

## Background

Adaptive laboratory evolution (ALE) has been used to modulate the phenotype of insect cells during Virus-Like Particles (VLPs) production<sup>1,2</sup>. However, little is known on the underlying biological mechanisms essential for improved production of Influenza VLPs. This study is focused on identifying gene expression differences between adapted and non-adapted cells during HA-VLPs production using transcriptome analysis (RNA-seq), paving the way for rational cell and/or bioprocess engineering.

## Aim

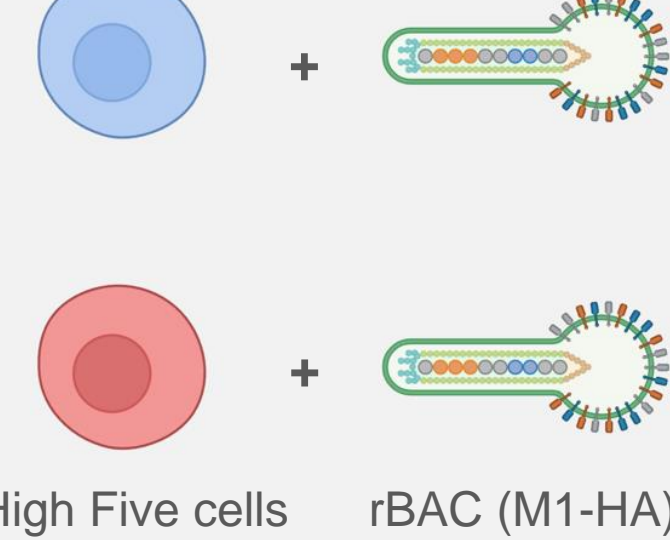
Understand the impact of adaptation process on insect cell phenotype via RNA-seq

## Strategy

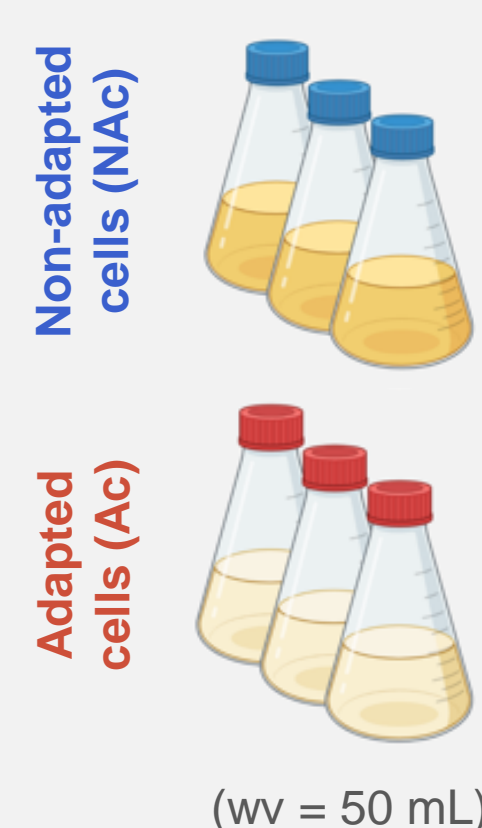
### Adaptive Laboratory Evolution (ALE)



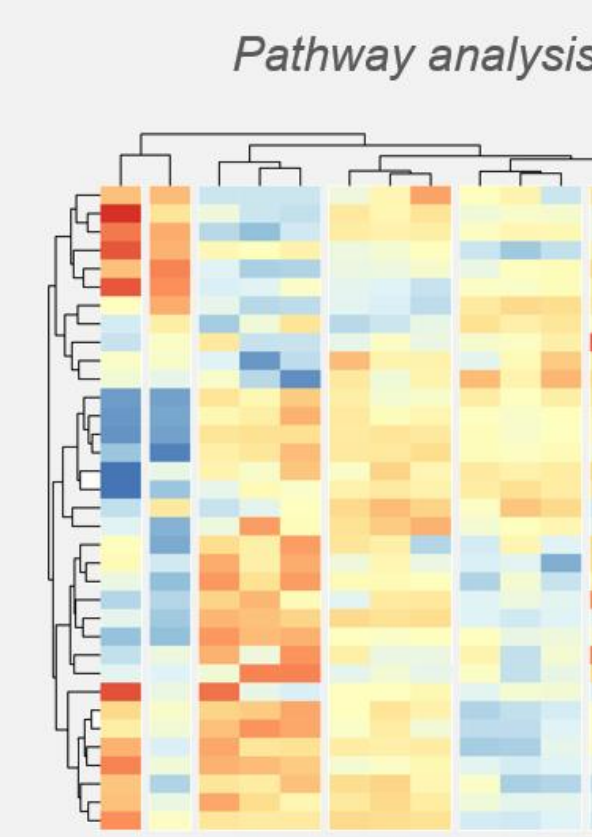
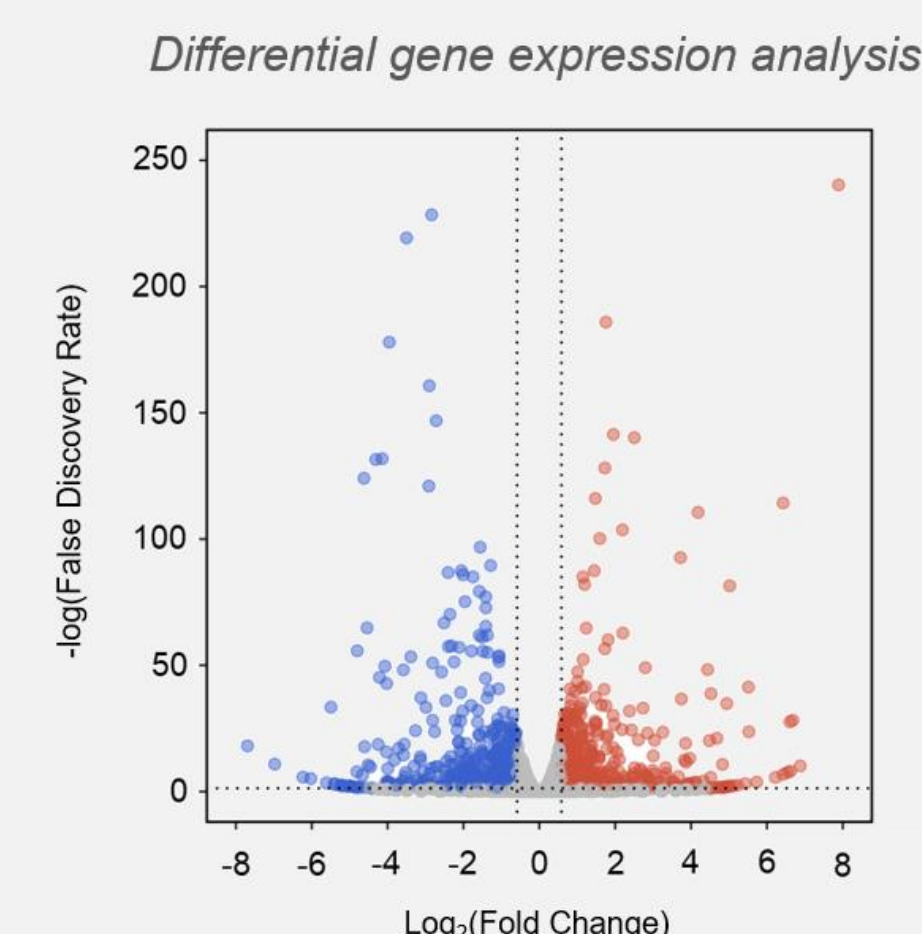
### Production of Influenza VLPs



### RNA extraction (12 and 24 hpi)

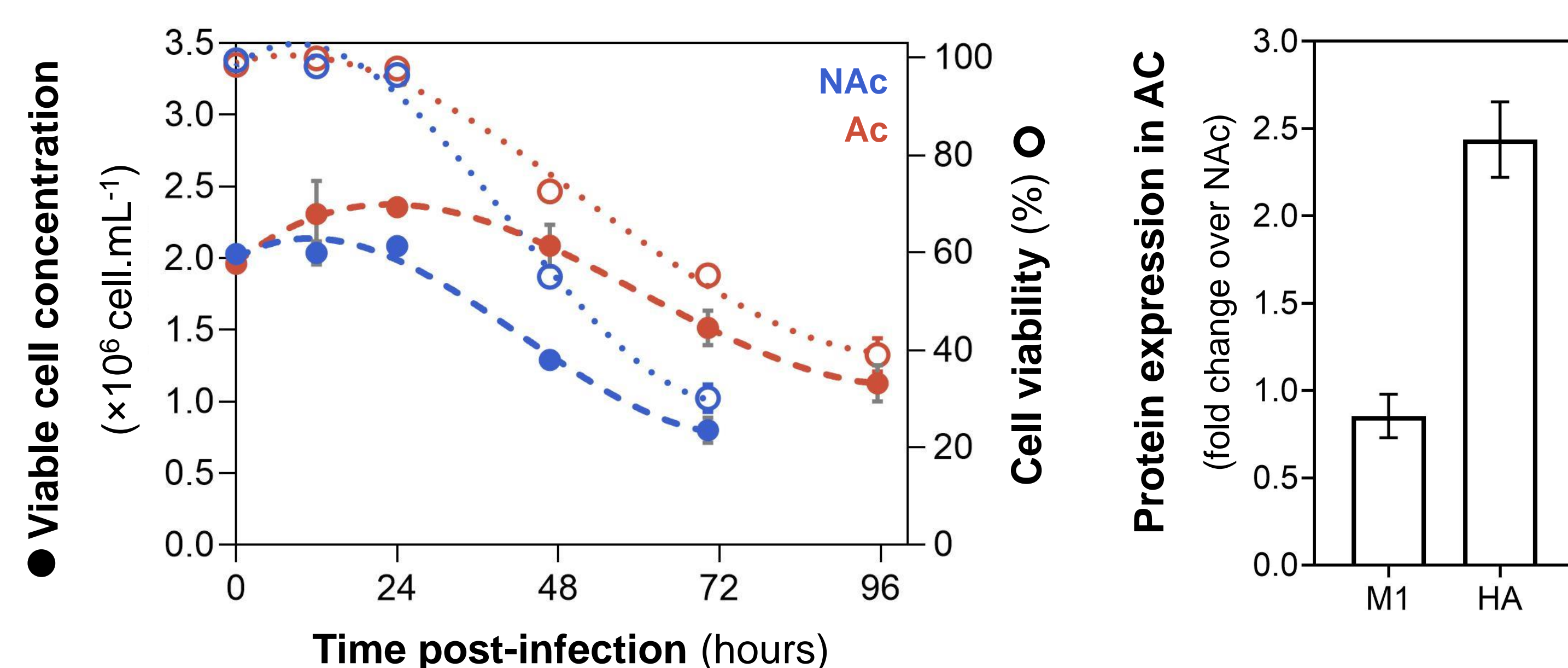


### Whole Transcriptome Analysis



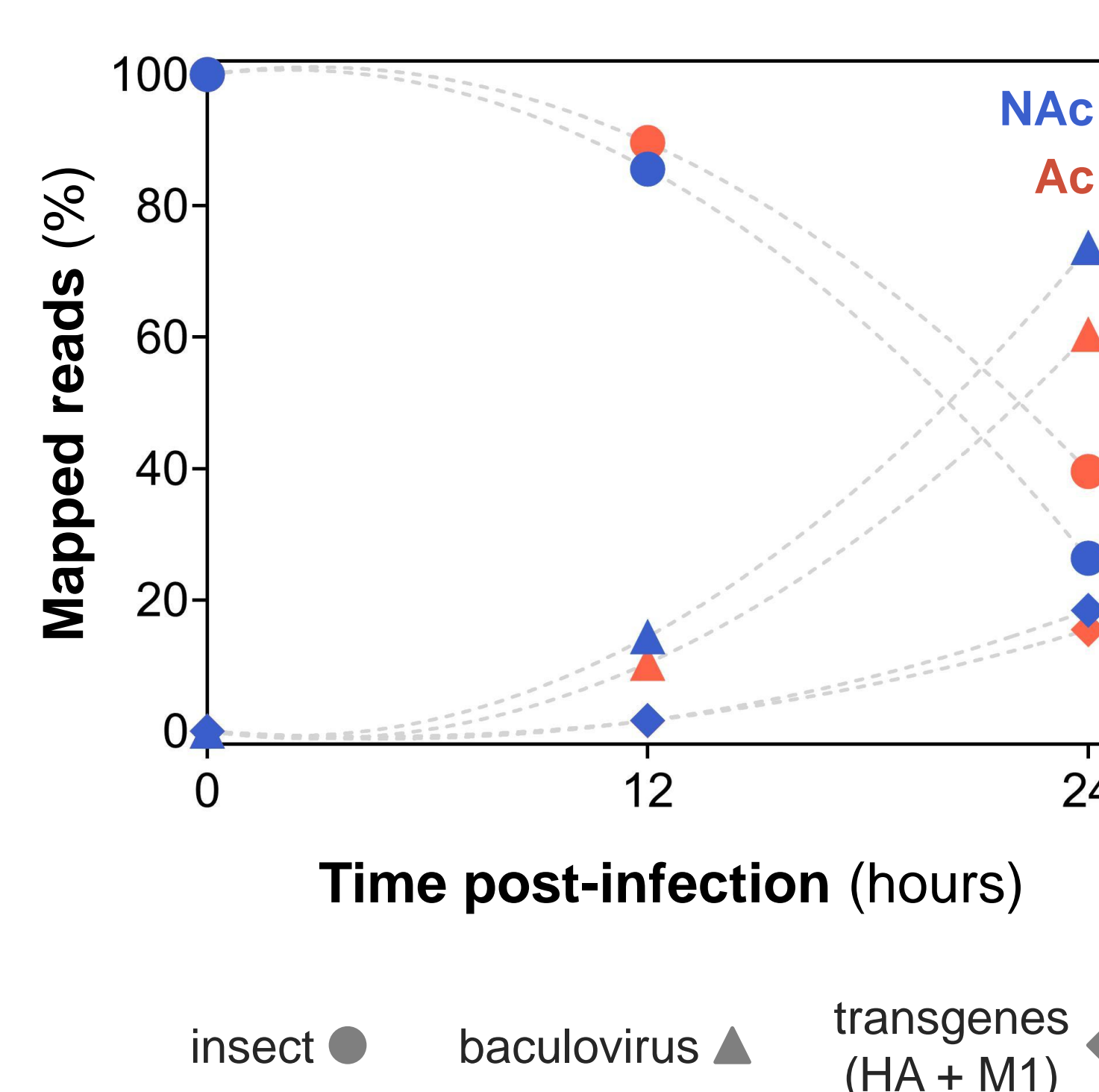
## Results

### Infection kinetics and HA production

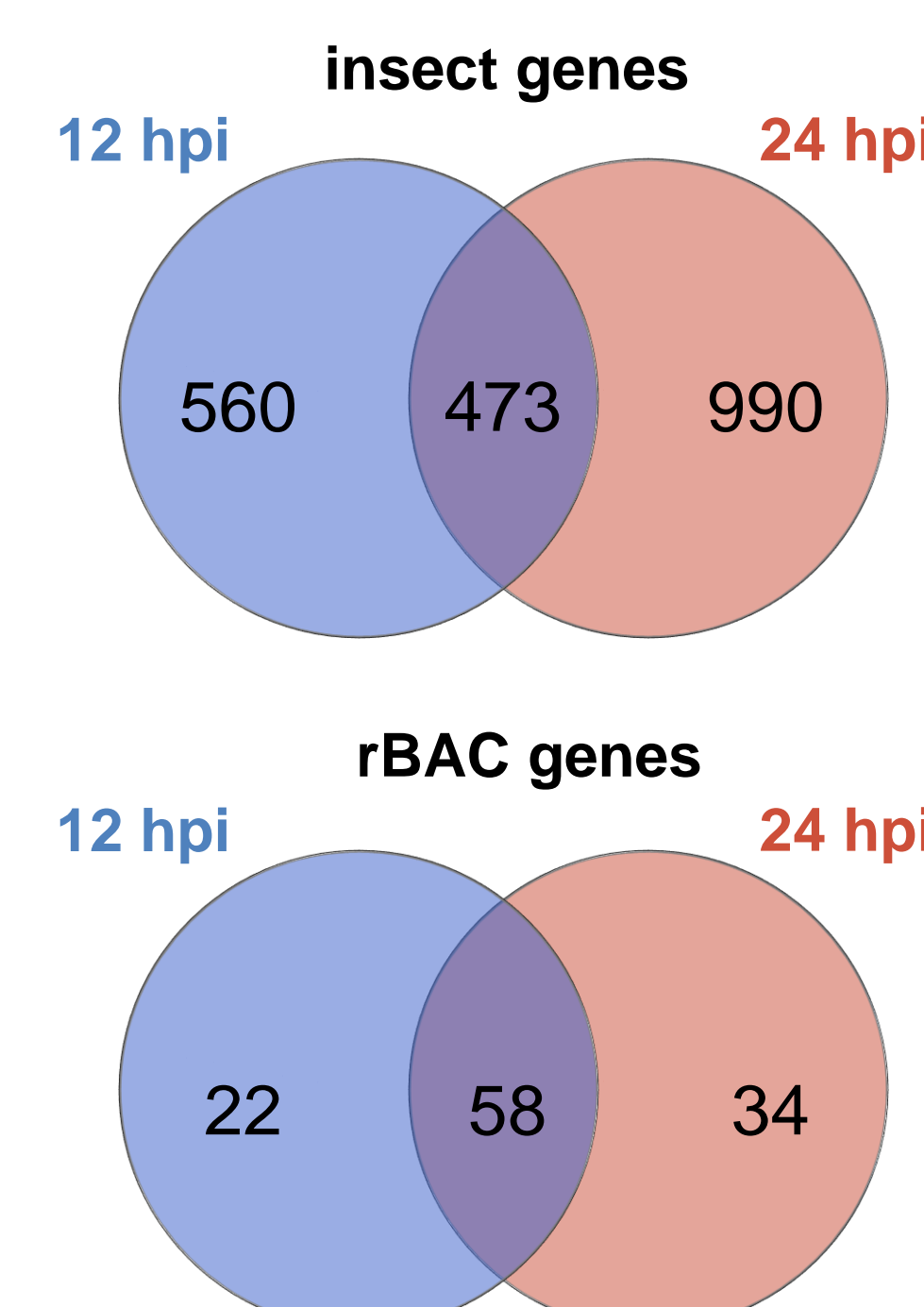


Adapted cells show delayed cell lysis and higher HA production

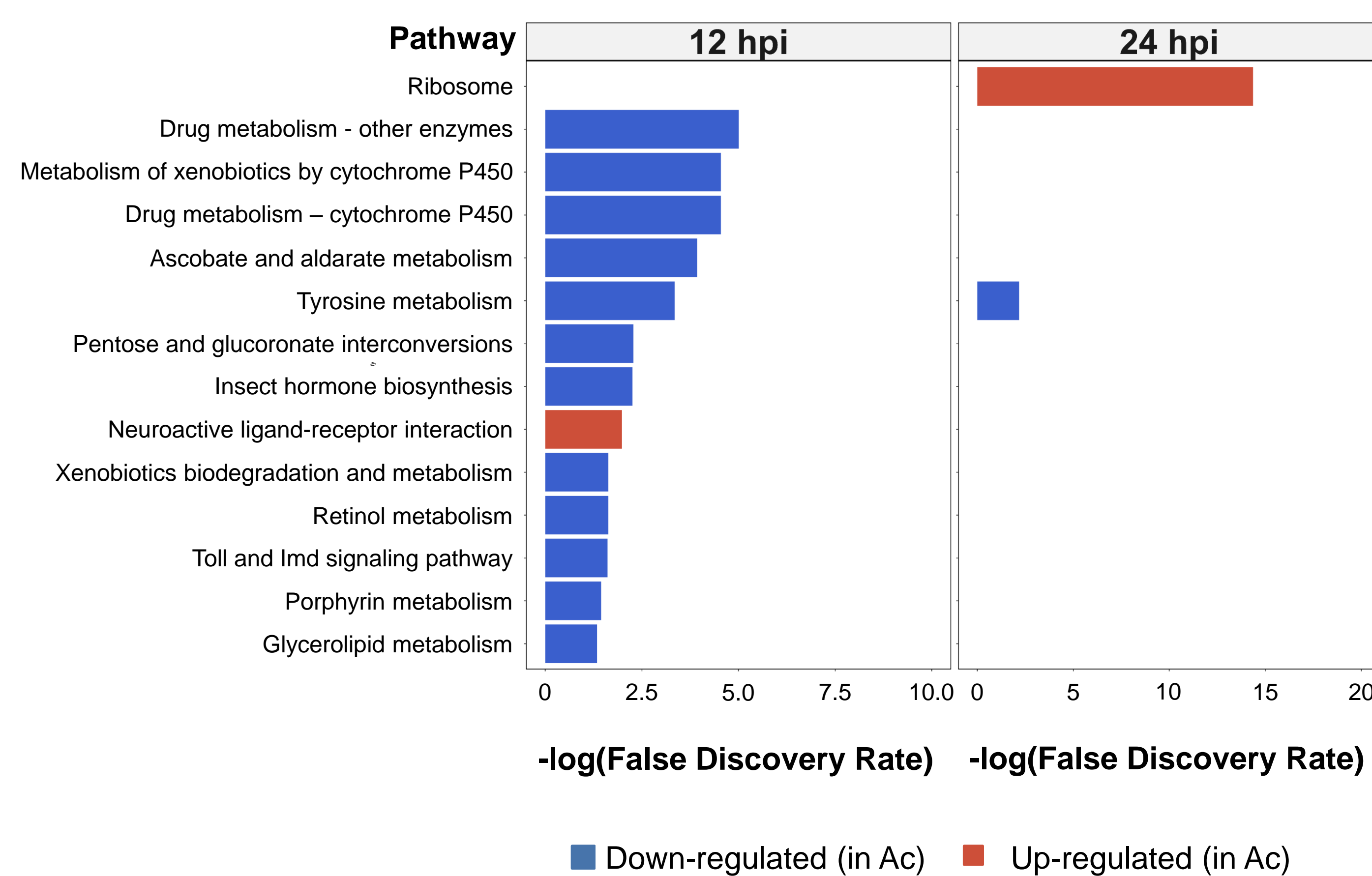
### Differential gene expression analysis



### Number of DEGs

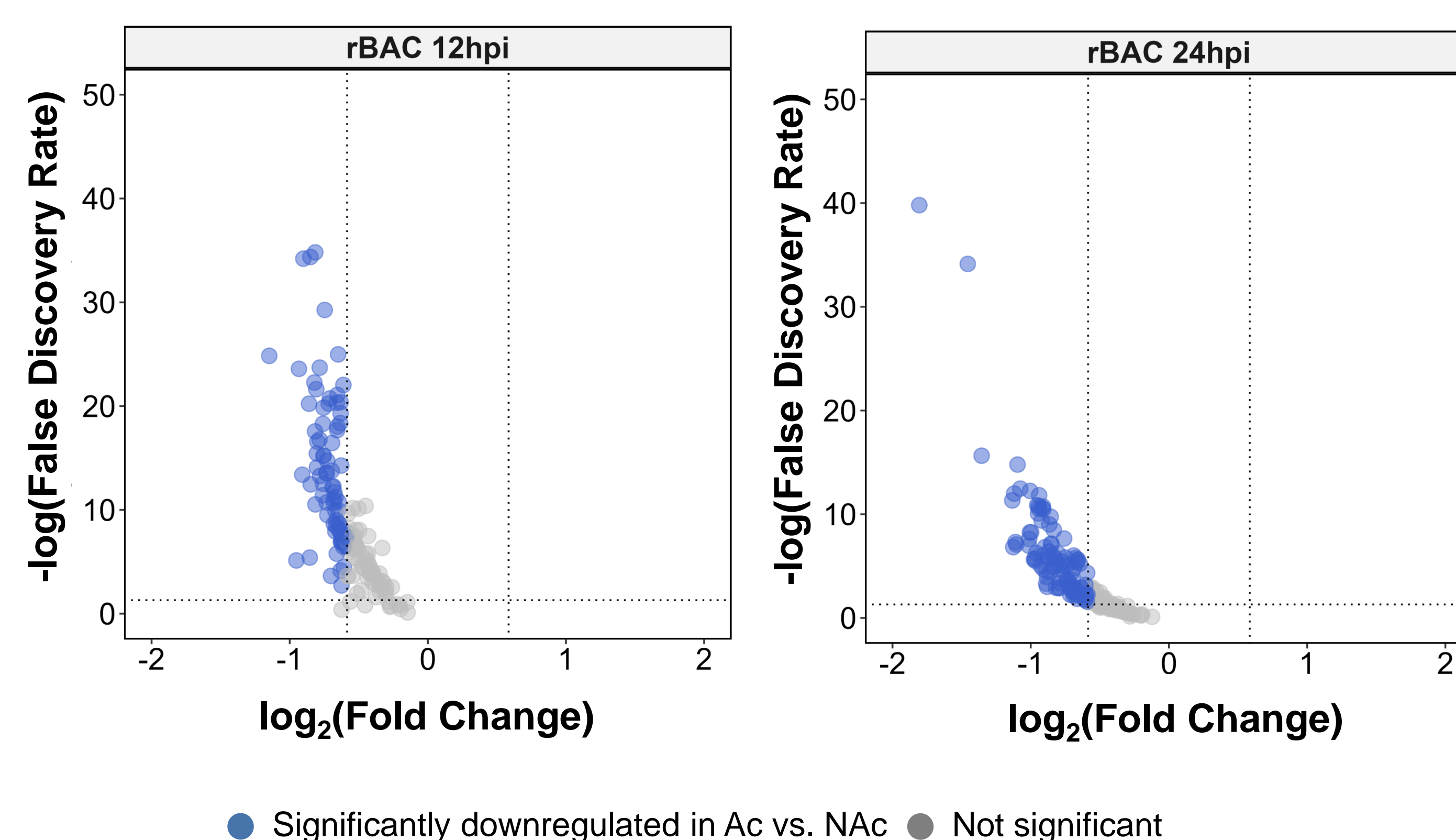


### Pathway analysis



Enriched pathways are mostly down-regulated and associated to rBAC infection

Adaptation process induces significant gene expression changes upon infection



Down-regulation of rBAC genes in infected adapted cells

## Conclusion

- Infection of Ac and NAc results in **significant gene expression changes**
- Pathways associated with rBAC infection are down-regulated** in adapted cells

**References:** 1. Fernandes B et al. Adaptive laboratory evolution of stable insect cell lines for improved HIV-Gag VLPs production. Journal of Biotechnology 307, 139-147 (2020). <https://doi.org/10.1016/j.jbiotec.2019.10.004>; 2. Correia R et al. Improving Influenza HA-Vlps Production in Insect High Five Cells via Adaptive Laboratory Evolution. Vaccines. 2020 Oct 7;8(4):589. doi: 10.3390/vaccines8040589.

### Acknowledgements

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