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Julia Papail, Ligia Prado, Nathalie Daniel, Brenda Silva Rosa da Luz, Daniele Vassaux, Yann Le Gouar, Nadia Berkova, Julien Jardin, Svetlana Chabelskaia, Yves Le Loir, et al.

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Extracellular vesicles from *Staphylococcus aureus* follow different pathways to manipulate host cells

**Julia PAPAIL¹, Ligia PRADO^{1,2}, Nathalie DANIEL¹, Daniele VASSAUX¹, Yann LE GOUAR¹, Nadejda BERKOVA¹,
Julien JARDIN¹, Svetlana CHABELSKAIA³, Yves LE LOIR¹, Vasco AZEVEDO⁴, Éric GUÉDON¹**

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

²Institute of Biological and Natural Sciences, Federal University of Triângulo Mineiro, Uberaba, Brazil;

³Université de Rennes, INSERM U1230, BRM, Rennes, France;

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



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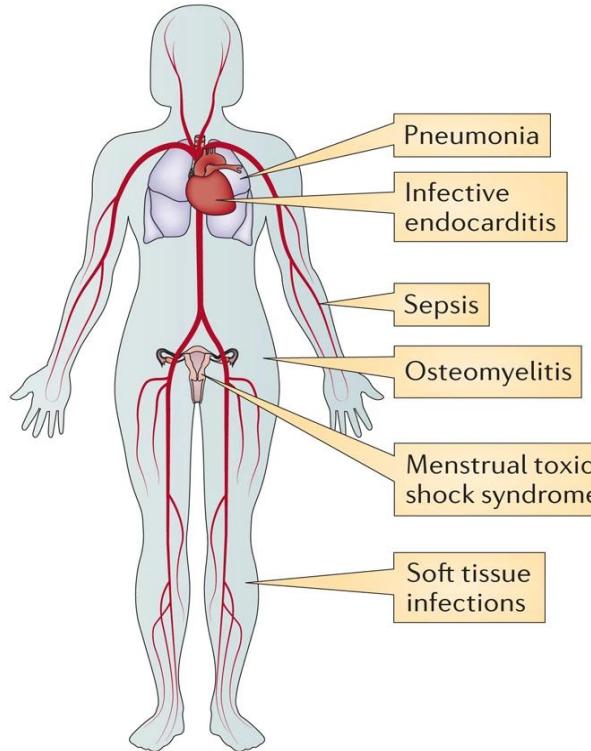


Conflict of interest declaration

For this presentation,
I declare that I have no conflict of interest.

✓ *Staphylococcus aureus*

- Human opportunist pathogen



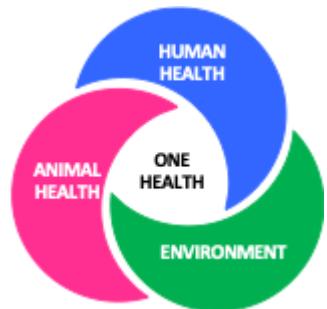
Diseases caused by *Staphylococcus aureus*
Salgado-Pabón W and Schlievert P., 2014

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

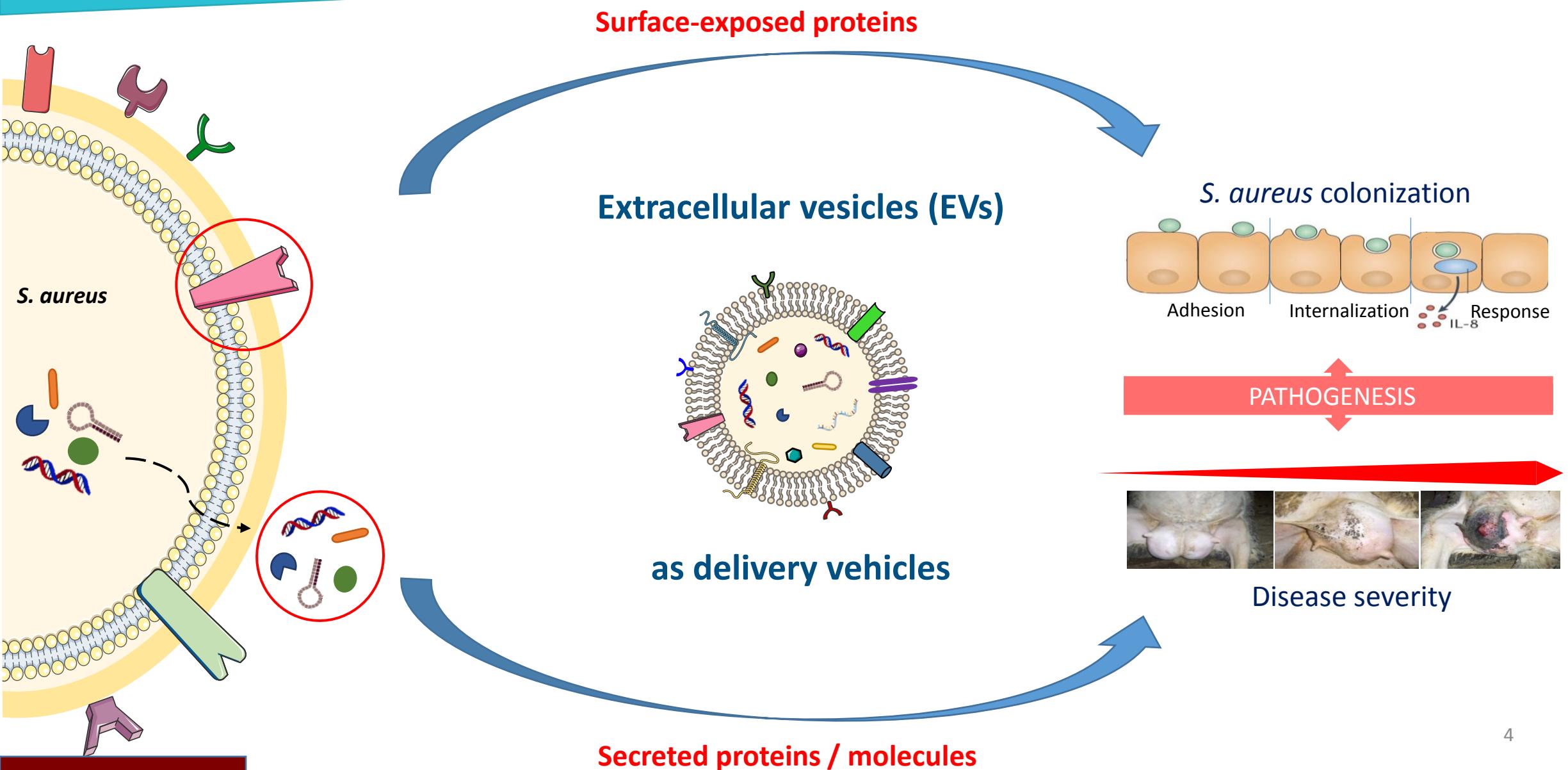


- The six highly virulent and antibiotic resistant bacterial pathogens

ESKAPE

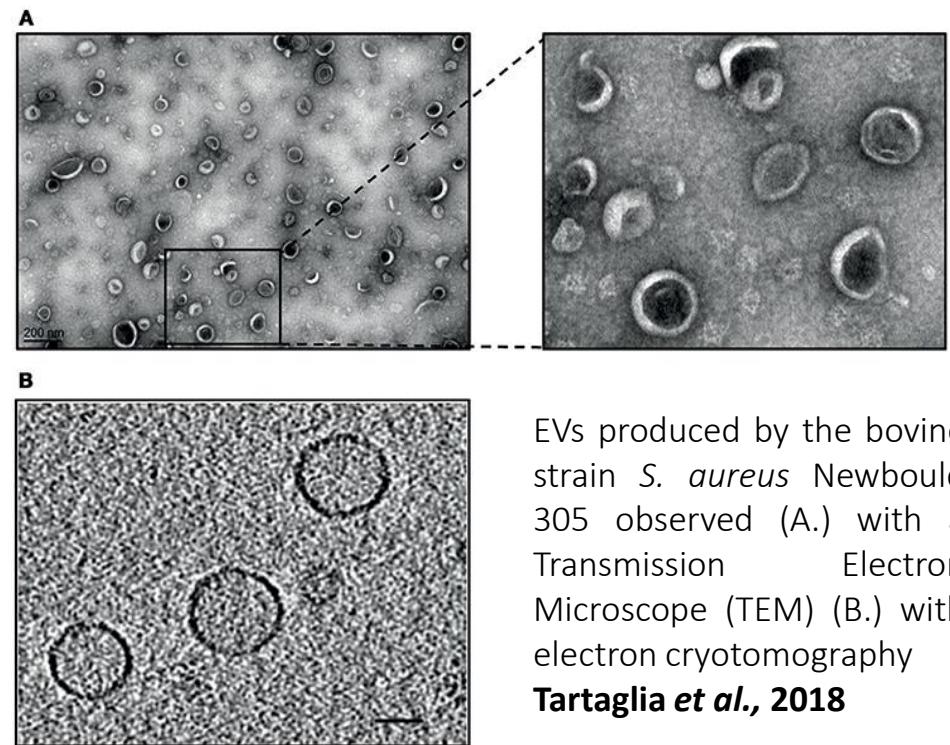


✓ *Staphylococcus aureus* virulence factors



✓ 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

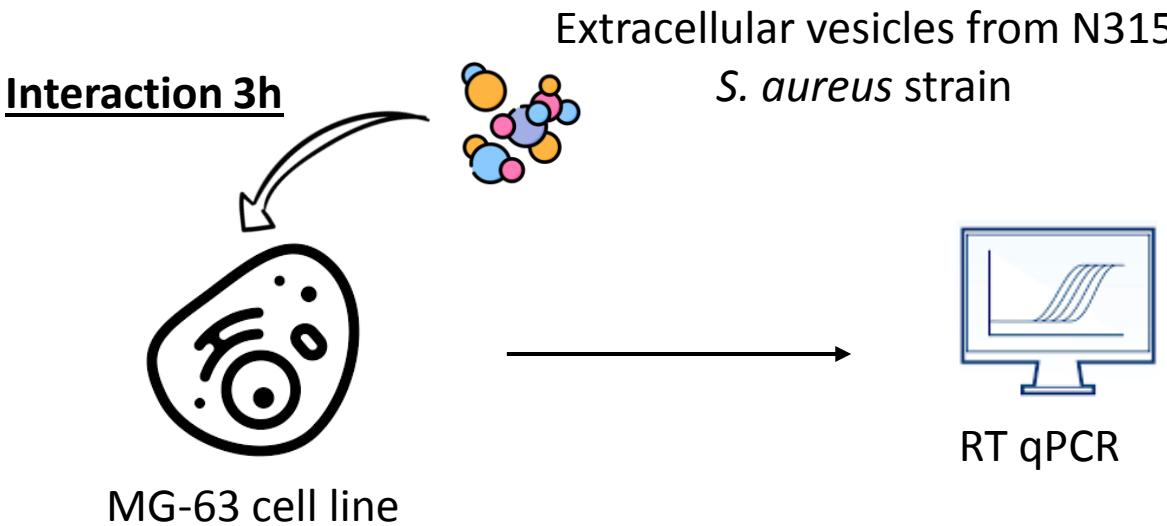


EVs produced by the bovine strain *S. aureus* Newbould 305 observed (A.) with a Transmission Electron Microscope (TEM) (B.) with electron cryotomography
Tartaglia et al., 2018

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

✓ Role of extracellular vesicles in pathogenesis

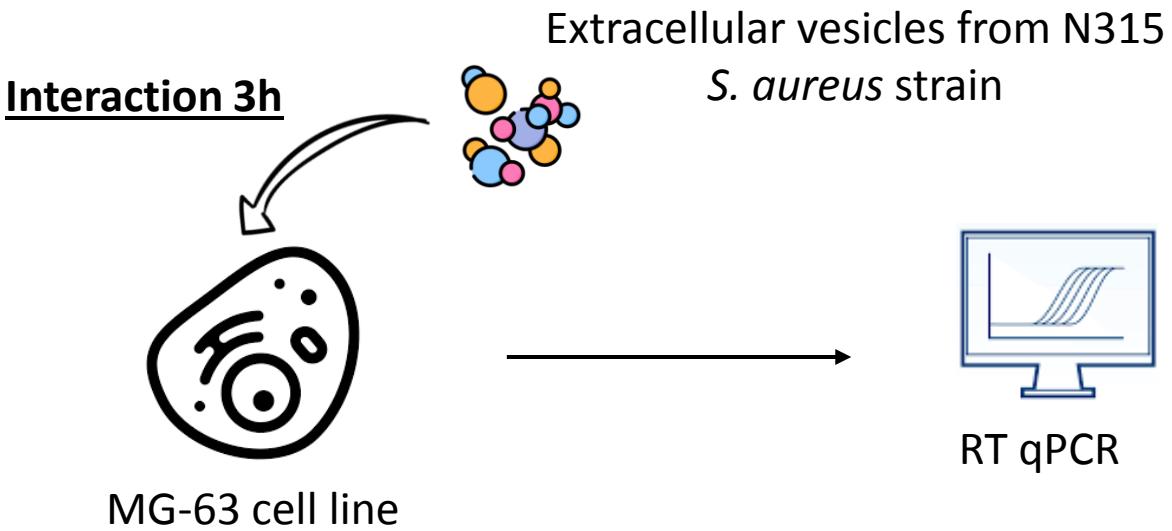
Impact of EVs on the expression of several inflammatory genes



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

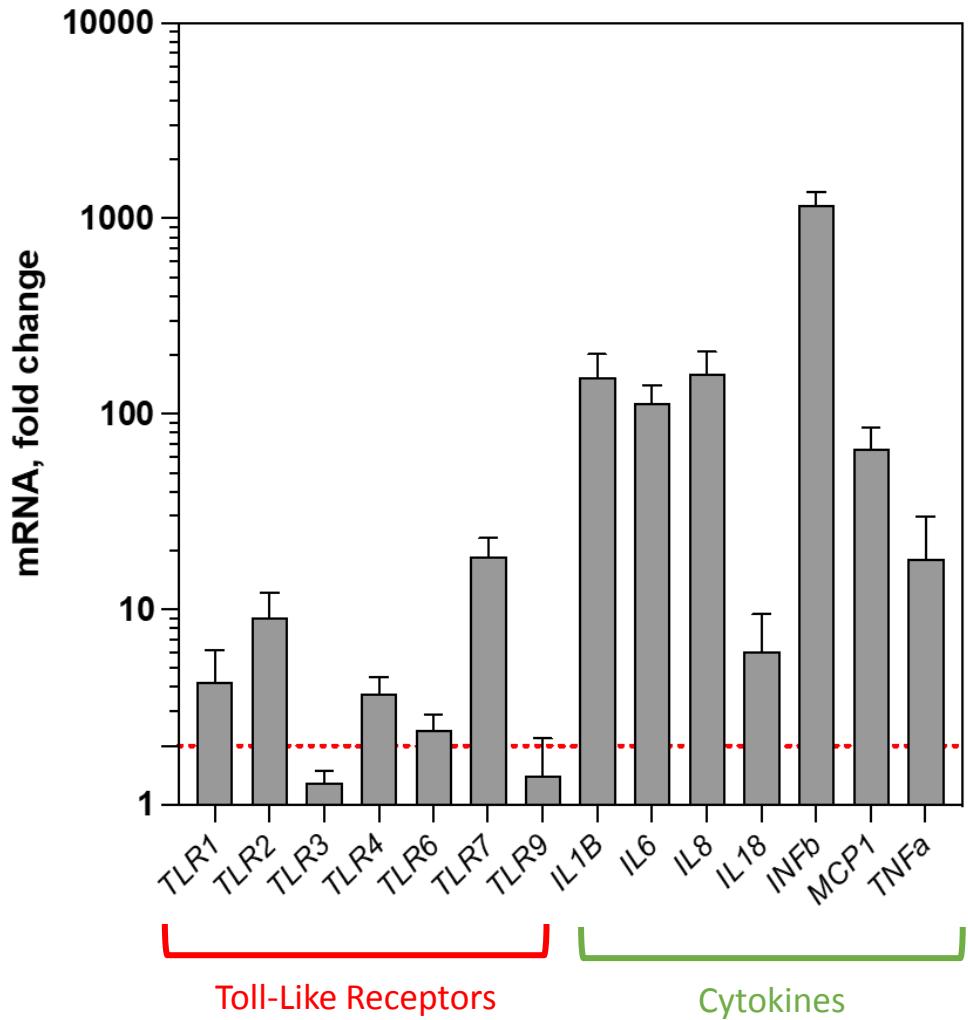
✓ Role of extracellular vesicles in pathogenesis

Impact of EVs on the expression of several inflammatory genes



Increased expression of genes coding for :

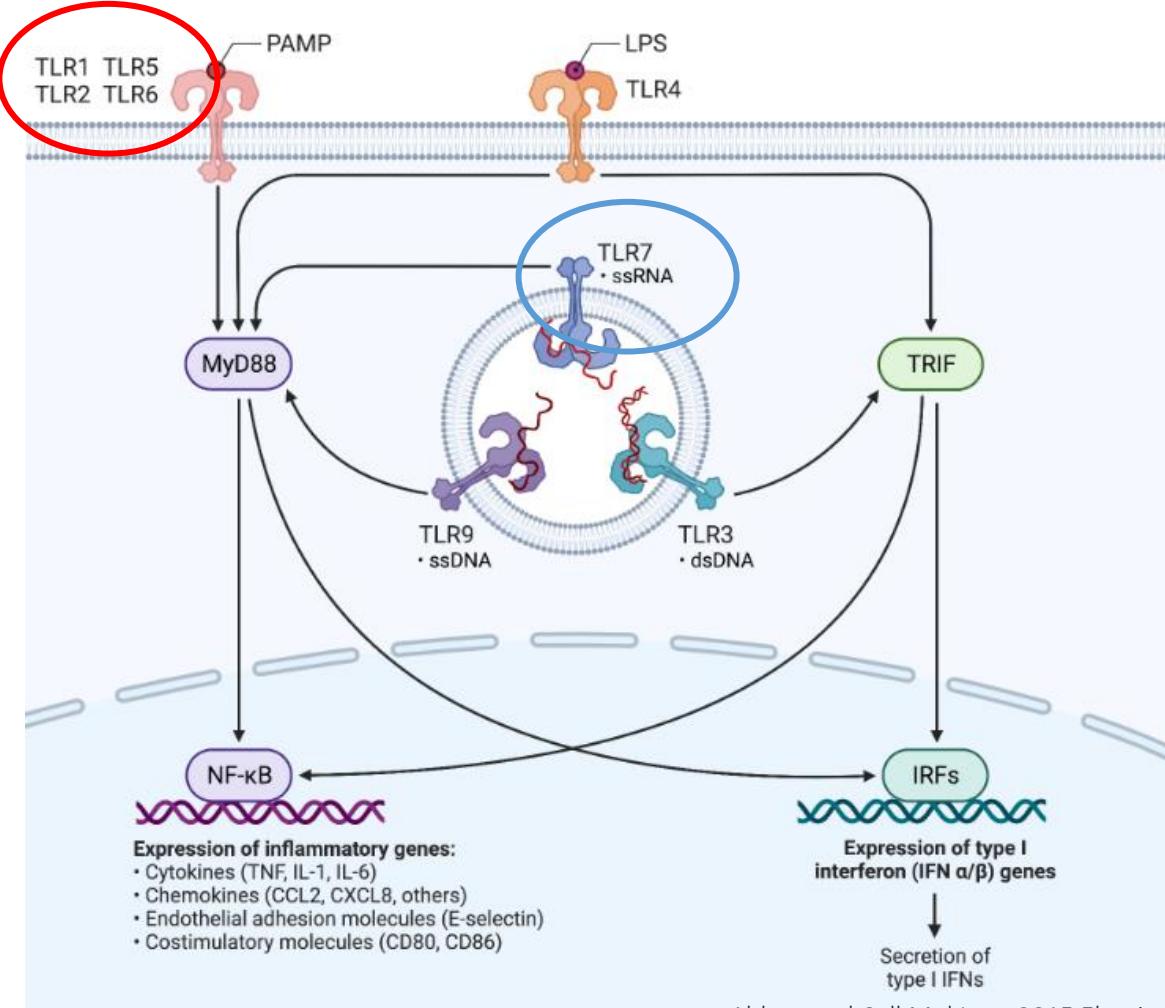
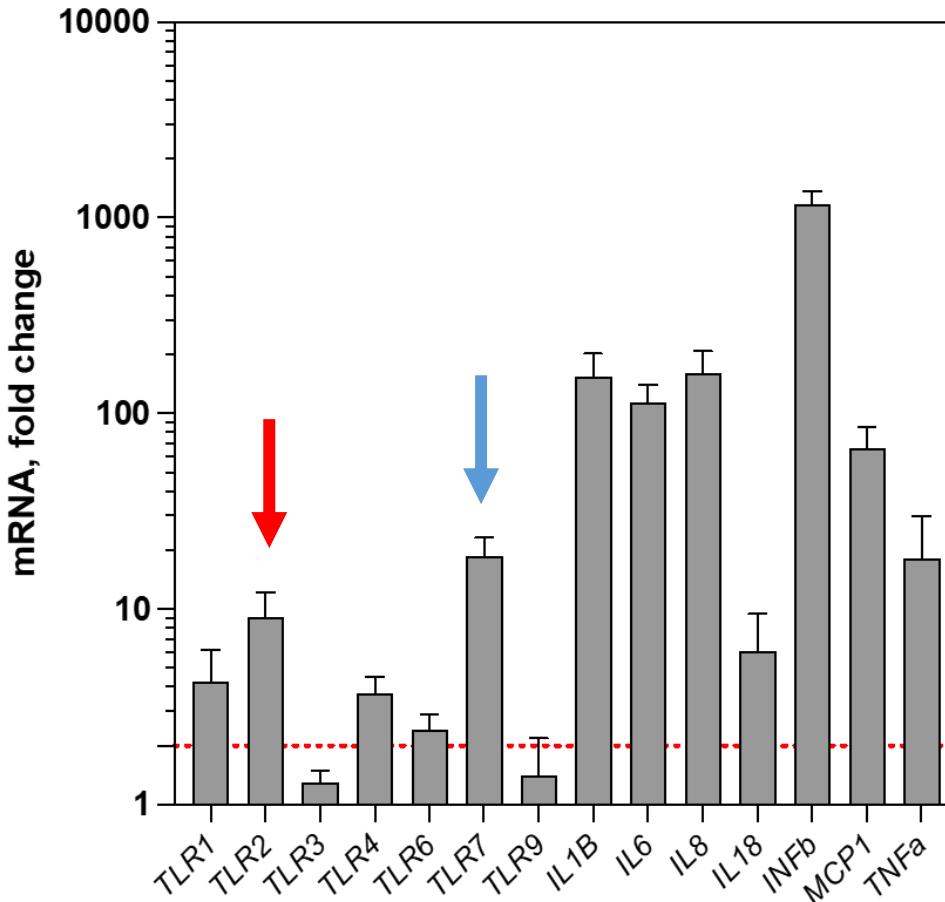
- ✓ Cytokines
- ✓ Toll-Like Receptors (TLR)



→ 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



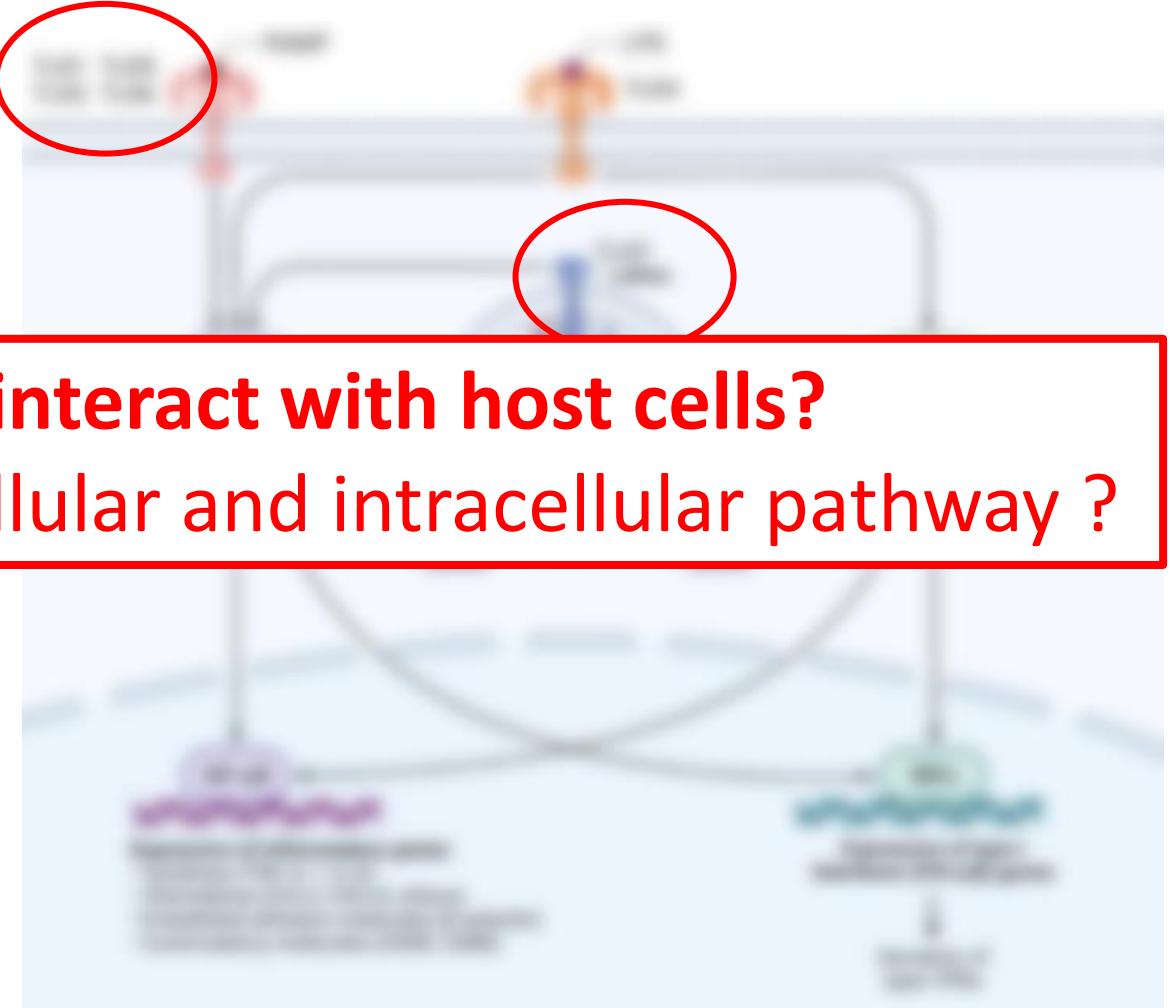
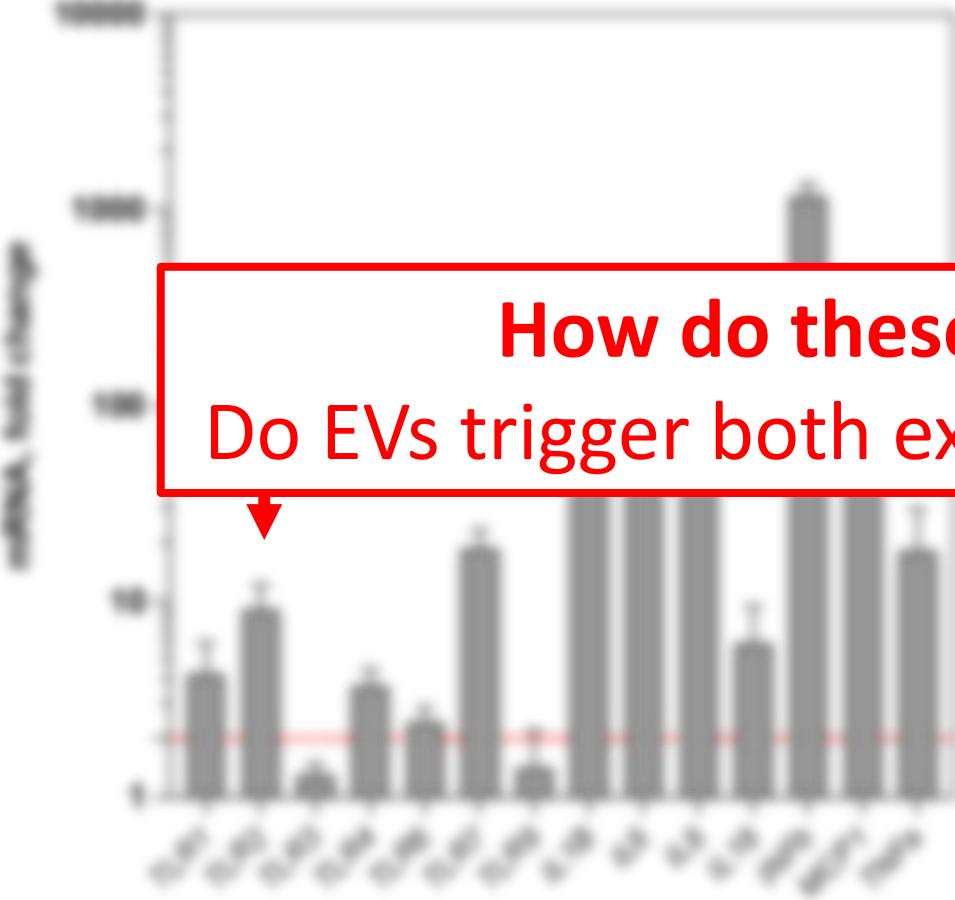
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✓ Role of extracellular vesicles in pathogenesis

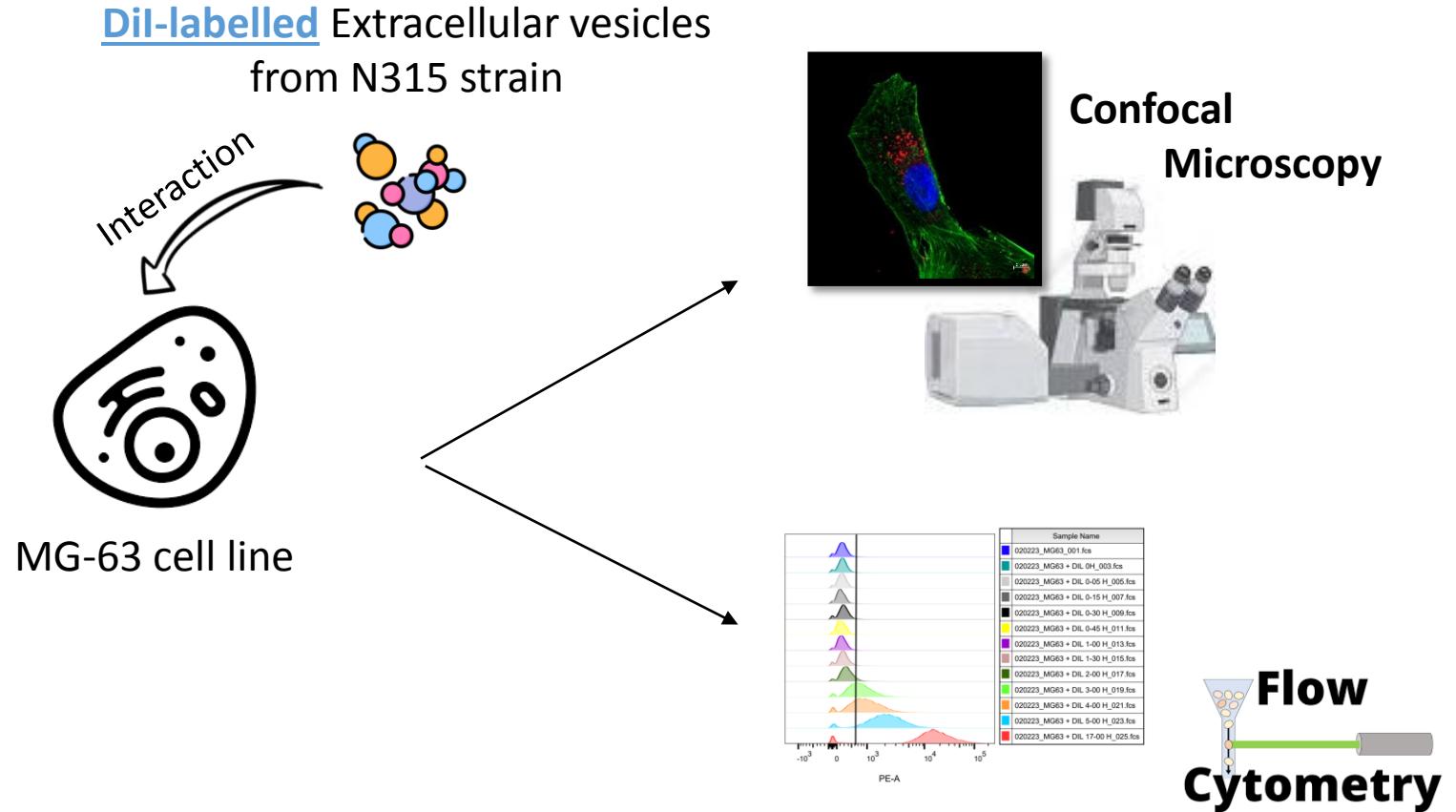
Impact of EVs on the expression of several inflammatory genes

How do these EVs interact with host cells?

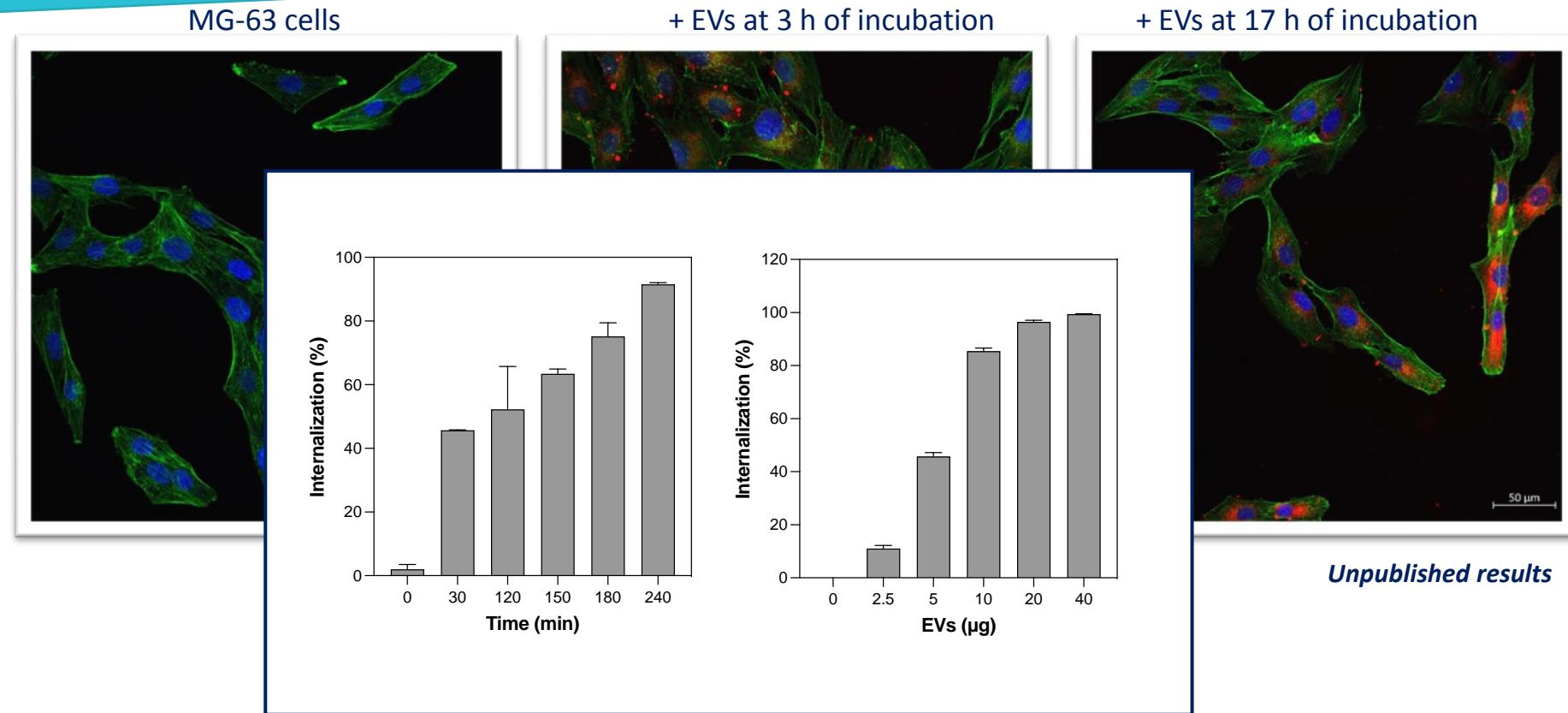
Do EVs trigger both extracellular and intracellular pathway ?



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



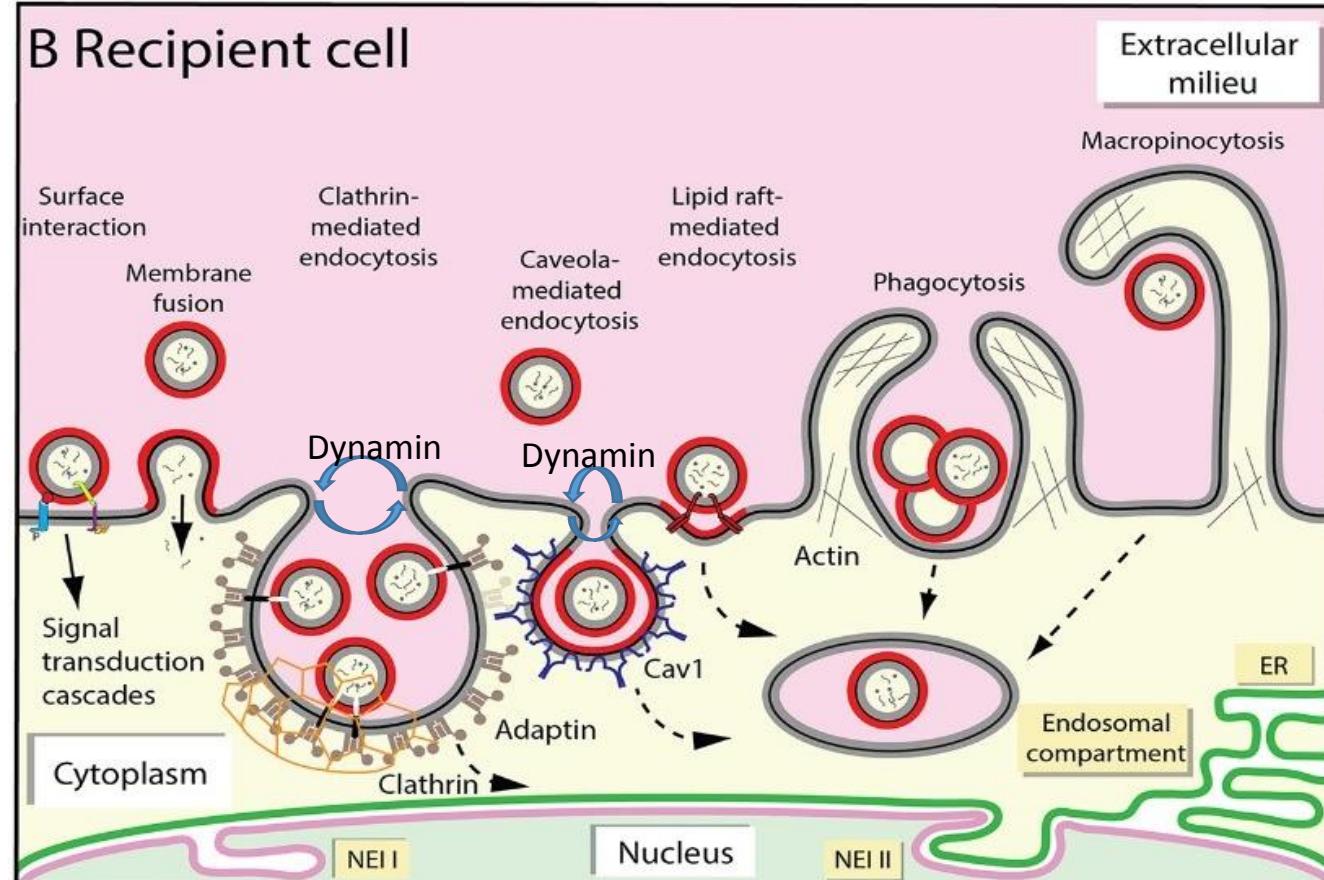
✓ Internalization of EVs by MG-63 cells



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

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

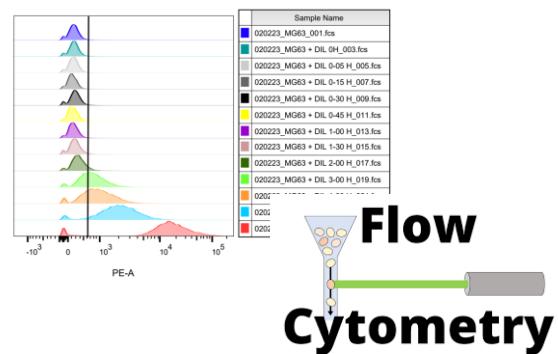
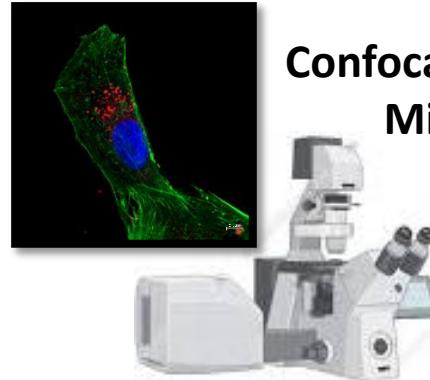
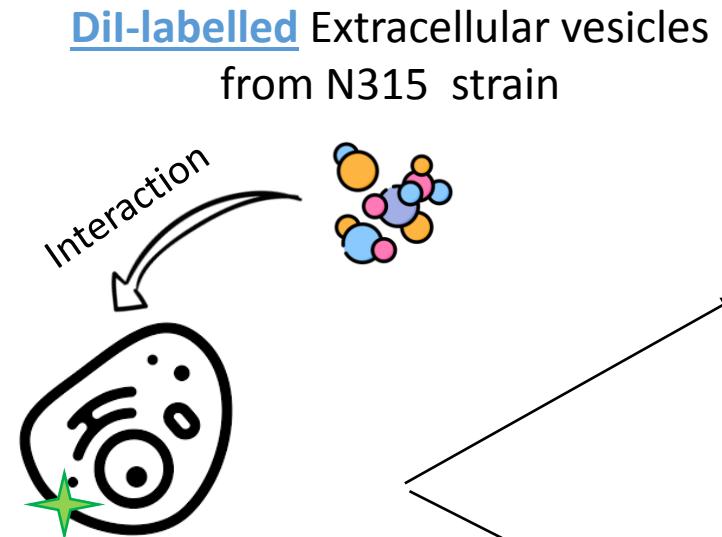
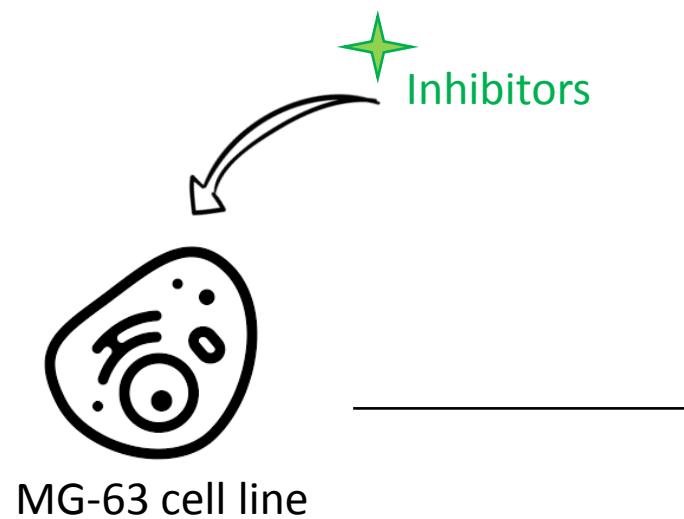
✓ Internalization of EVs by MG-63 cells



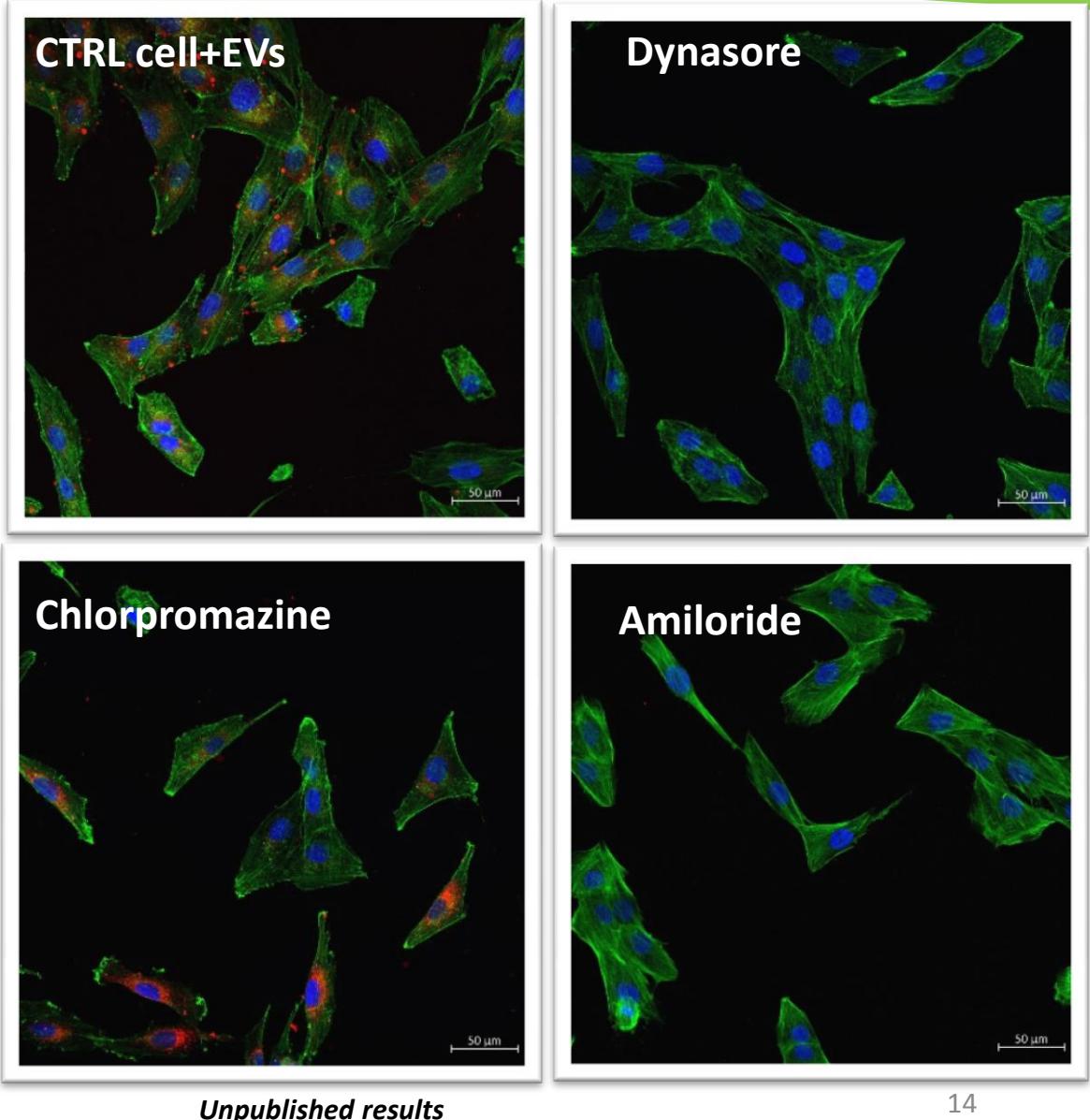
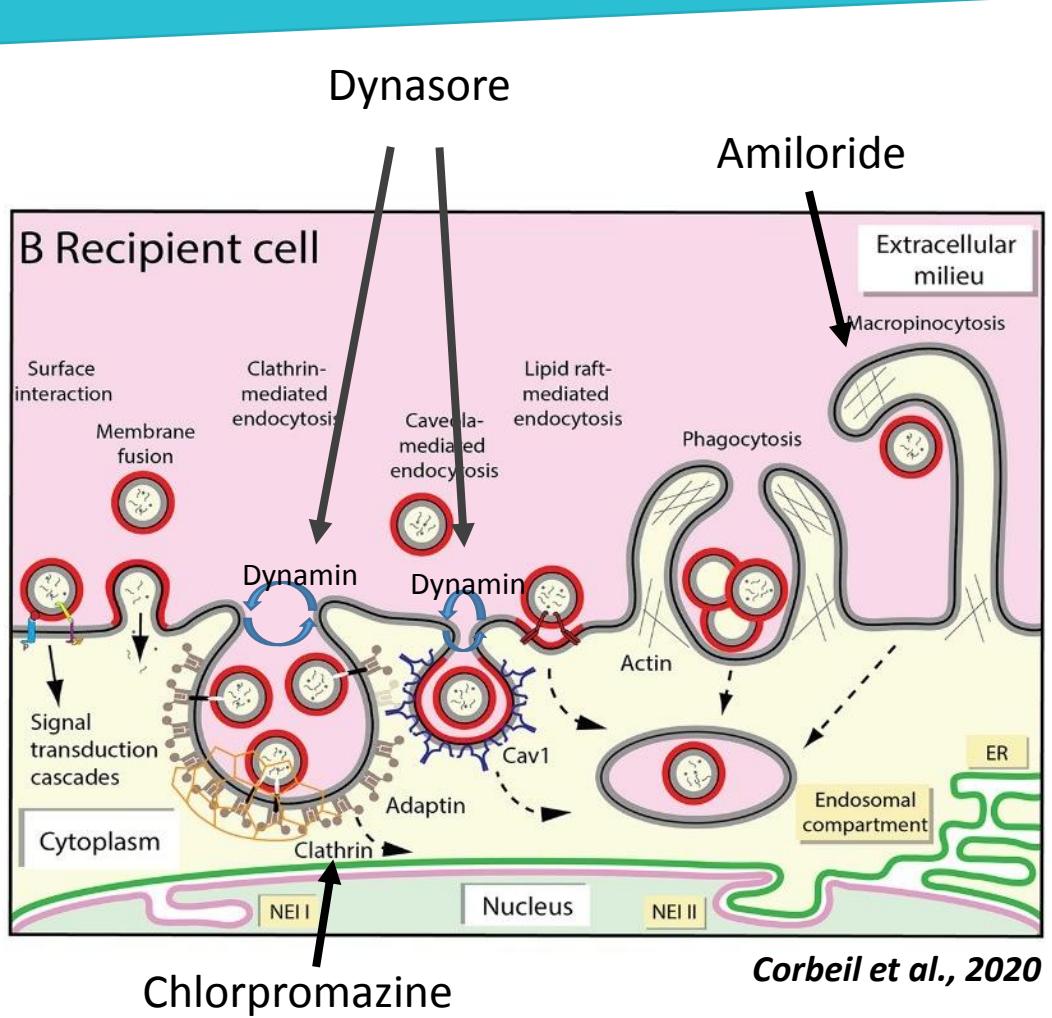
Corbeil et al., 2020

→ Several different pathways of internalization are possible

✓ Methods

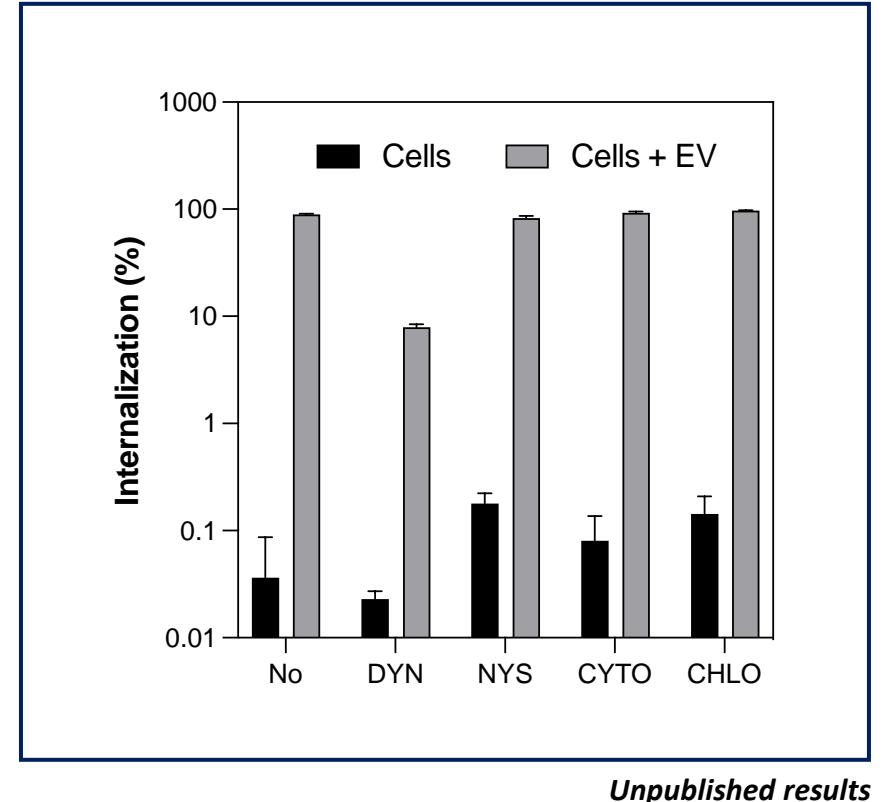
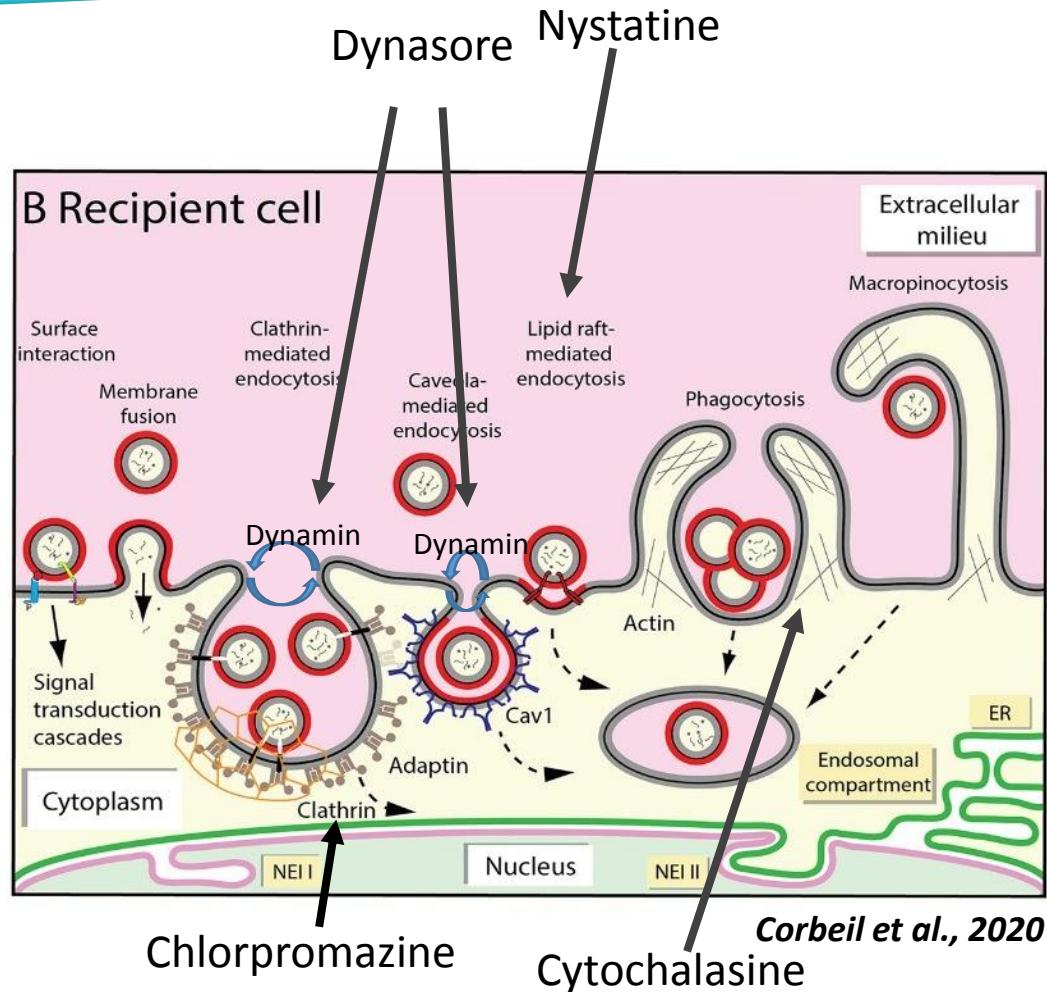


✓ Internalization of EVs by MG-63 cells



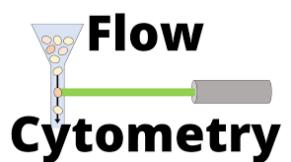
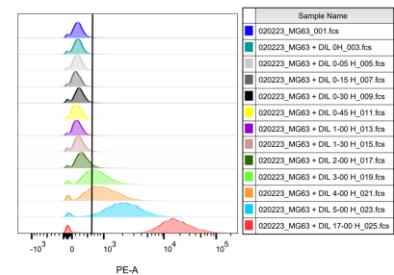
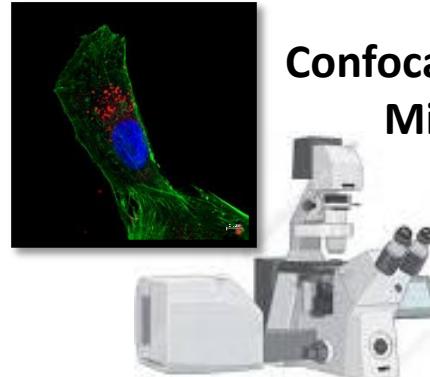
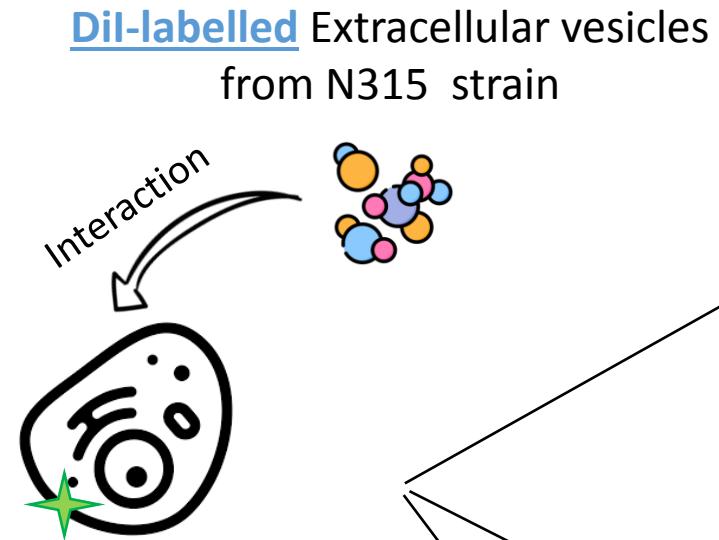
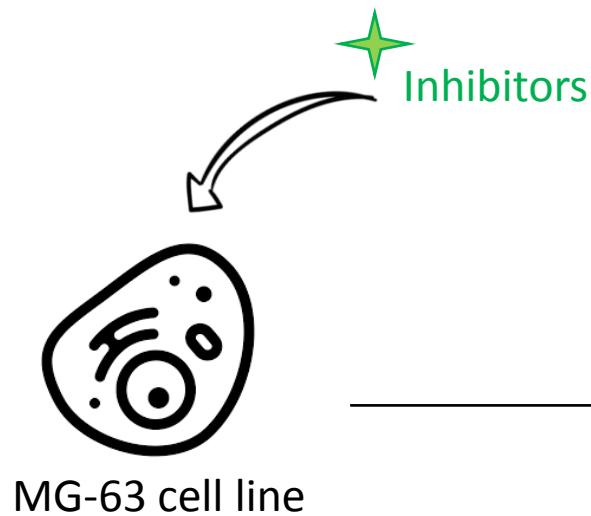
→ Internalization of N315 EVs can dependent upon dynamin-mediated endocytosis and macropinocytosis

✓ Internalization of EVs by MG-63 cells

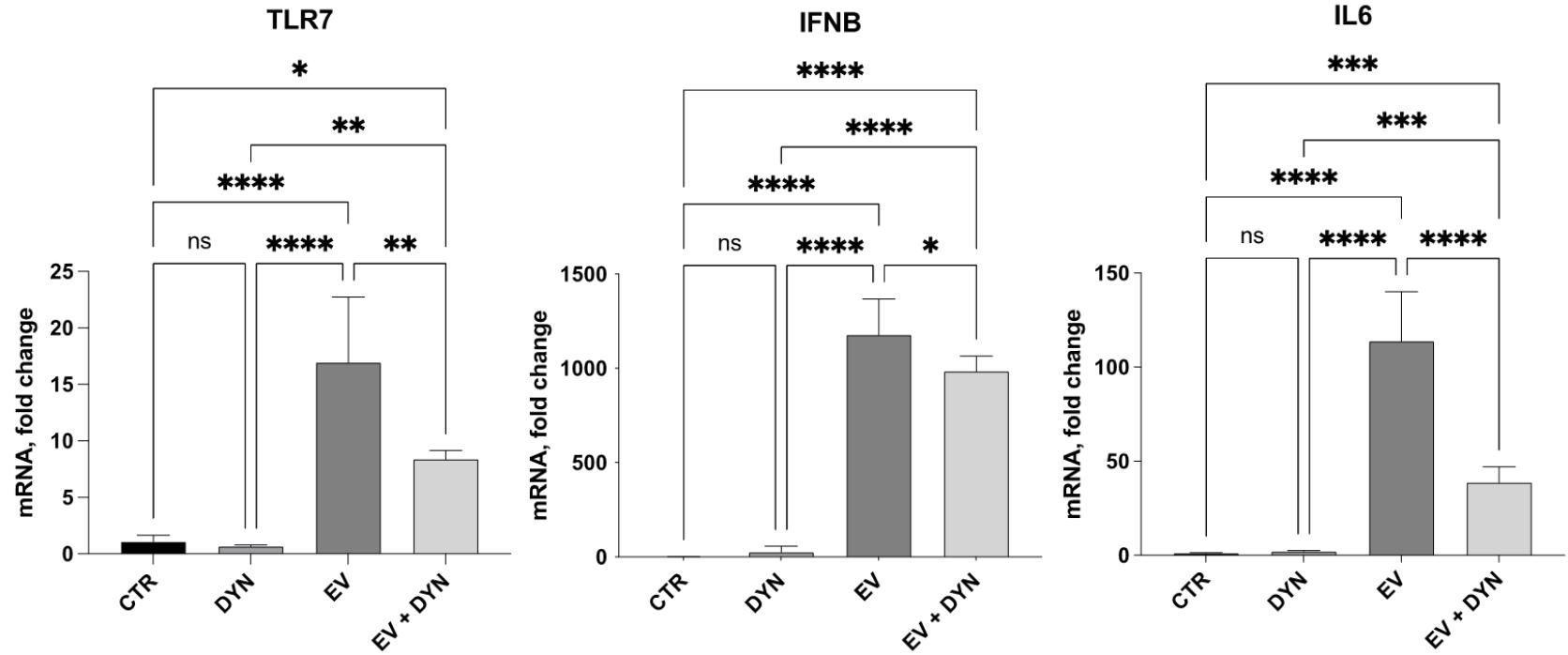


→ Internalization of N315 EVs can dependent upon dynamin-mediated endocytosis and macropinocytosis

✓ Methods



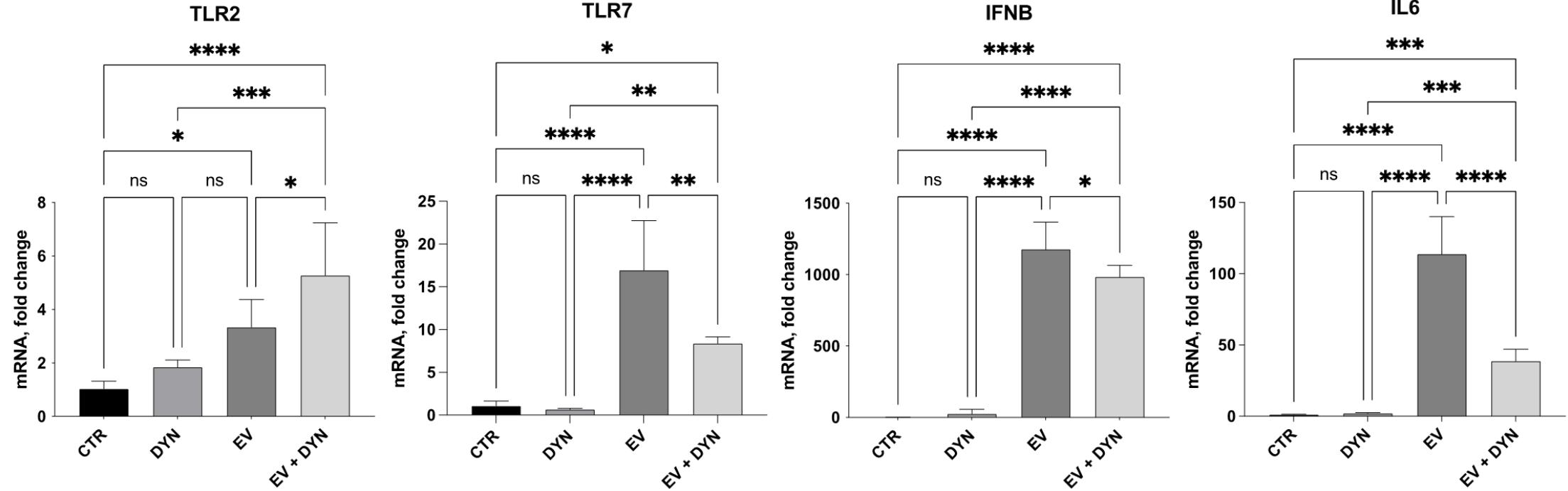
✓ Modulation of genes expression



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

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

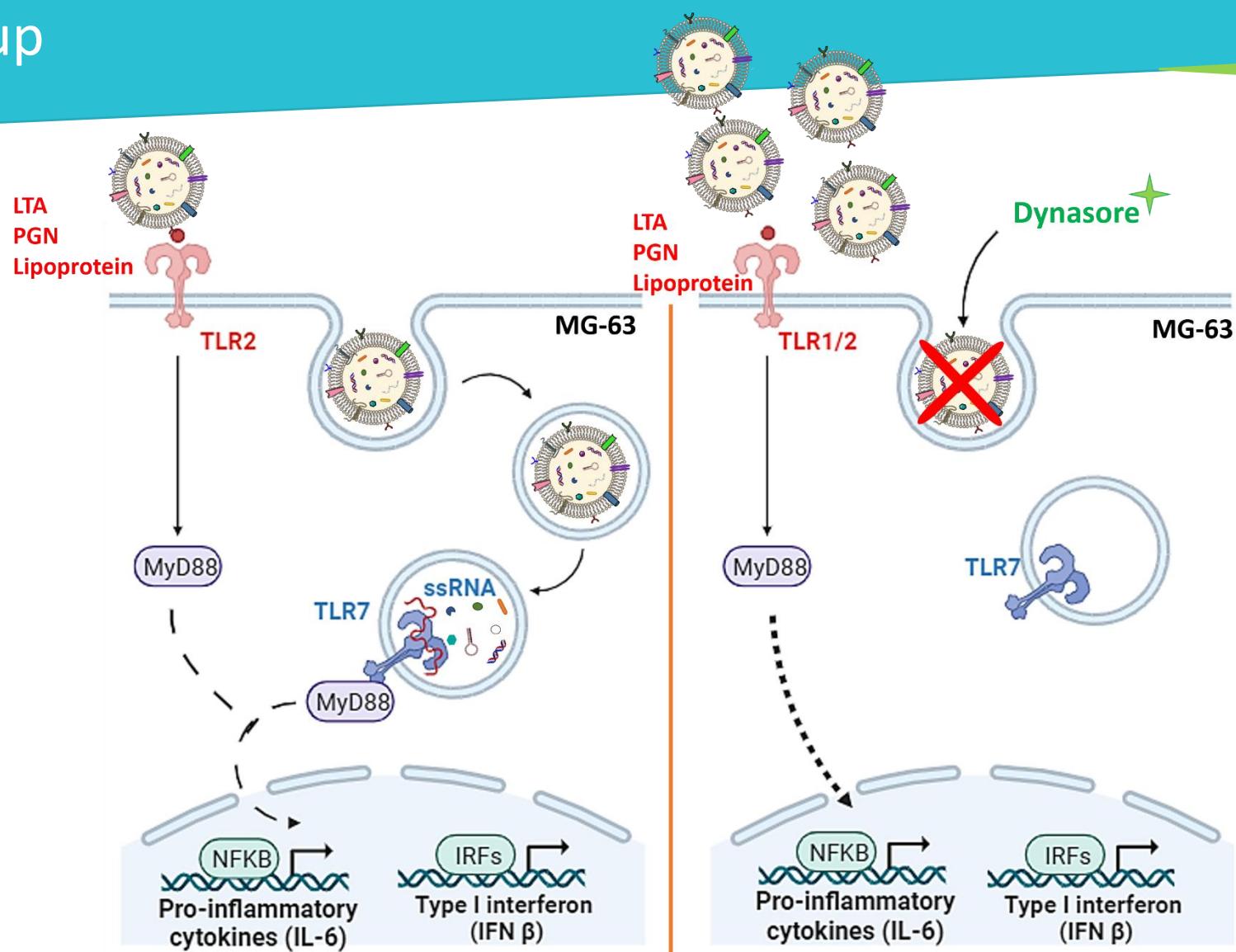
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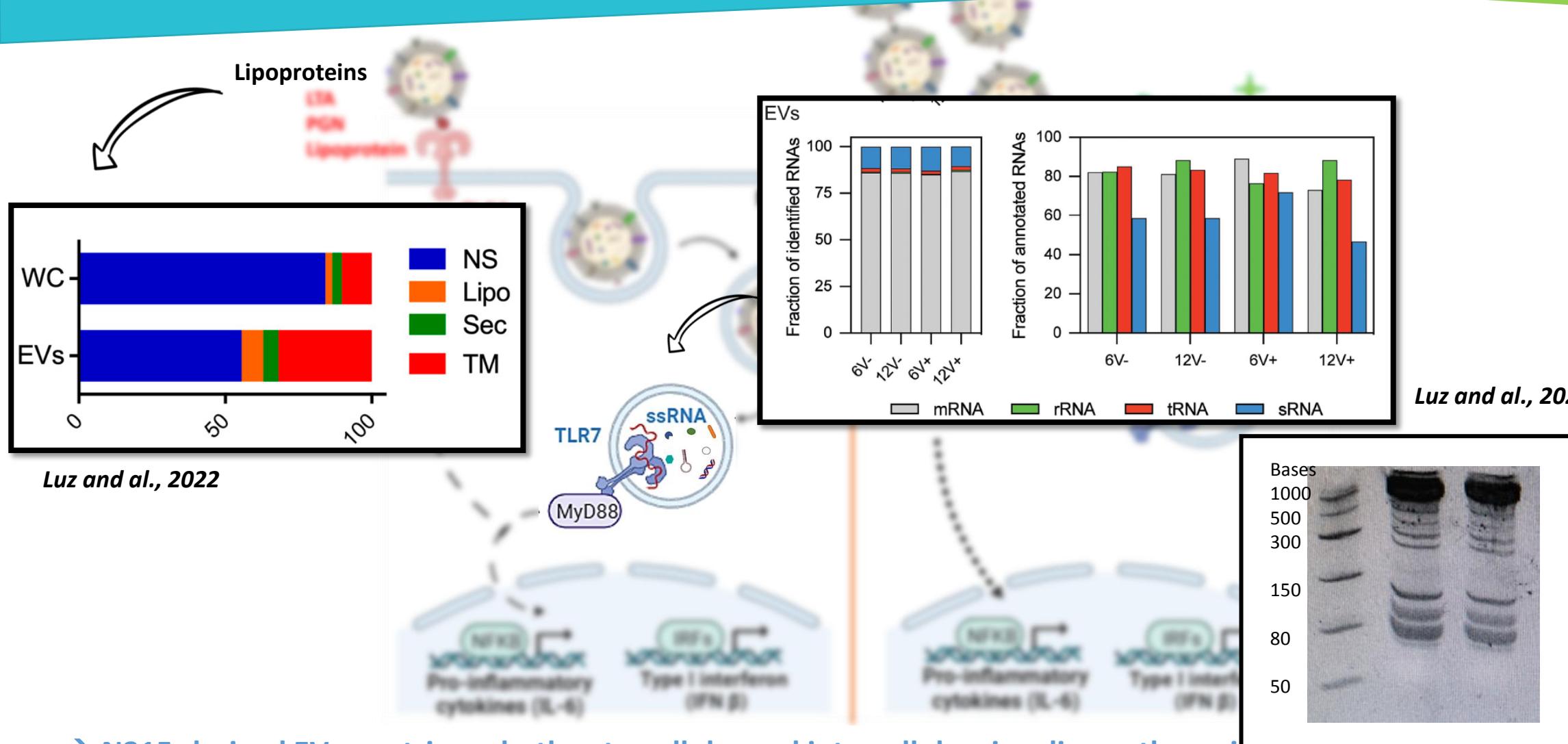
→ Several pathways can be used by EVs to interact with host cells

✓ To sum up



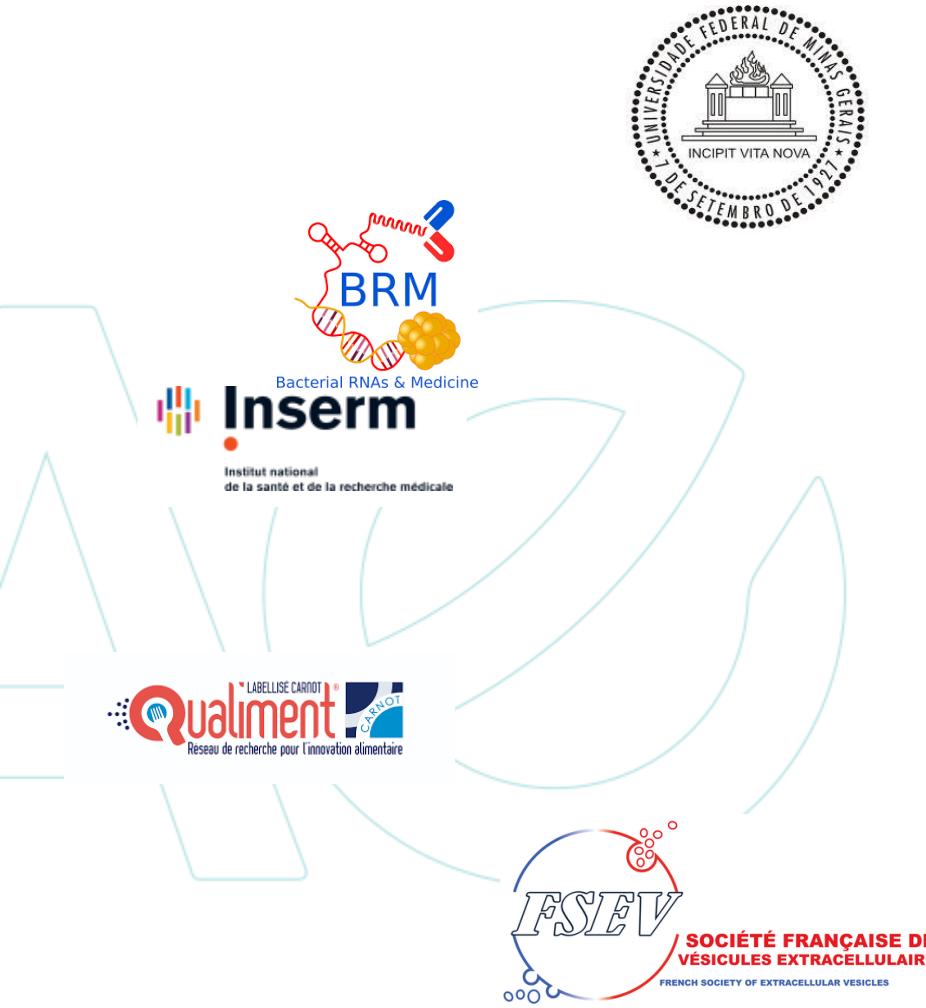
- N315-derived EVs can trigger both extracellular and intracellular signaling pathway in host cells
- Several EV components (proteins, RNA) can be involved in the interaction with host cells

✓ To sum up



- 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

Thanks



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Jordane Ossemond, STLO, Rennes

Brice Felden, BRM, Rennes
Svetlana Chabelskaia, BRM, Rennes

Vasco AZEVEDO, UFMG, Belo Horizonte, Brazil

