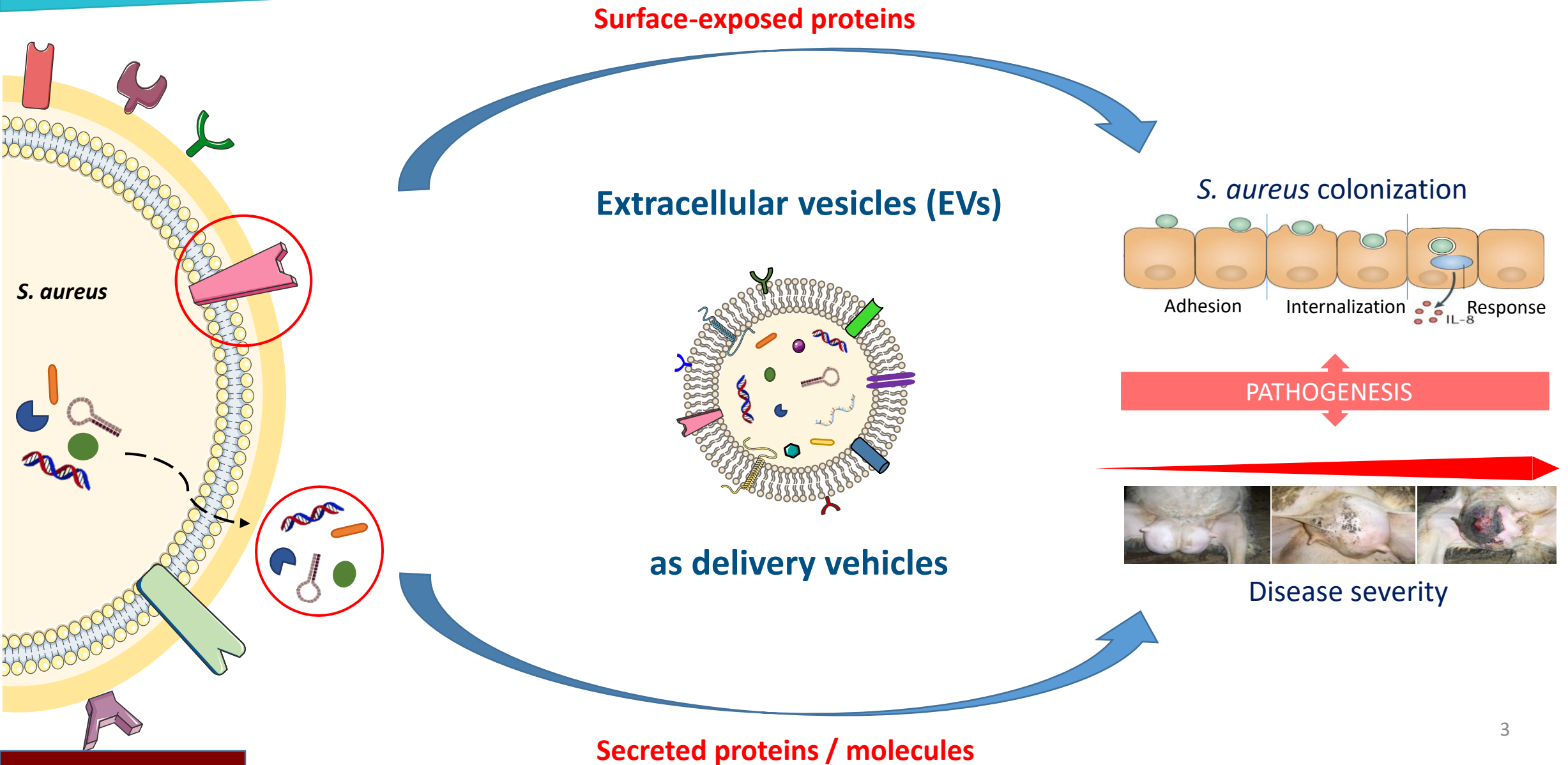


## ➤ The six highly virulent and antibiotic resistant bacterial pathogens

ESKAPE

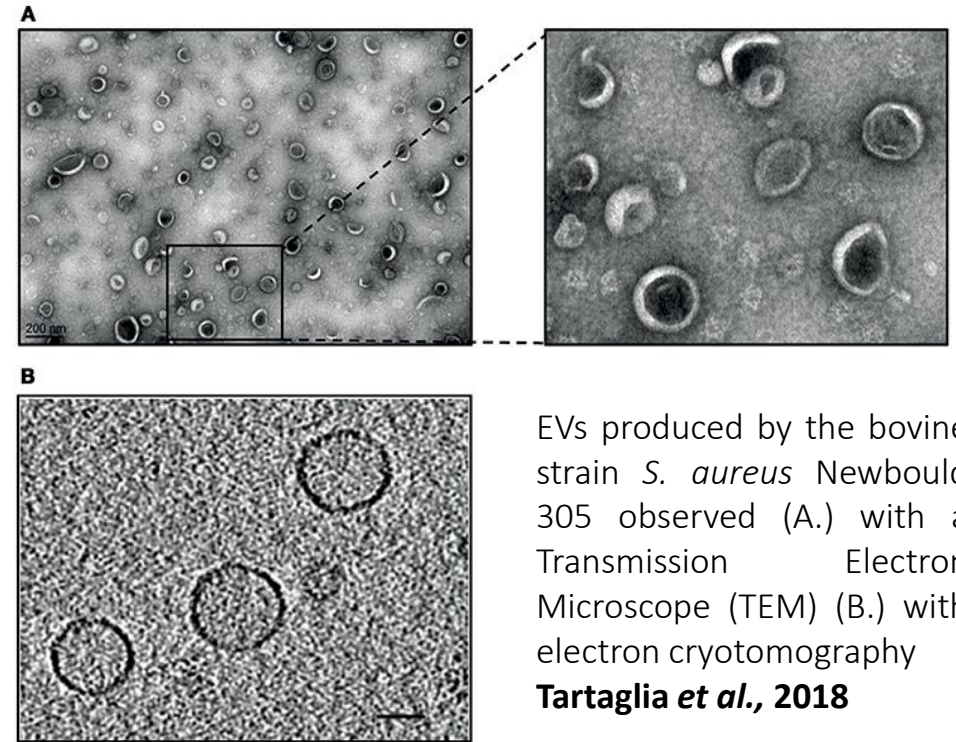


✓ *Staphylococcus aureus* virulence factors



# ✓ Extracellular vesicles (EVs)

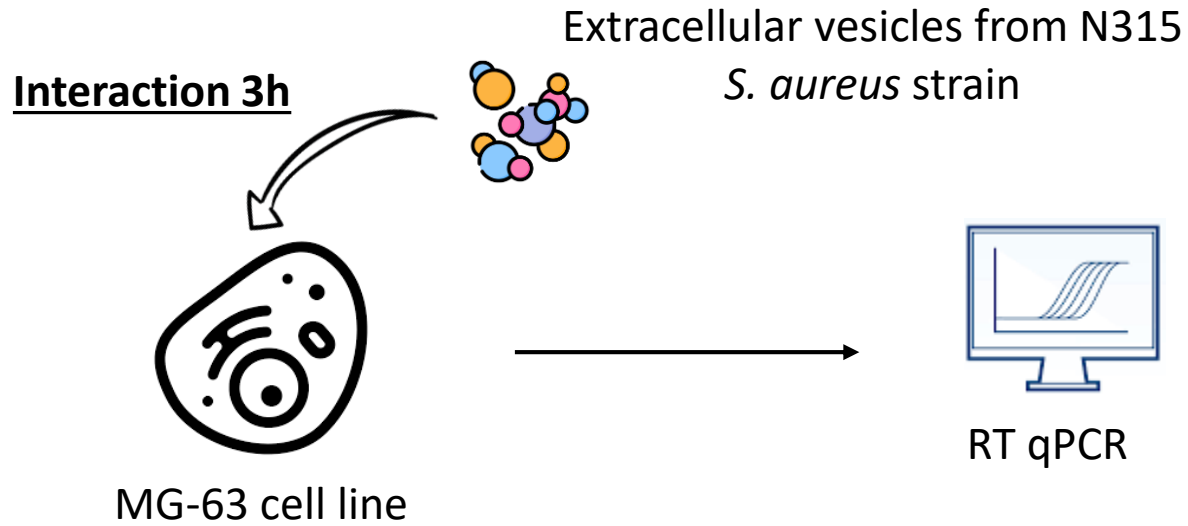
- Lipid bilayer spherical nano-sized particles (30-300 nm) which carry various molecules (eg, lipids, nucleic acids, proteins)
- Vehicles that transport and deliver molecules to local or distant cellular targets
- Imply in cell-to-cell communication and especially in host-pathogen interaction



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

# ✓ Role of extracellular vesicles in pathogenesis

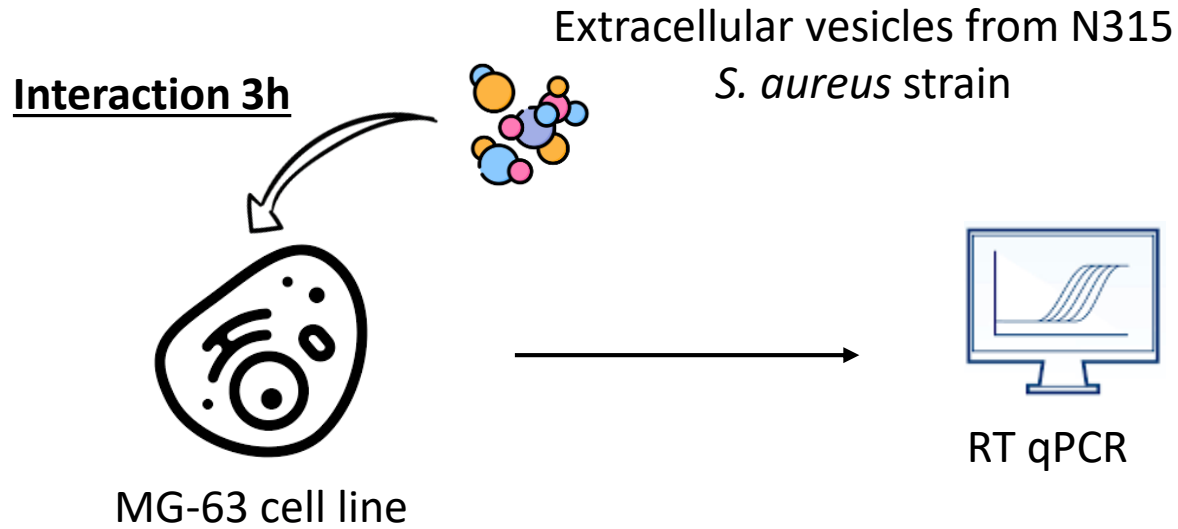
Impact of EVs on the expression of several inflammatory genes



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

# ✓ Role of extracellular vesicles in pathogenesis

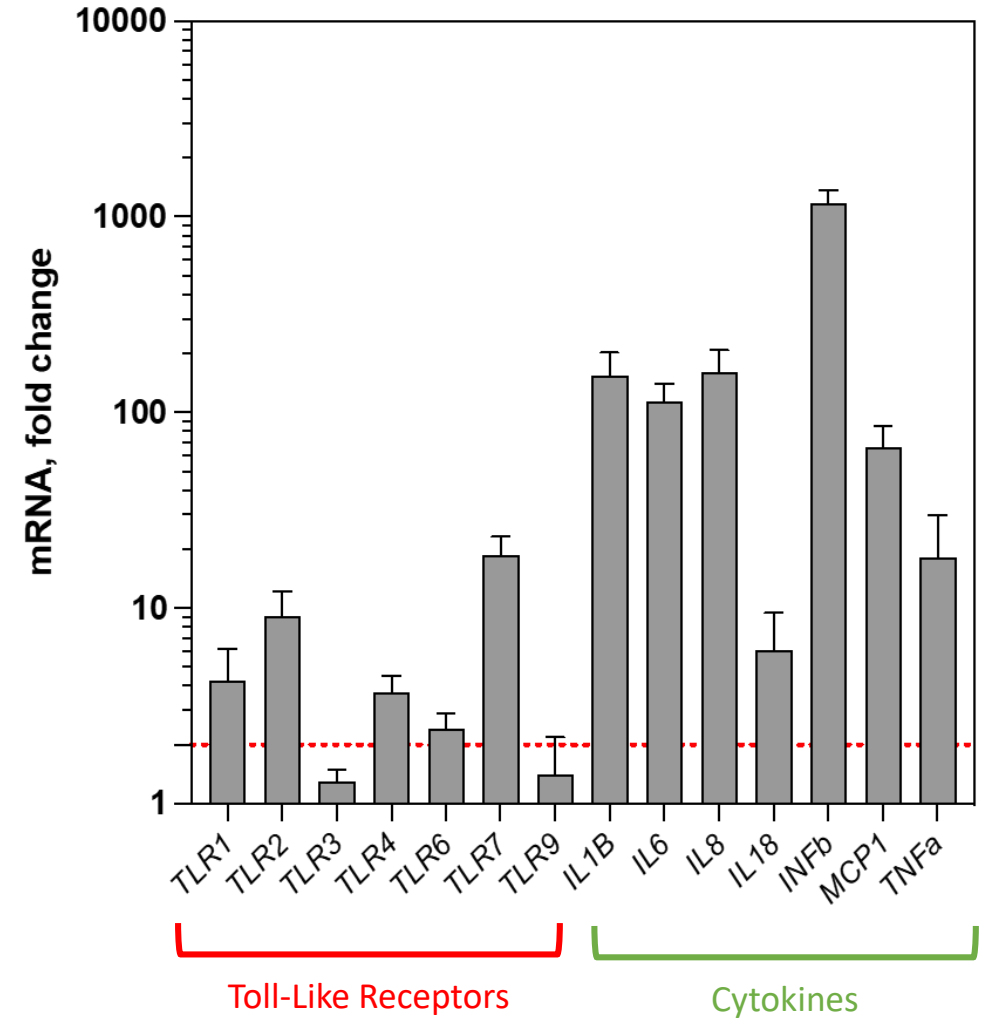
Impact of EVs on the expression of several inflammatory genes



Increased expression of genes coding for :

✓ Cytokines

✓ Toll-Like Receptors (TLR)

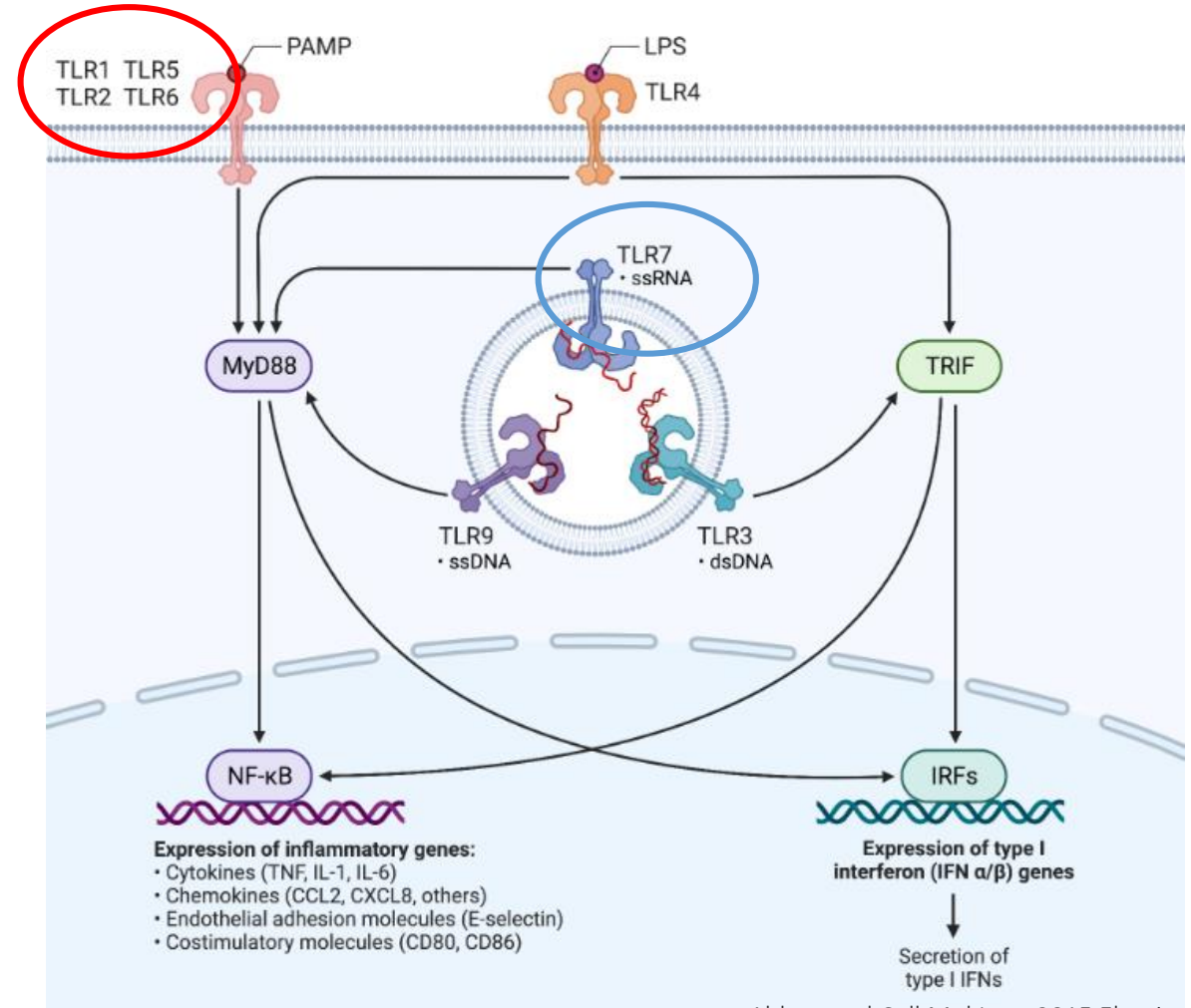
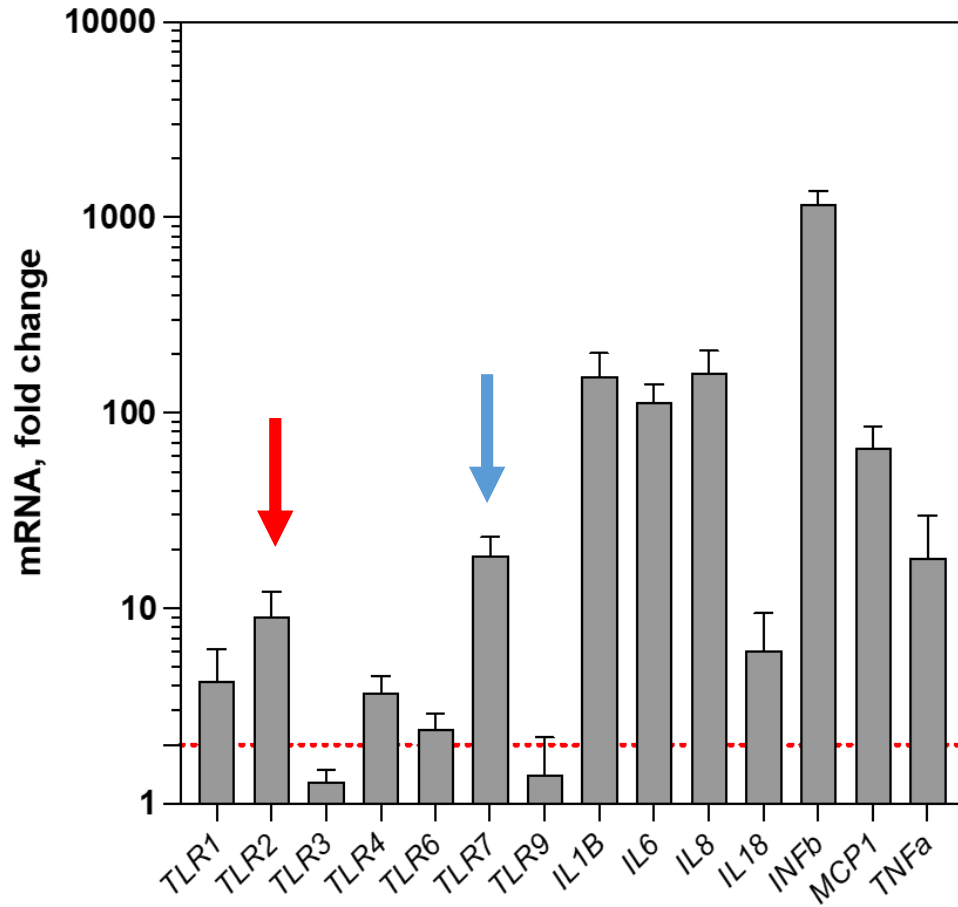


→ N315-derived EVs induce the expression of various *TLR* and immune genes in MG-63 cells



# ✓ Role of extracellular vesicles in pathogenesis

Impact of EVs on the expression of several inflammatory genes



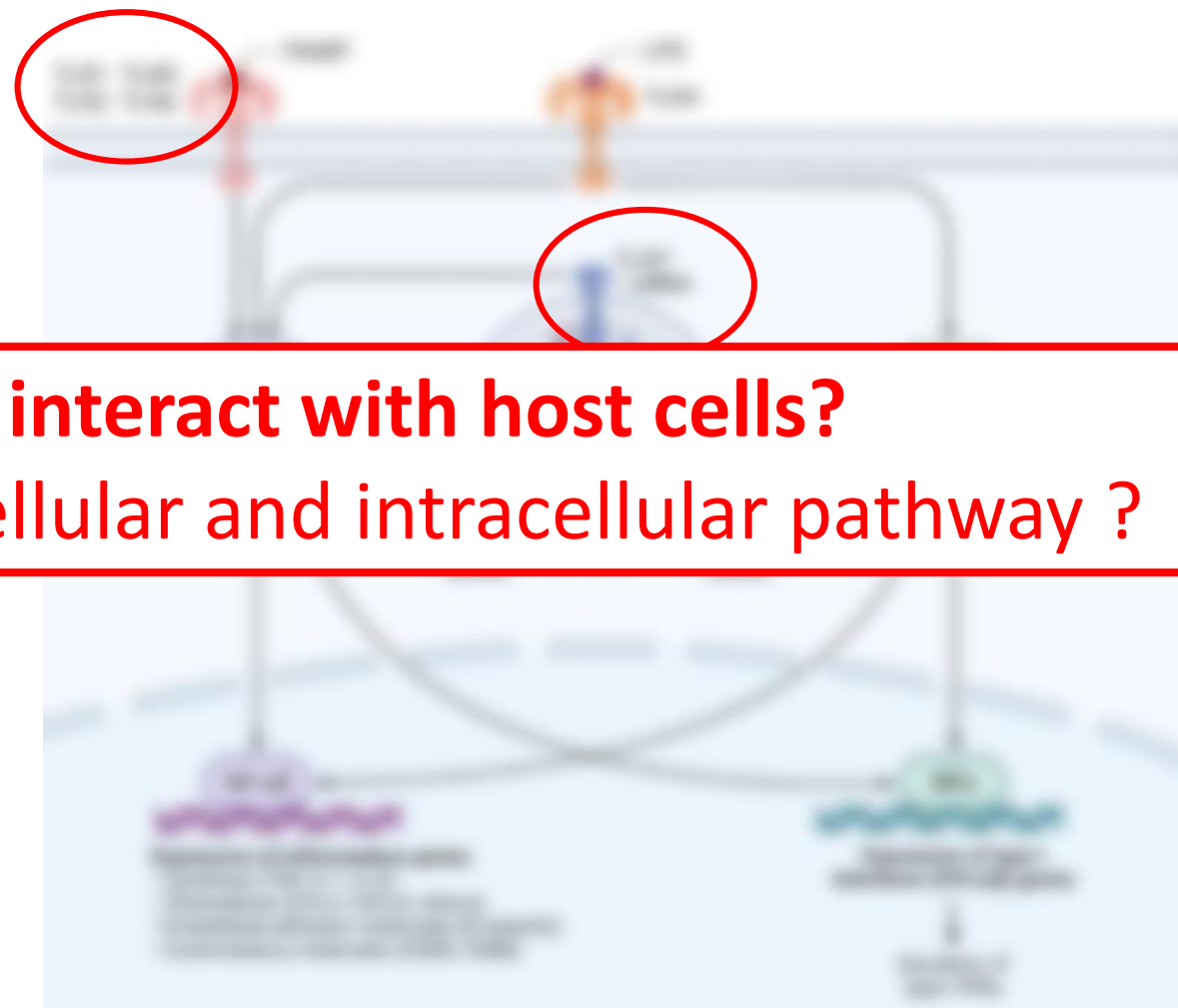
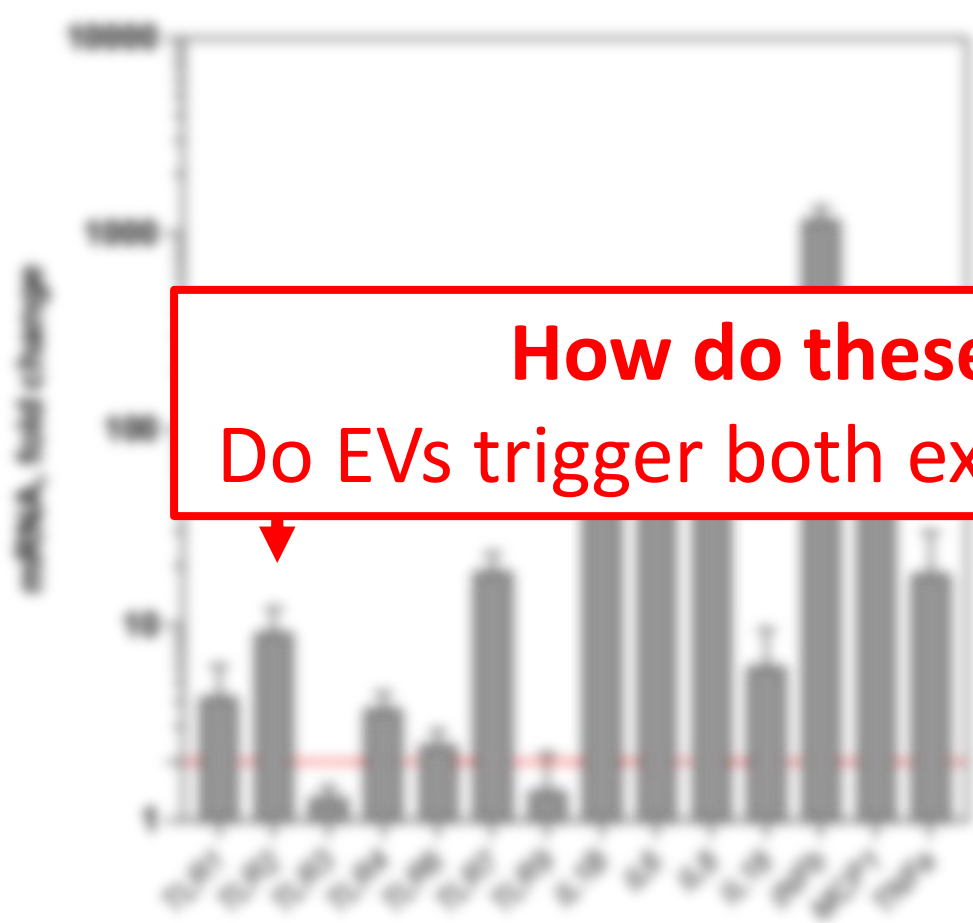
Abbas et al Cell Mol Imm 2015 Elsevier

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



# ✓ Role of extracellular vesicles in pathogenesis

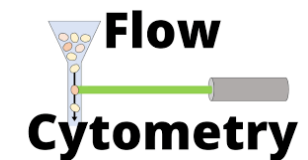
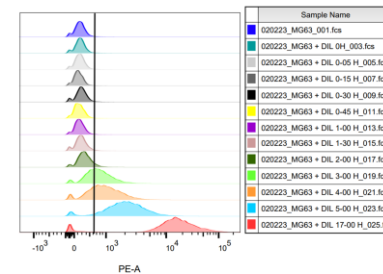
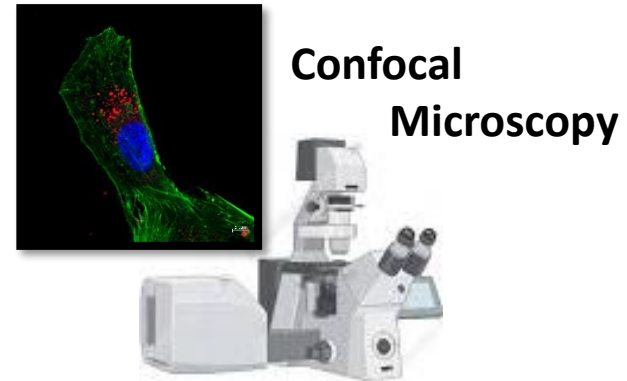
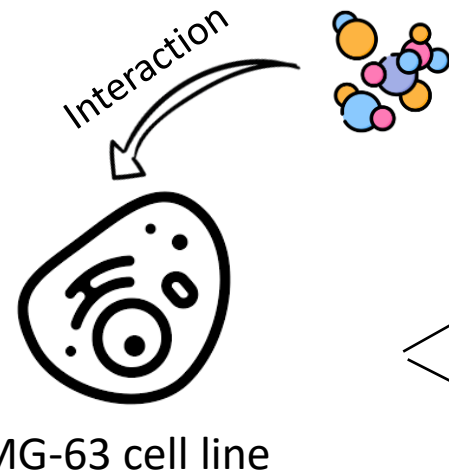
Impact of EVs on the expression of several inflammatory genes



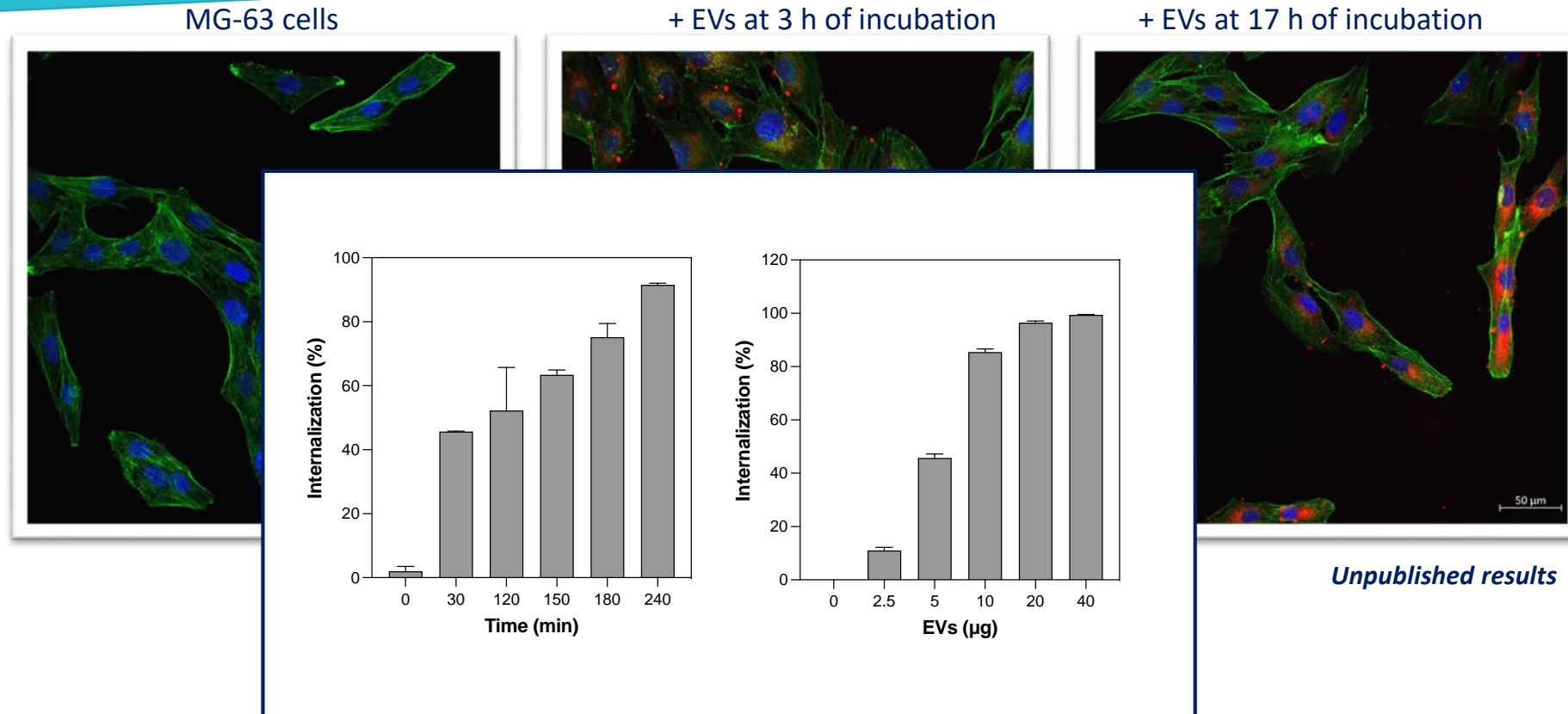
**How do these EVs interact with host cells?**  
Do EVs trigger both extracellular and intracellular pathway ?

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

Dil-labelled Extracellular vesicles  
from N315 strain



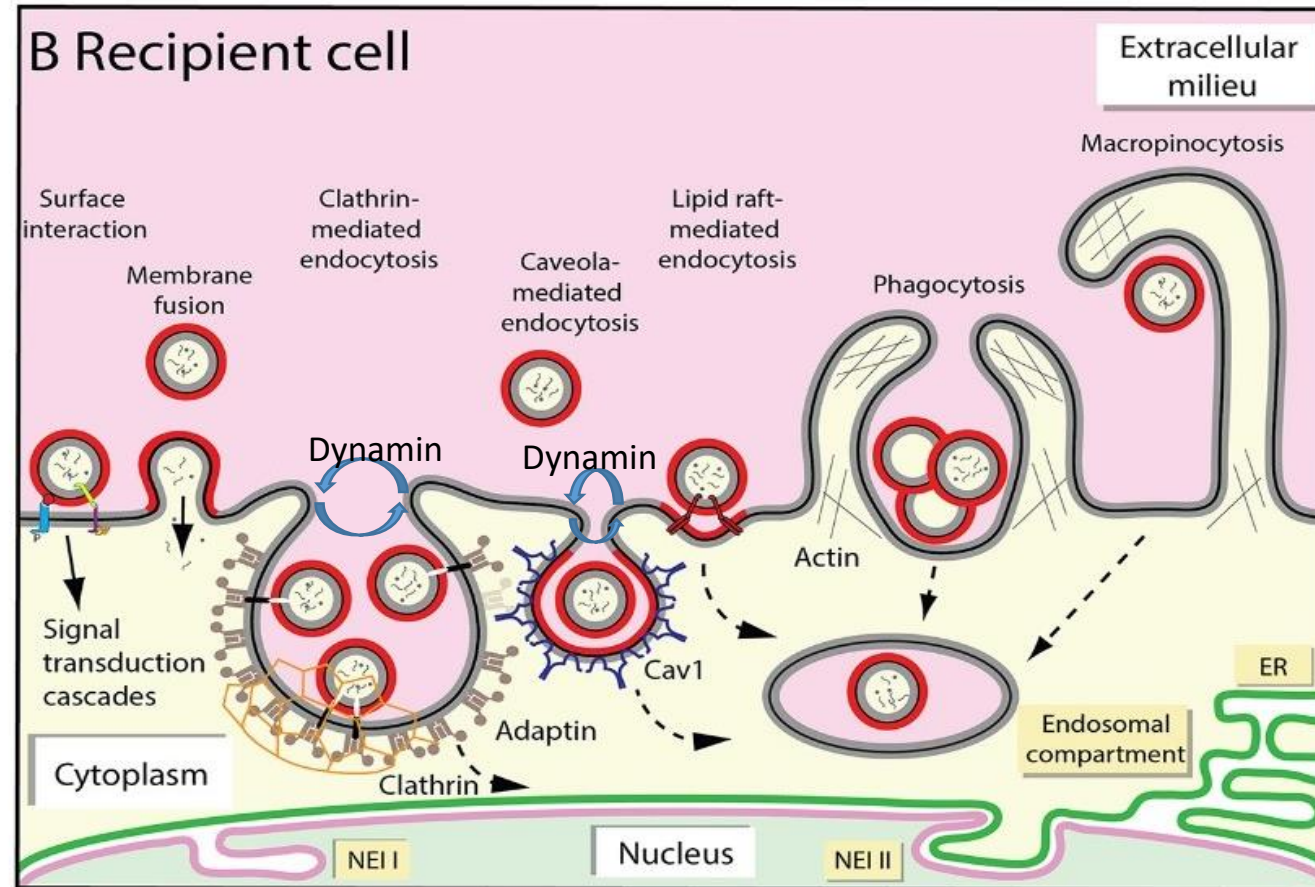
# ✓ Internalization of EVs by MG-63 cells



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

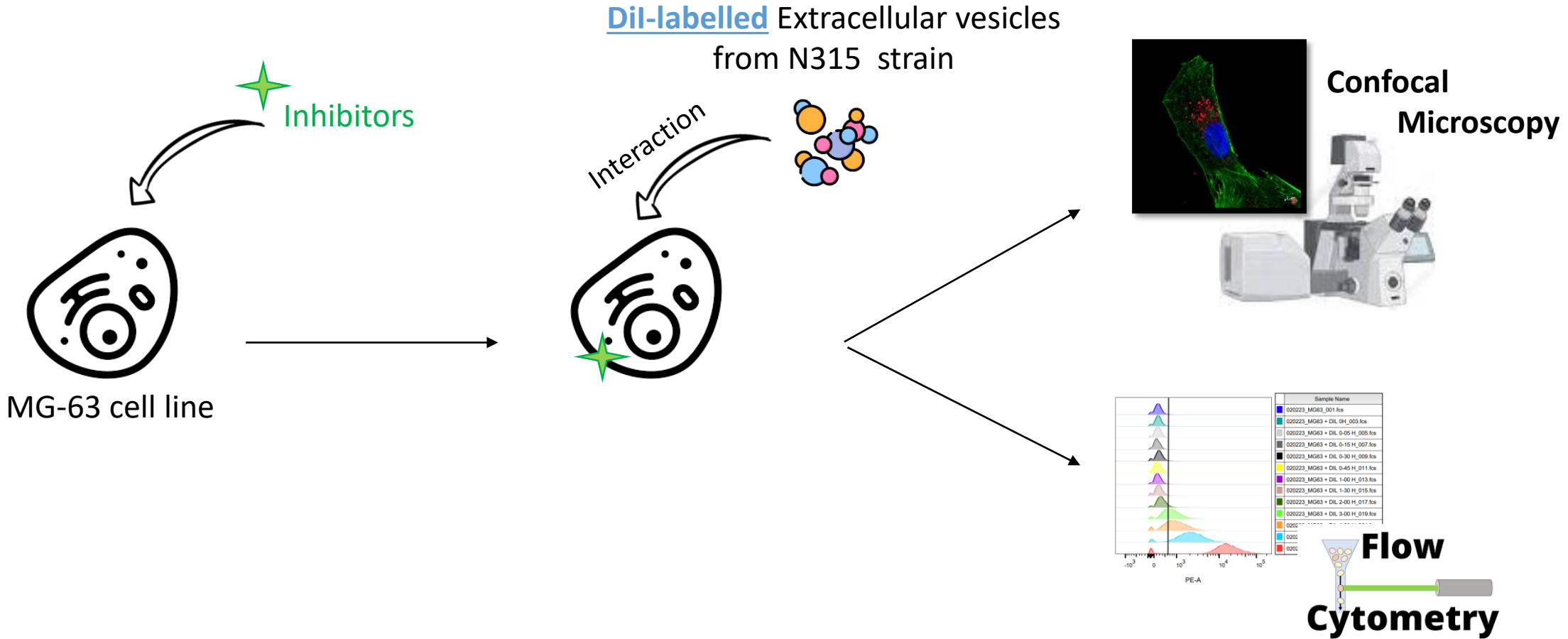
- in a dose-dependent manner
- in a time-dependent manner

# ✓ Internalization of EVs by MG-63 cells



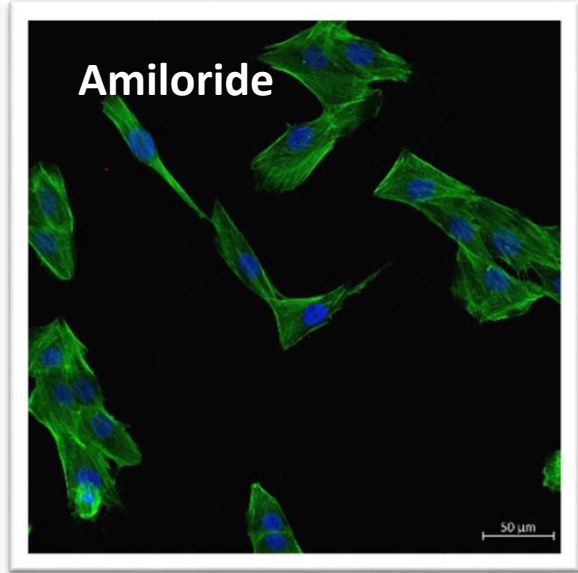
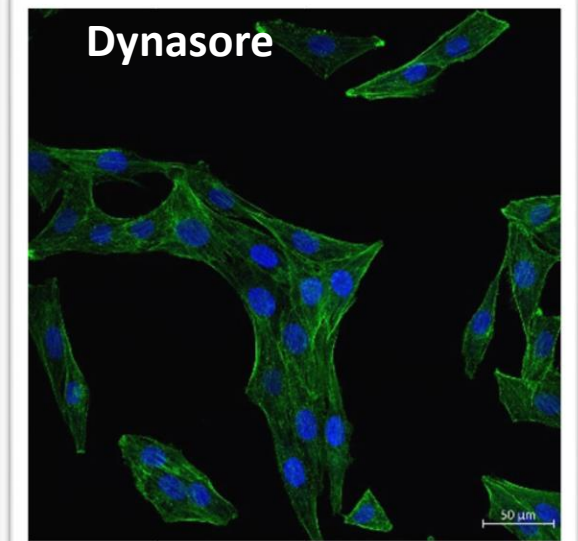
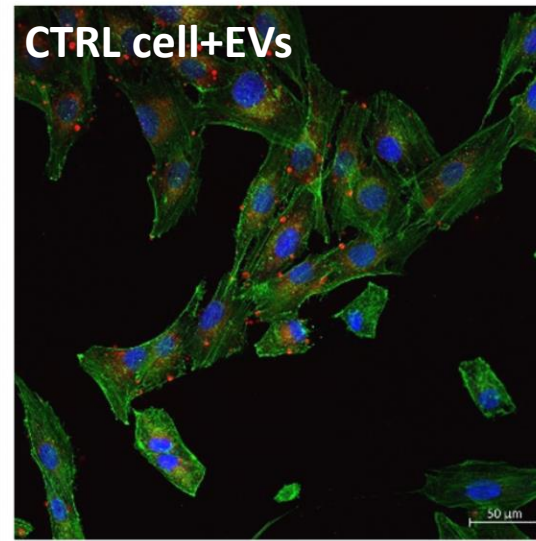
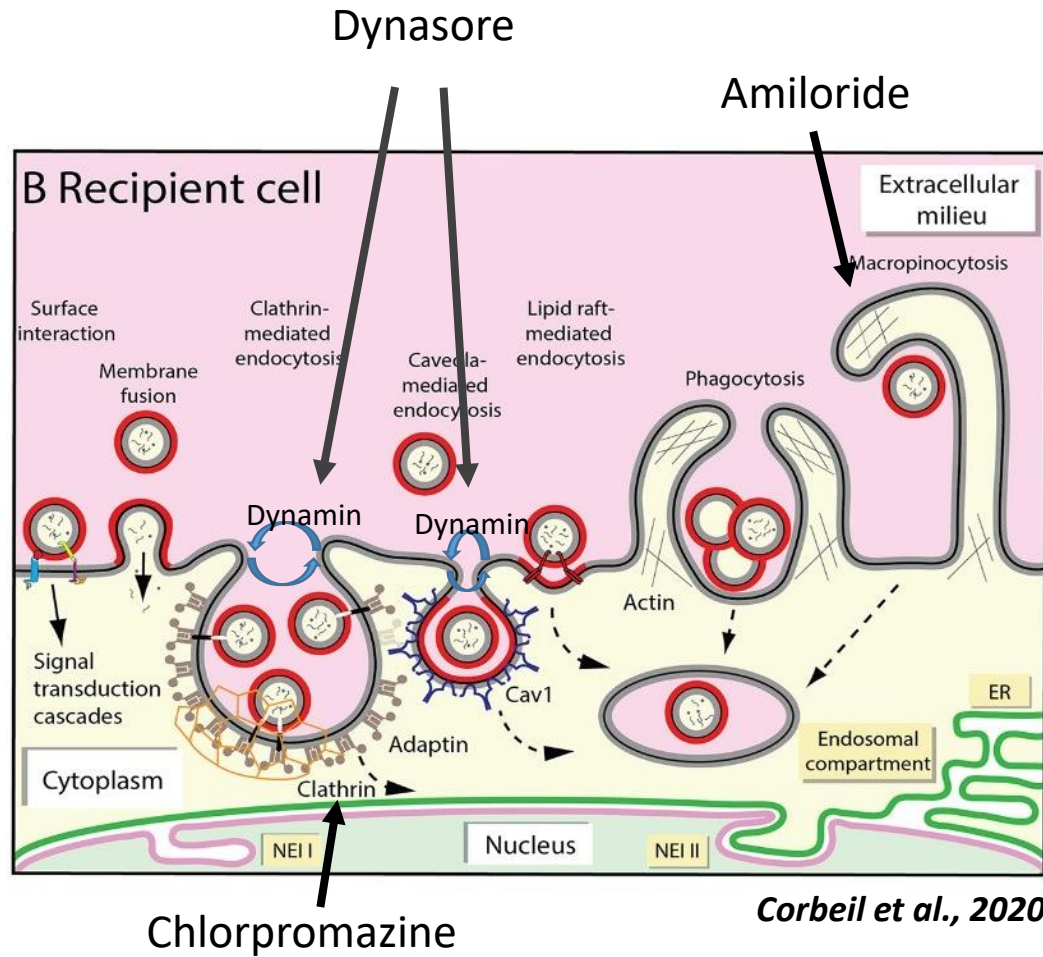
Corbeil et al., 2020

→ Several different pathways of internalization are possible





✓ Internalization of EVs by MG-63 cells

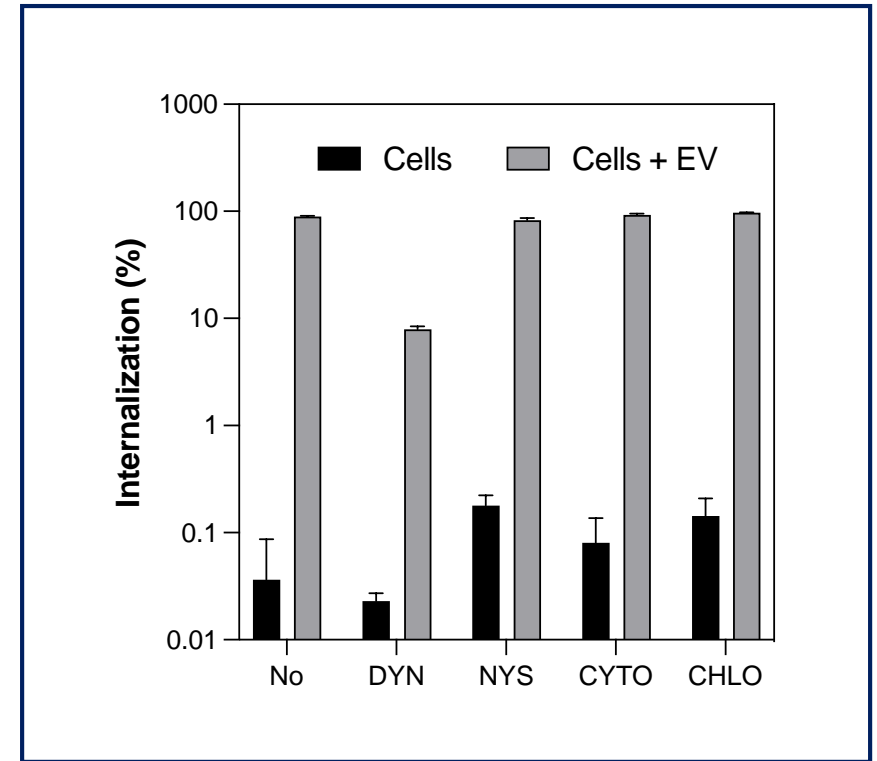
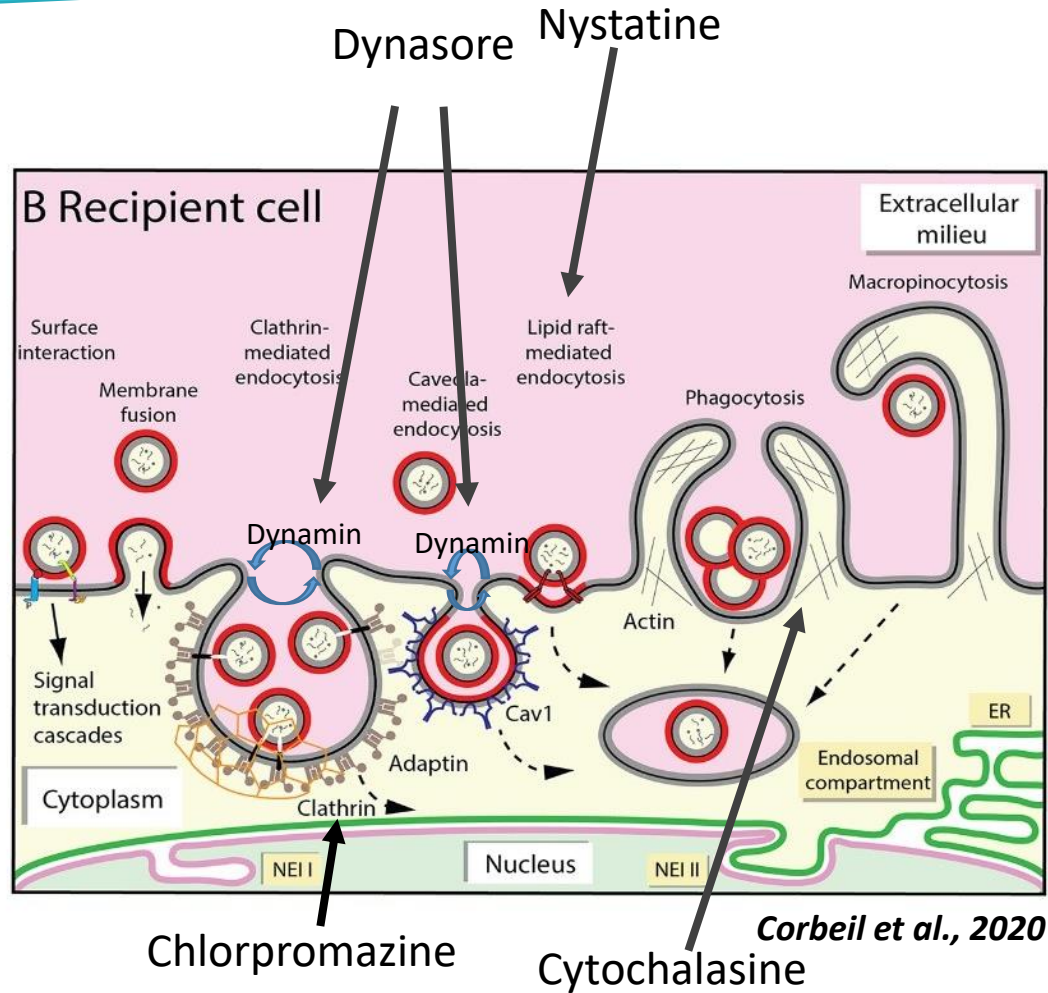


Unpublished results

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

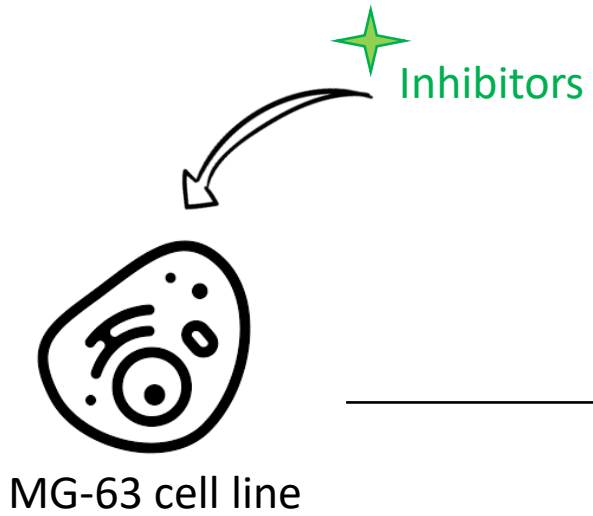


# ✓ Internalization of EVs by MG-63 cells

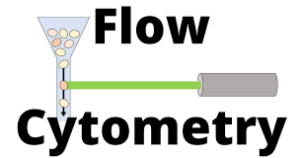
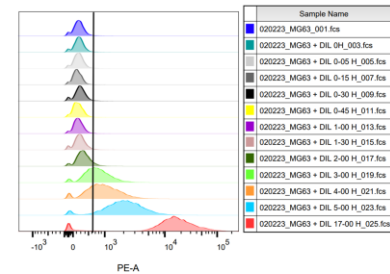
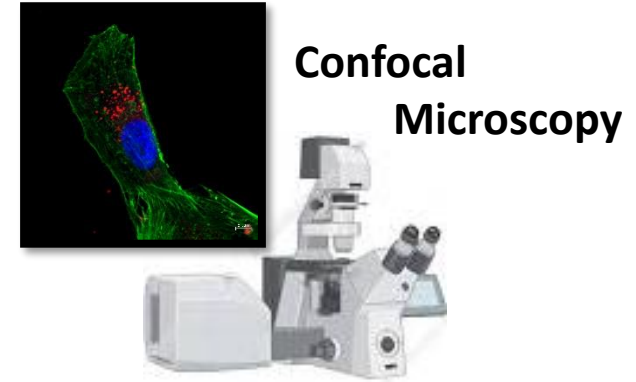
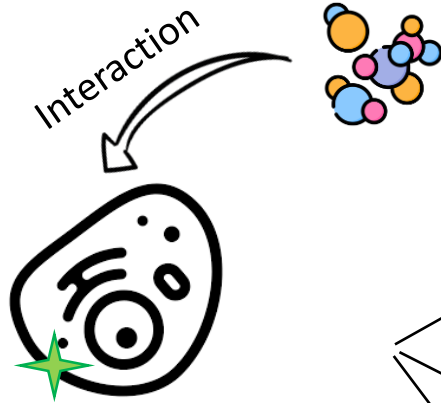


*Unpublished results*

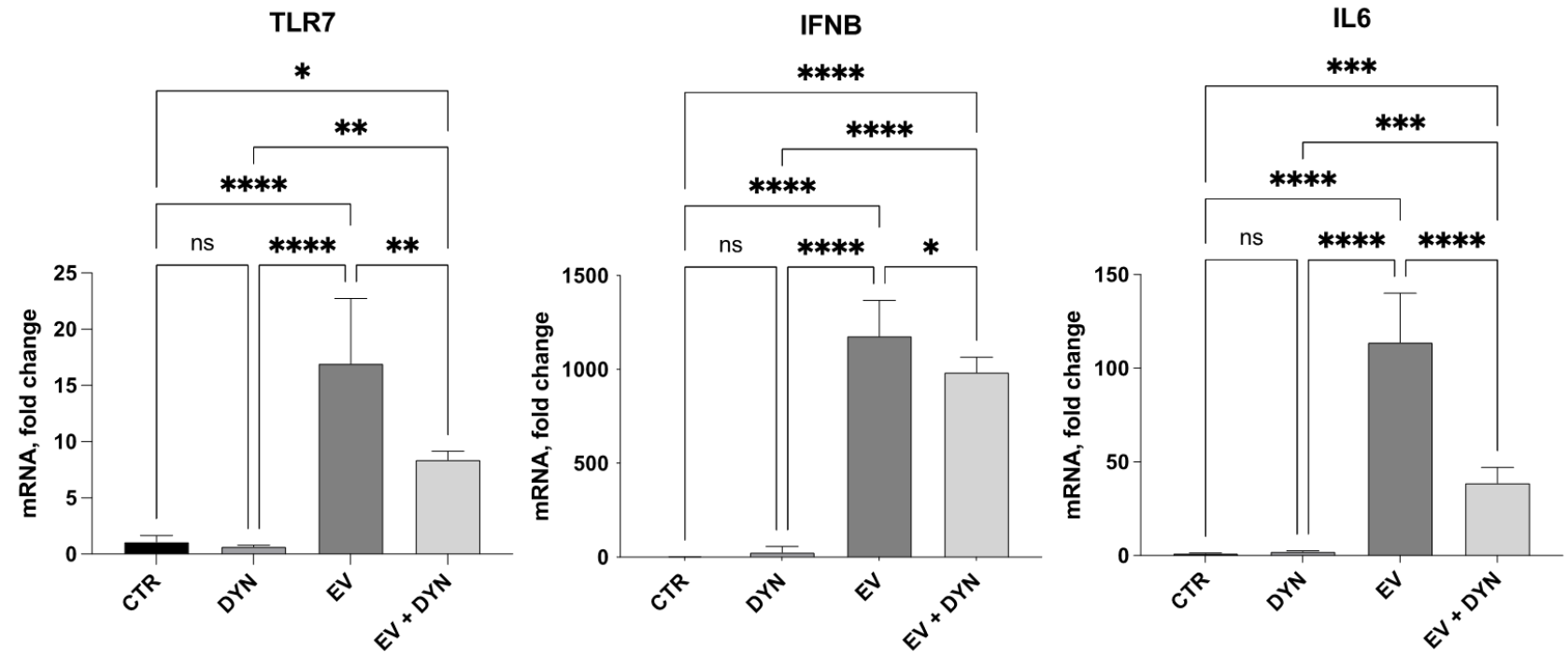
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Dil-labelled Extracellular vesicles from N315 strain



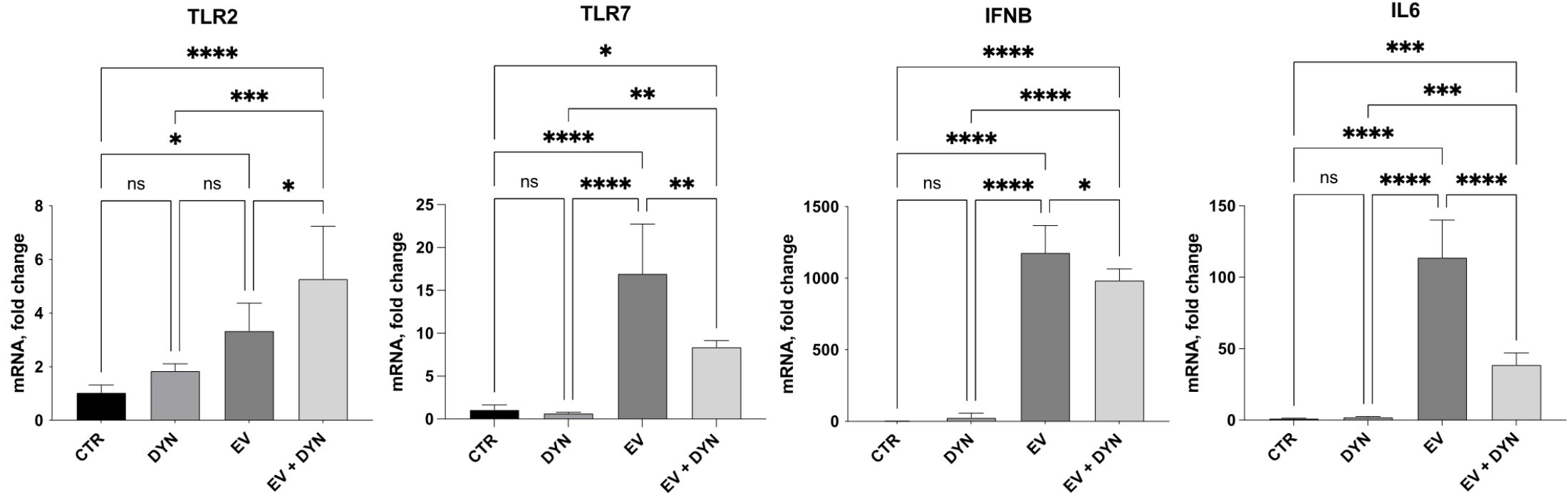
# ✓ Modulation of genes expression



→ 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

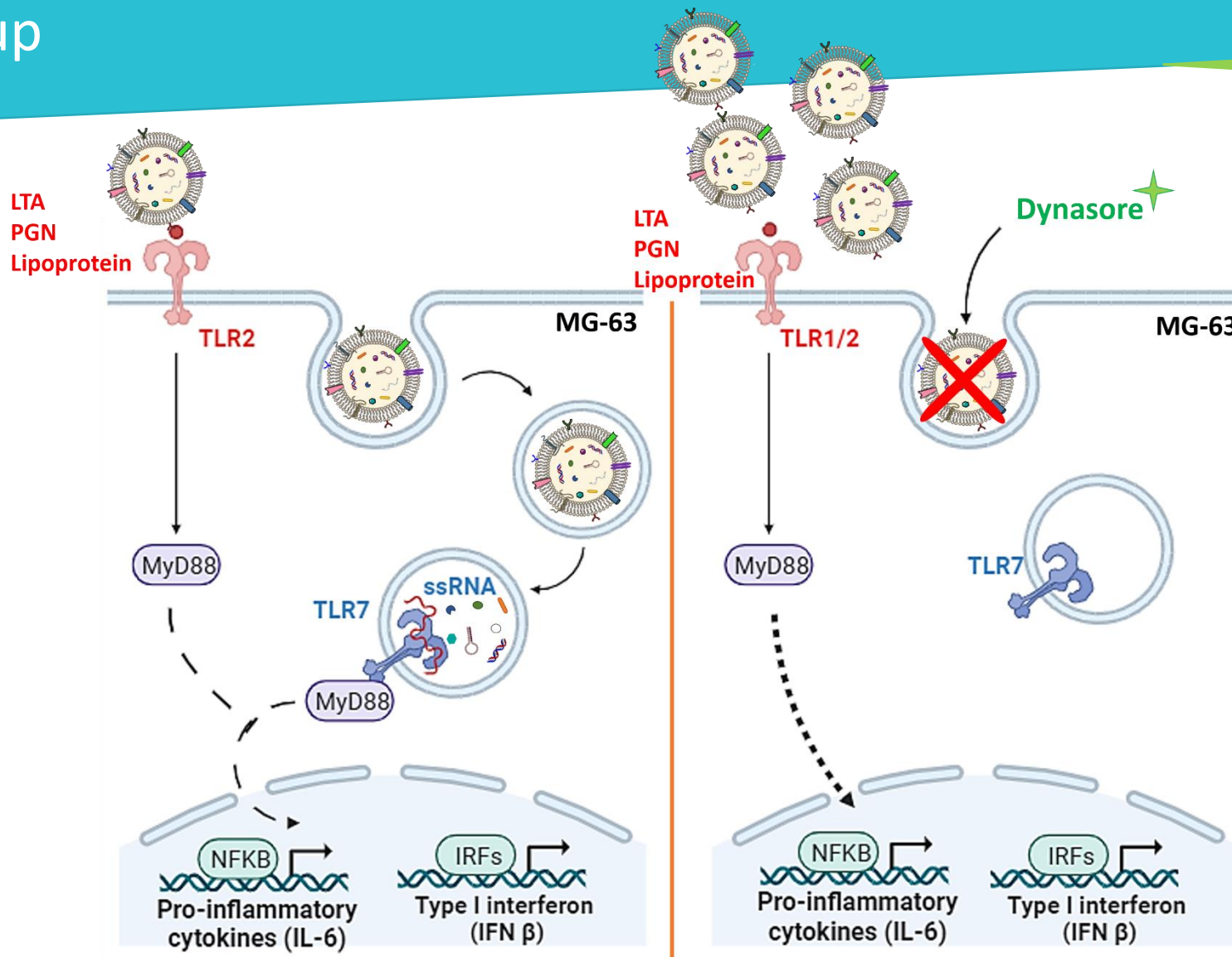
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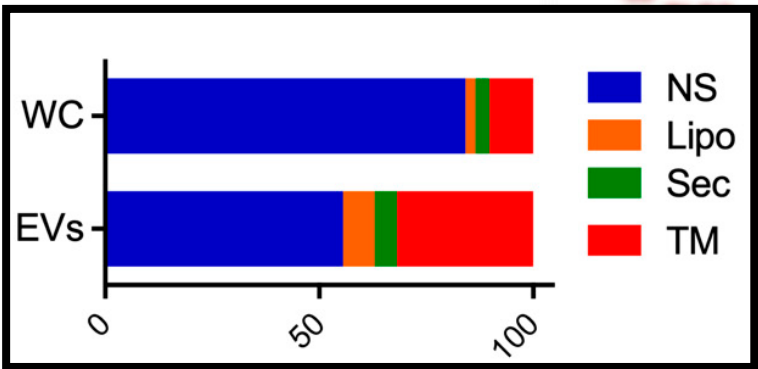
✓ To sum up



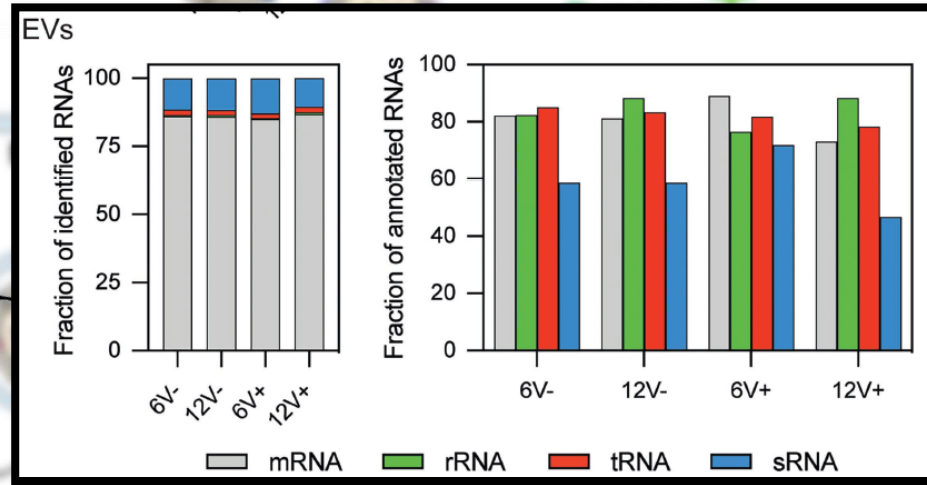
- N315-derived EVs can trigger both extracellular and intracellular signaling pathway in host cells
- Several EV components (proteins, RNA) can be involved in the interaction with host cells

✓ To sum up

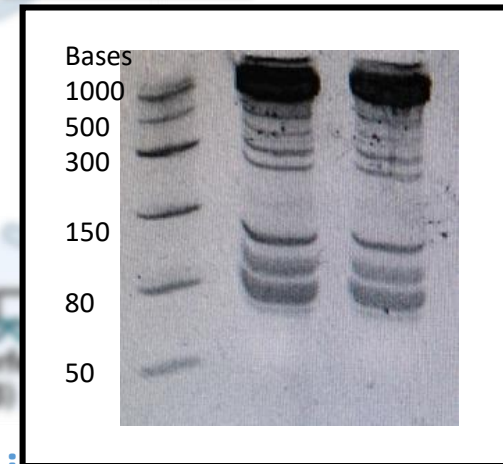
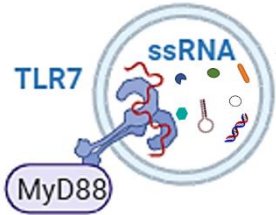
Lipoproteins



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



Institut national  
de la santé et de la recherche médicale



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