

FOURTEENTH INTERNATIONAL

# ROTAVIRUS SYMPOSIUM

MARCH 14–16 2023 BALI INDONESIA

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# Understanding the interplay between host, microbiome and an orally delivered probiotic rotavirus vaccine platform

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Colorado State University



Imagine if we could deliver vaccines . . .

Quickly, cheaply, conveniently



Imagine if we could deliver vaccines . . .

Where people gather each day

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Imagine if we could  
deliver vaccines . . .

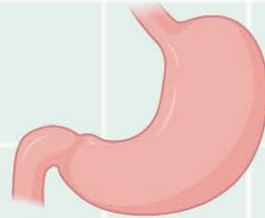
Anywhere in the  
world

# Advantages of *Lactobacillus acidophilus* as a vaccine platform

Oral  
Delivery



Acid/Bile  
Stable



Inexpensive



Easy



No Cold  
Chain



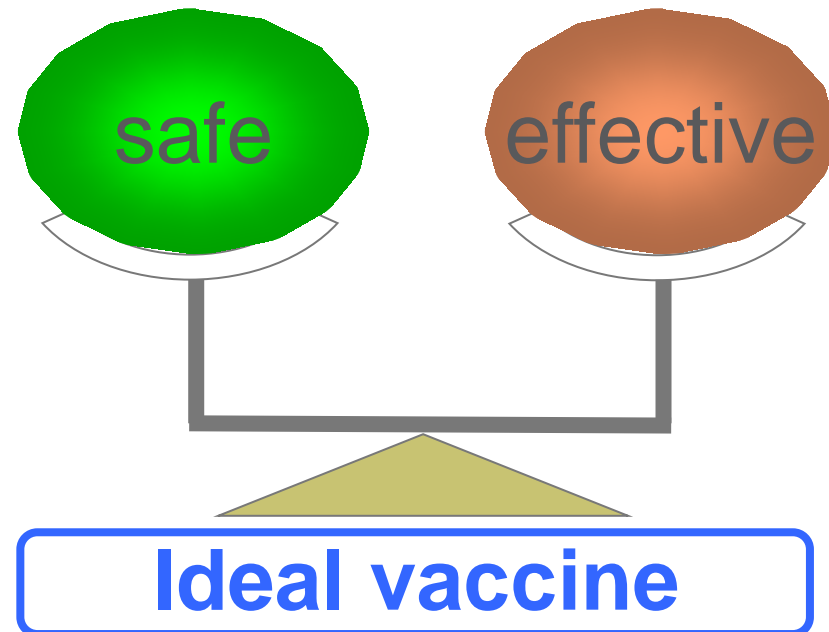
Increased access and acceptance



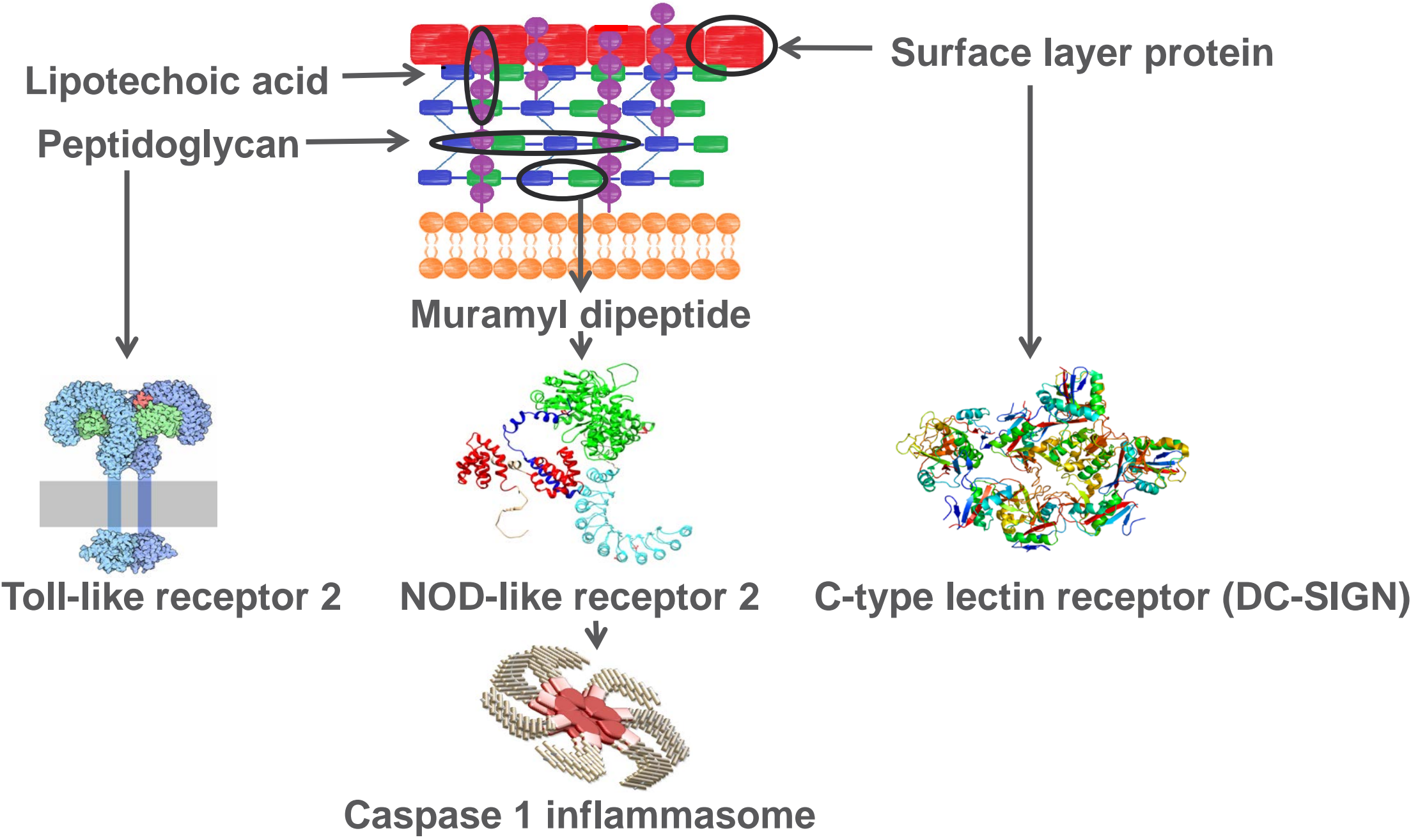
# Challenges of LA platform

Low immunogenicity

No regulatory precedent

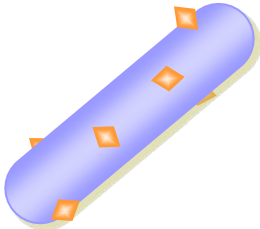


# Innate immune activation by LA

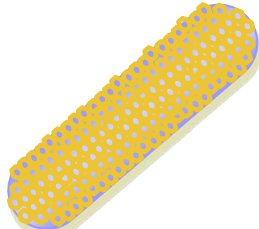




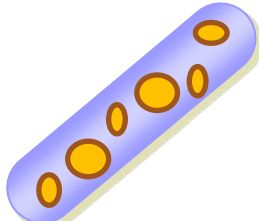
# Antigen/adjuvant expression strategies



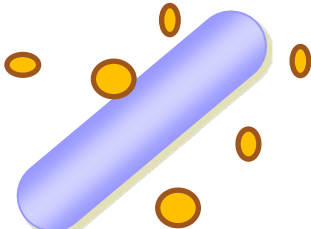
Surface Layer Associated Proteins



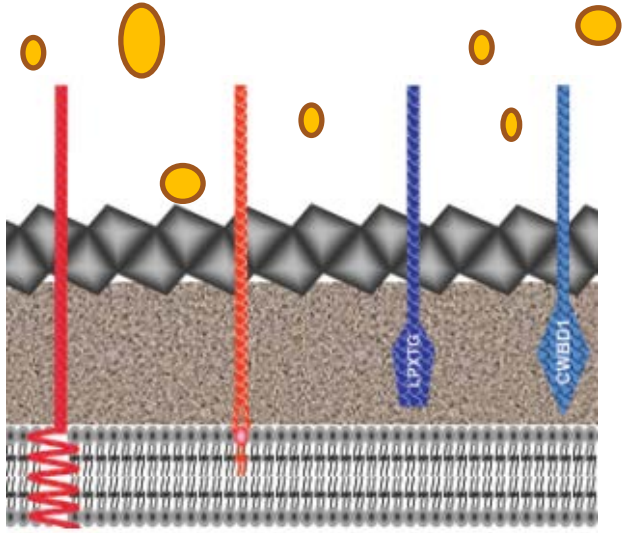
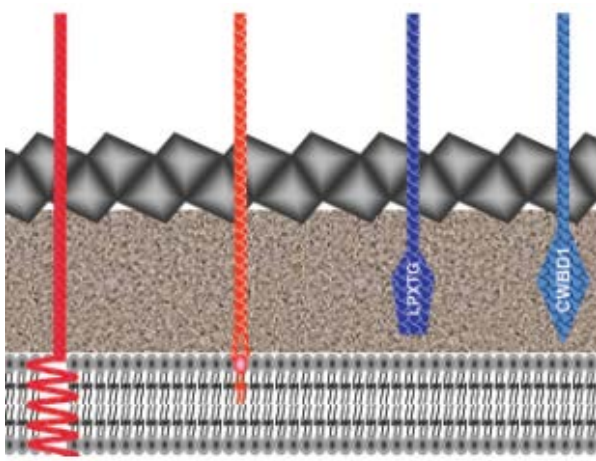
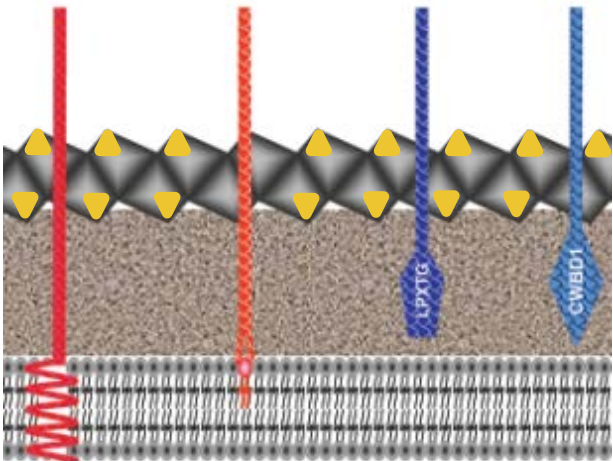
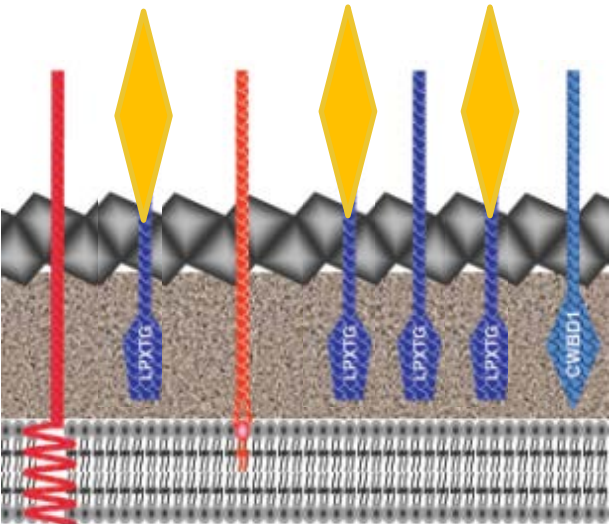
Surface Layer Protein



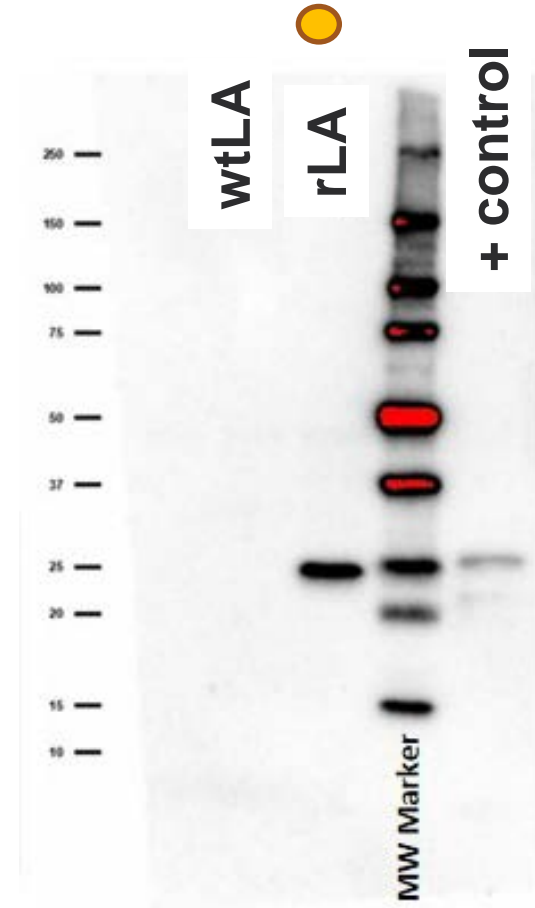
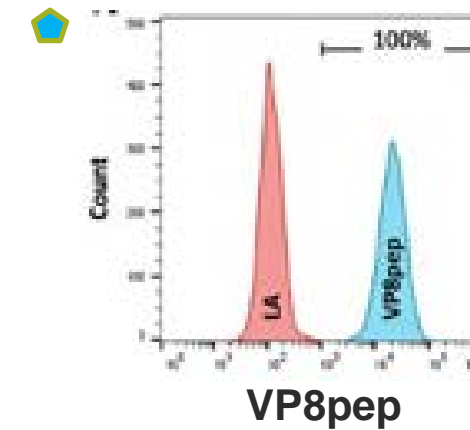
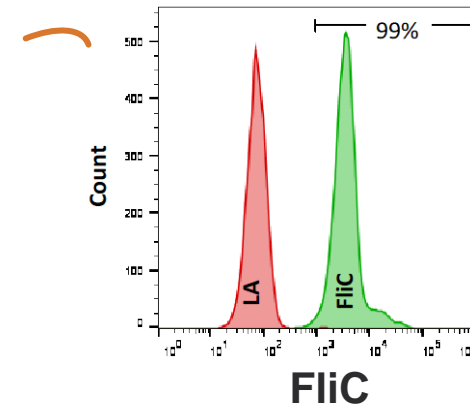
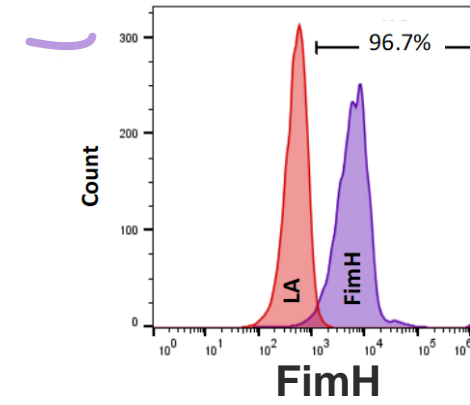
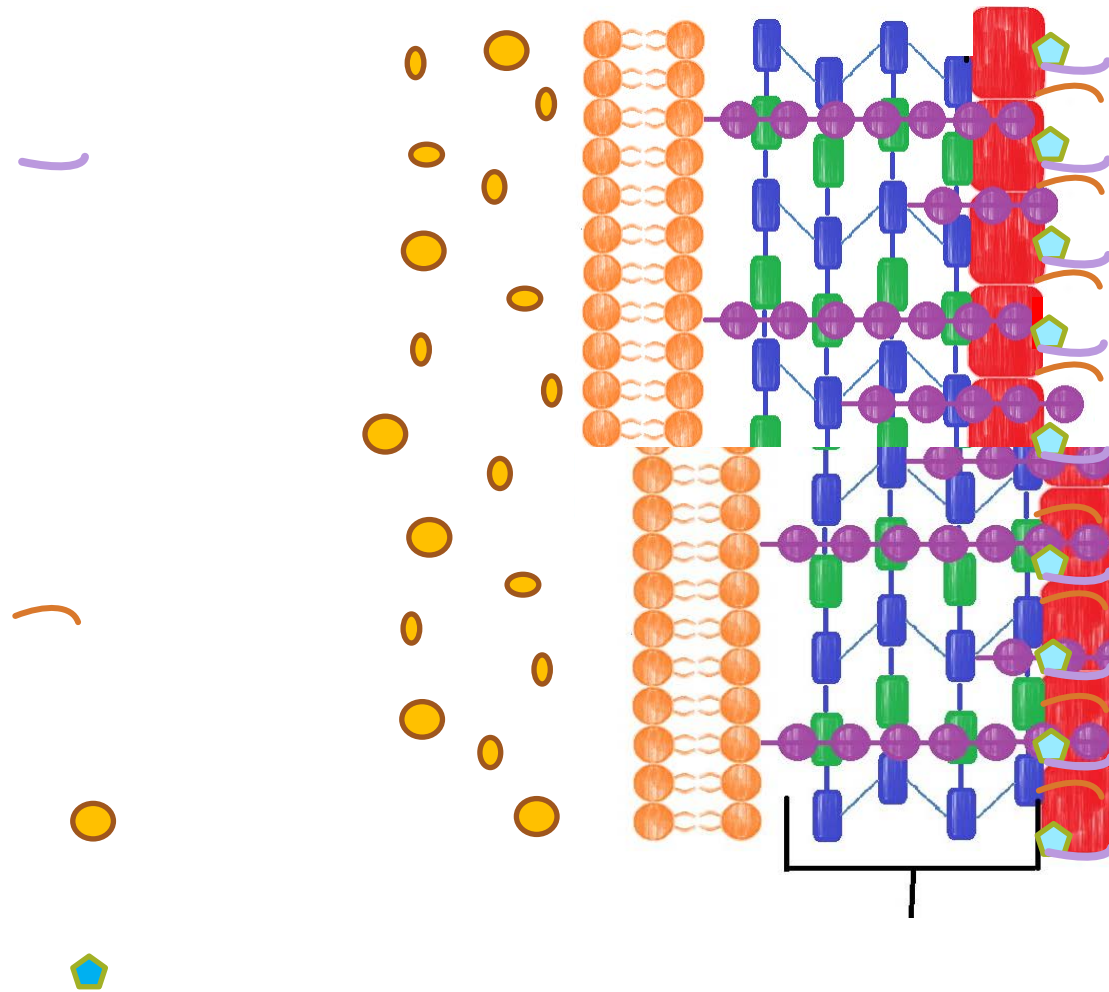
Cytosol

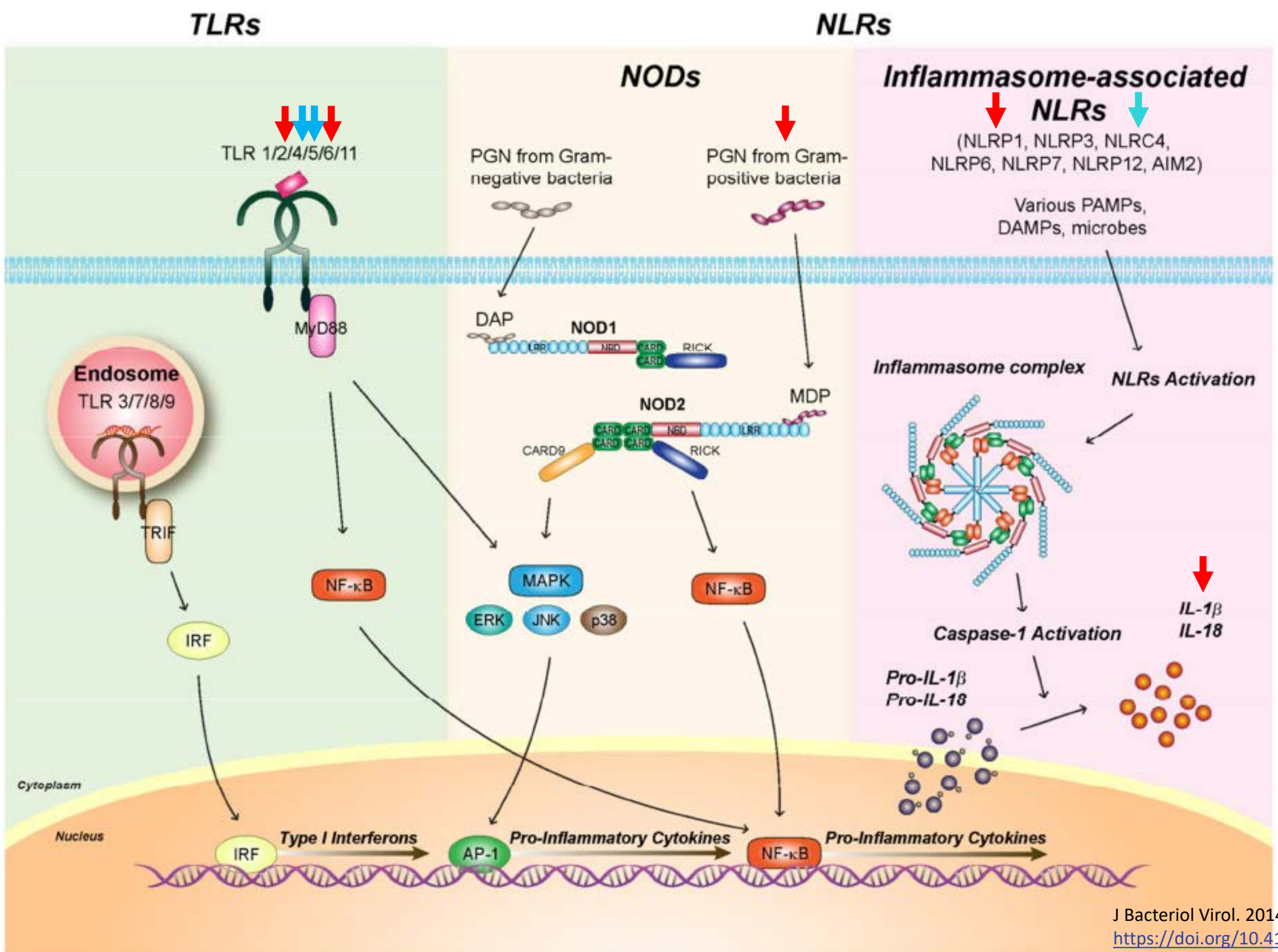


Secreted



# Innovation: Expression of multiple adjuvants/antigens

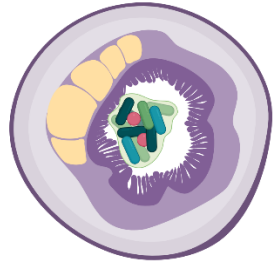




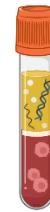
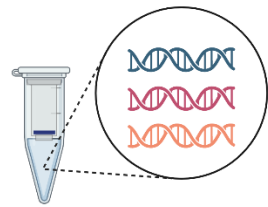
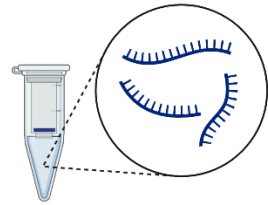
# Conclusion

- *Lactobacillus acidophilus* can be engineered as a subunit vaccine platform to express **multiple adjuvants and antigens**

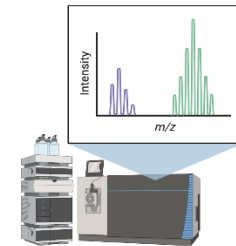
## Sample collection



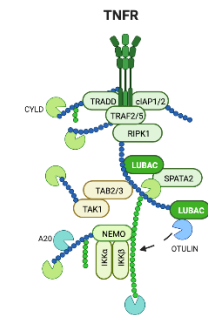
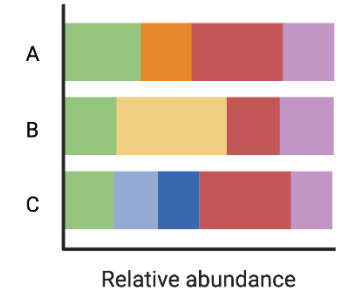
## Sample processing



## Sample analysis



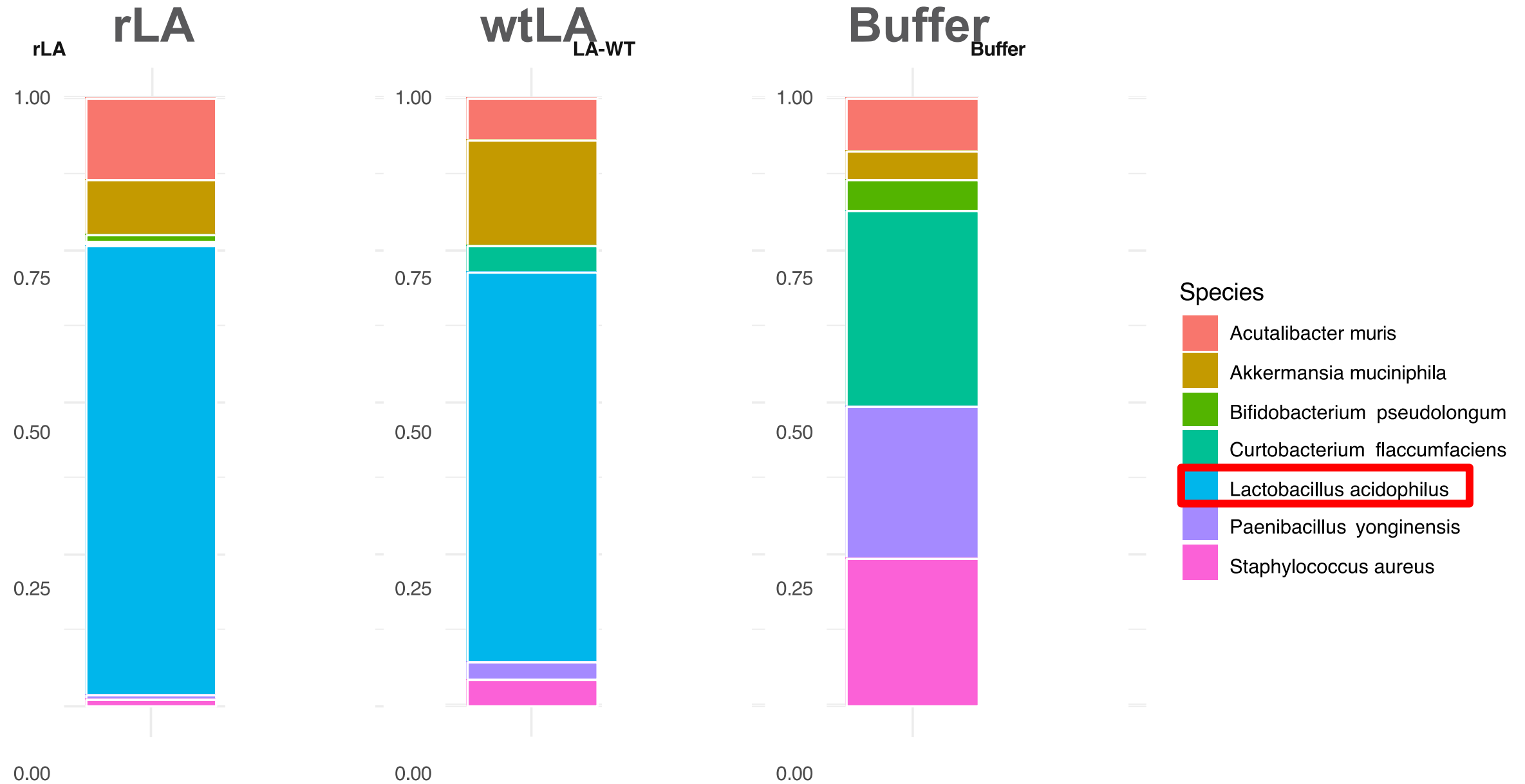
## Data processing



# Systems Vaccinology

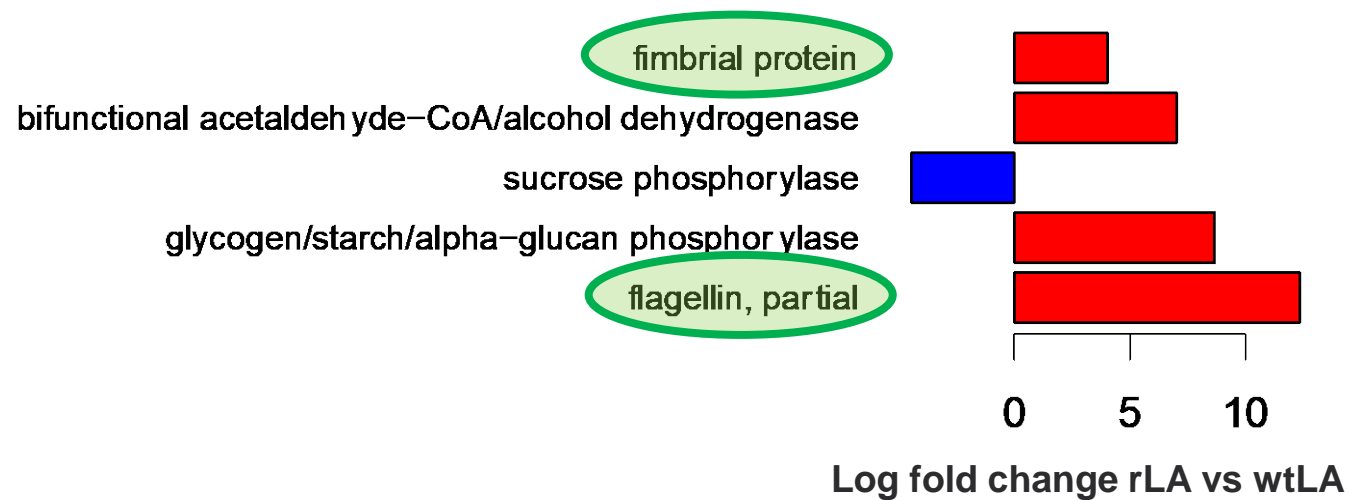
metagenomics  
metatranscriptomics  
host transcriptomics  
metabolomics  
pathway analysis

# Metagenomic comparison: small intestine

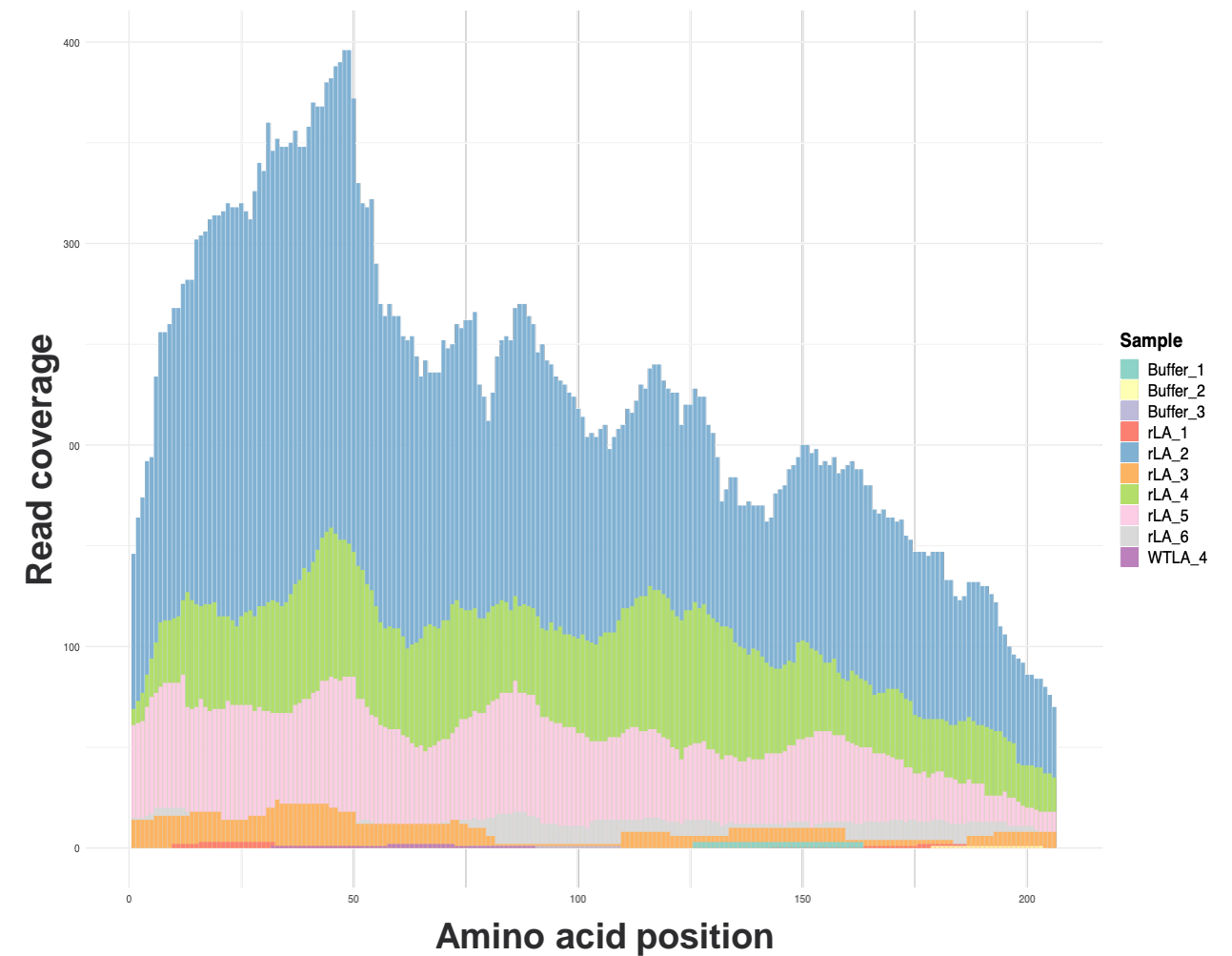


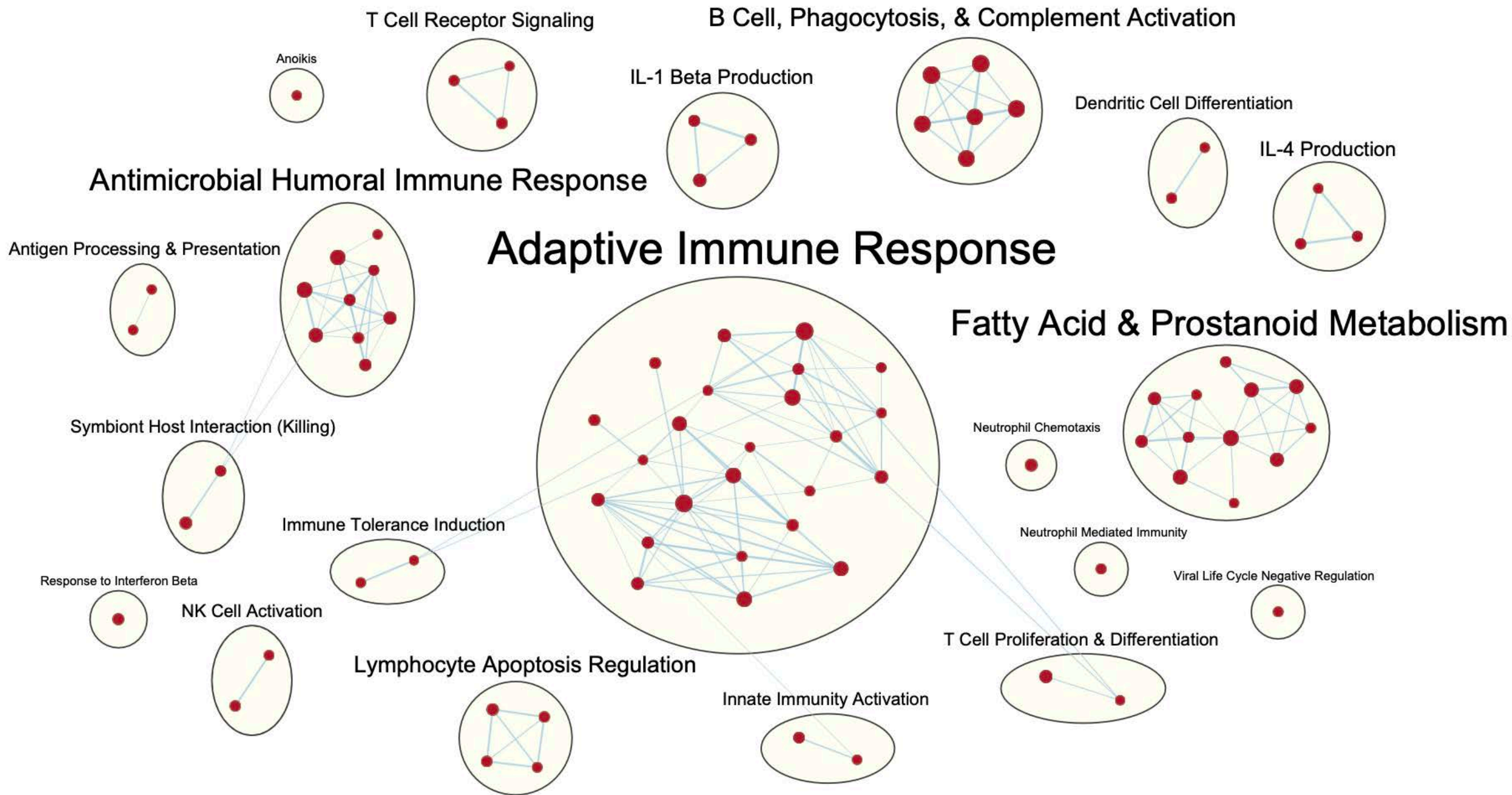
# Metatranscriptomics: rLA performance in vivo

## Adjuvant Expression



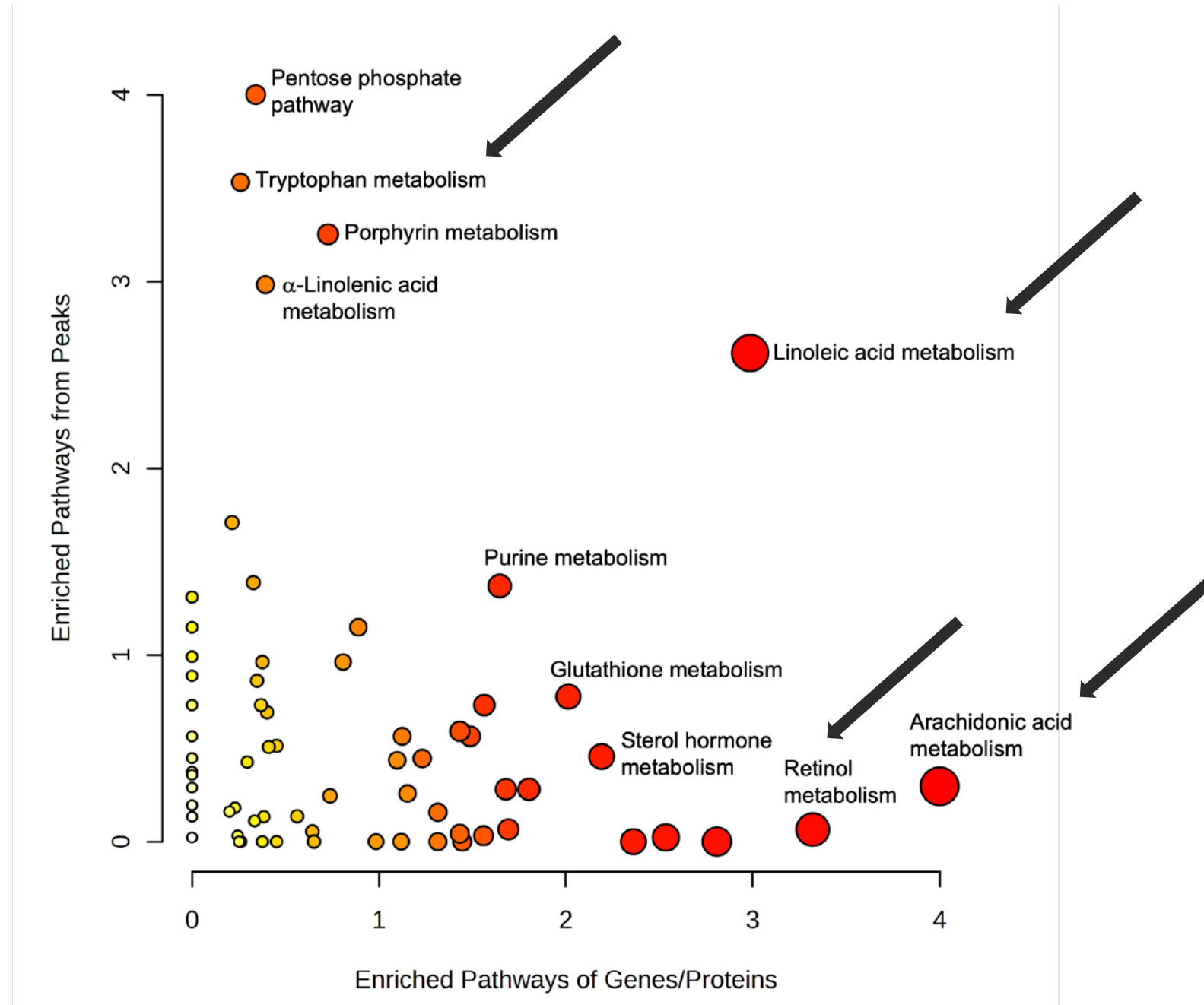
## VP8-1 Expression



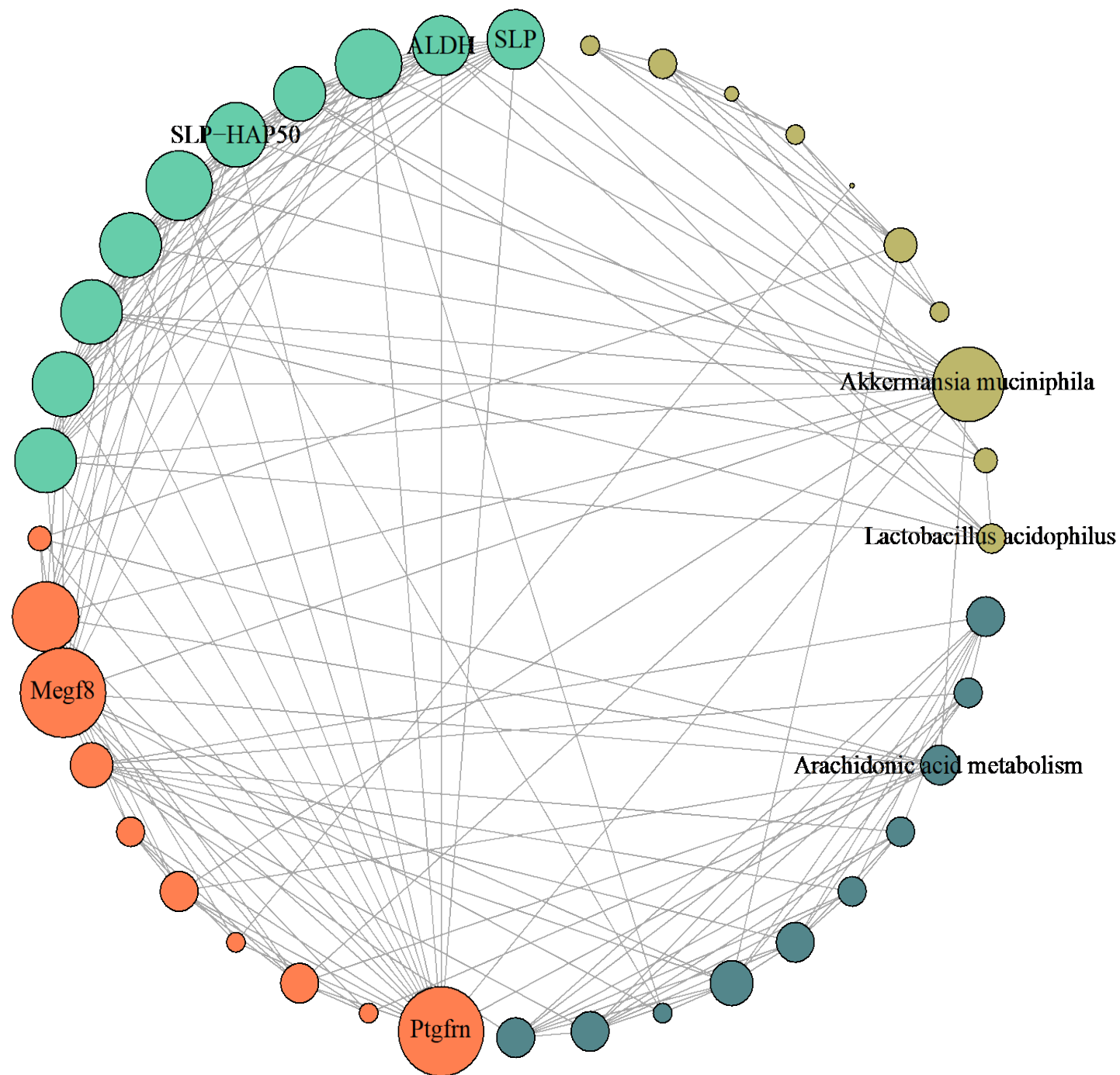




# Host, vaccine, microbiome interactions



# Host, vaccine, microbiome interactions



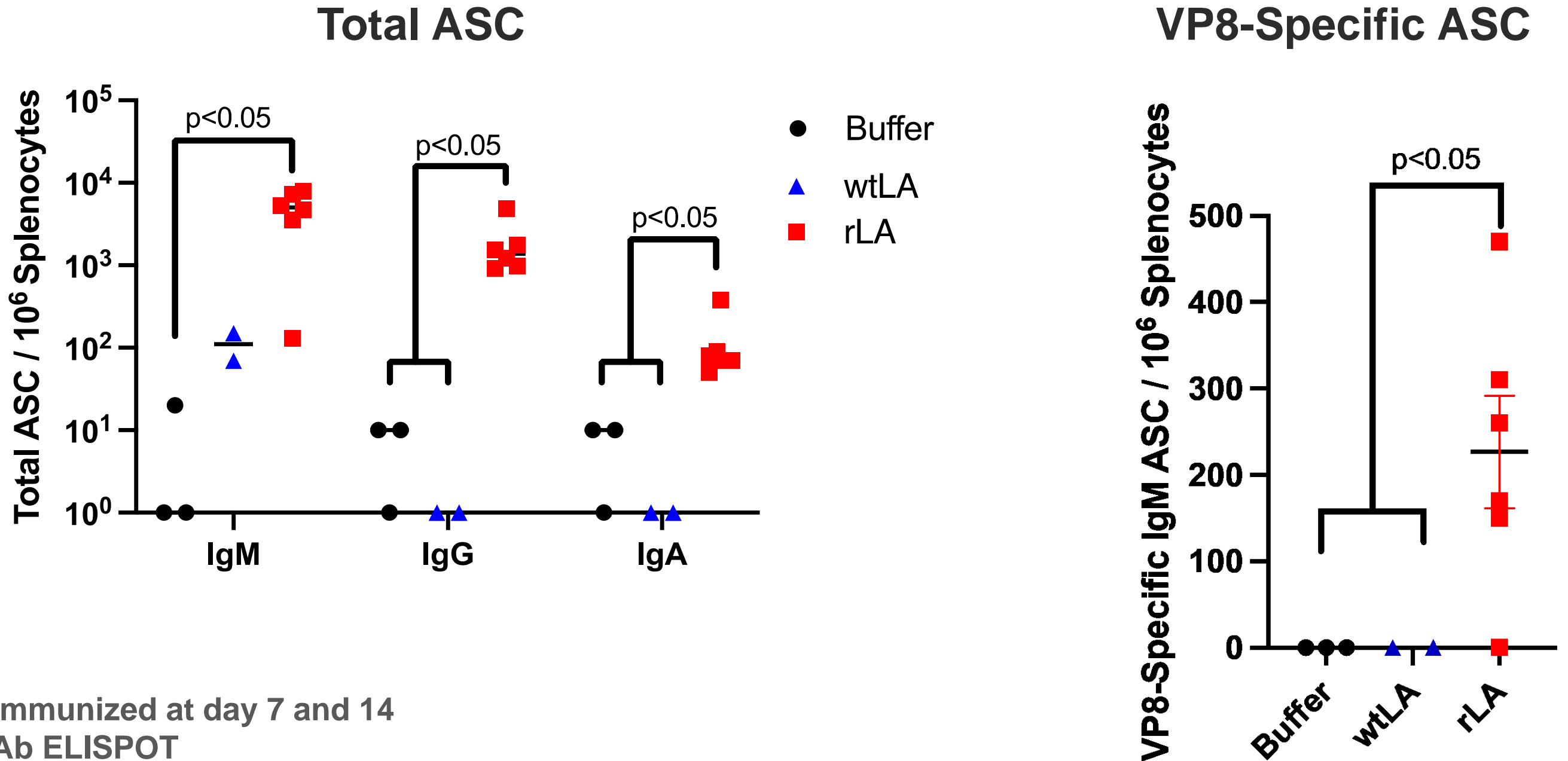
## 'omics data

- metagenomics
- metatranscriptomics
- transcriptomics
- metabolomics

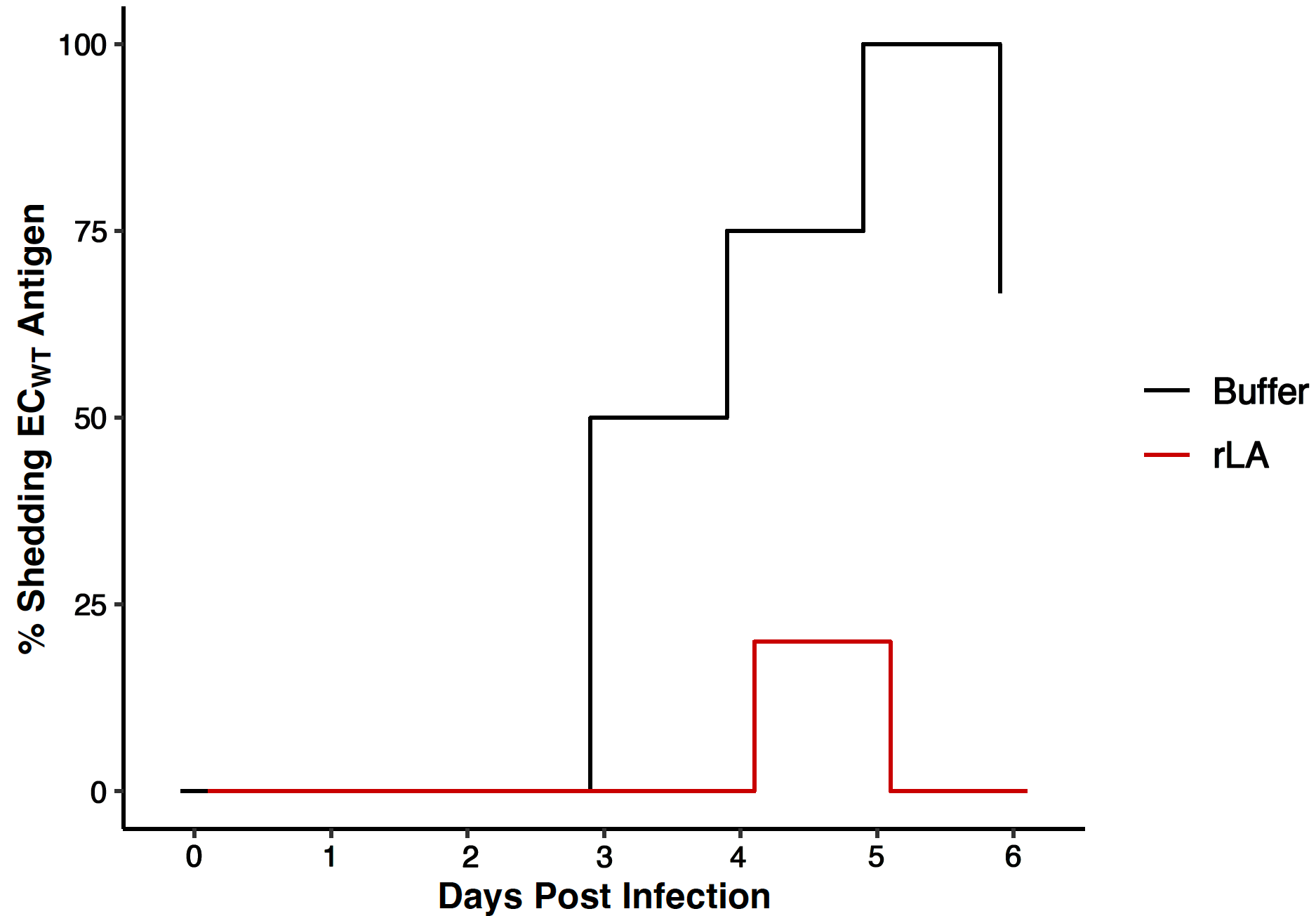
# Conclusion

- **Systems vaccinology** provides an understanding of the **host-microbiome-vaccine interactions** and allows **rapid testing** of different constructs (adjuvants) under different clinical conditions (maternal pre-exposure, dysbiosis, etc)

# Neonatal antibody response to rLA immunization



# rLA protects neonatal mice against challenge



# Conclusions

- rLA induces VP8-specific antibody production in neonates
- Maternal exposure to rotavirus does not interfere with neonatal immune responses upon immunization with rLA
- Neonates immunized with rLA were protected against challenge
- **See Dr. Vilander, poster #117 for more detail on in vivo studies**

# Acknowledgements

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