Defining how two avian double-stranded RNA viruses affect lipid droplet (LD) formation and lipid metabolism *in vitro*

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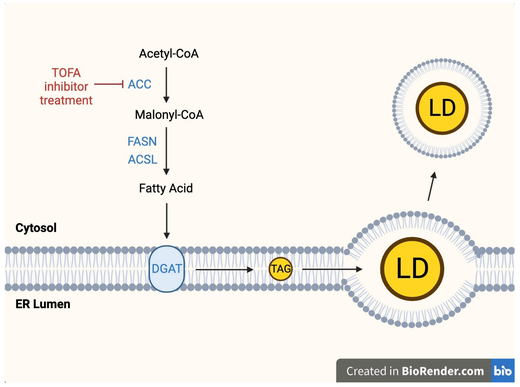
Introduction

- **Cellular lipid droplets (LDs)** consist of a neutral lipid core surrounded by a phospholipid monolayer with LD-associated proteins such as perilipins (PLIN). LDs have important functions in cellular metabolism and signaling.[1]
- **Virus factories (VFs)** are cytoplasmic inclusions in infected cells that serve as sites of viral genome replication and virus particle assembly.[1,2]
- Some mammalian and fish double-stranded (ds)RNA viruses hijack lipid droplets (LDs) during their replication cycle in favor of viral replication.[1,3,4]
- Our understanding of how avian dsRNA viruses, including avian reovirus (ARV) and infectious bursal disease virus (IBDV) impact lipid metabolism and utilize LDs in infected cells is incomplete
- This information is important to know as ARV and IBDV both show promise in oncolytic virotherapy, so we need to better understand how they impact cellular lipid metabolism in infected cells.[5,6]



The *de novo* LD synthesis pathway. Figure adapted from Criglar et al., 2022.

Objectives

- Characterize ARV and IBDV-mediated changes in LD formation in infected cells by quantifying LD size and number in ARV and IBDV-infected cells
- Identify mechanisms of how ARV and IBDV infection change LD formation by quantifying lipogenesis enzyme gene expression following ARV and IBDV infection
- Evaluate the role of LDs in viral replication by quantifying viral replication following inhibition or upregulation of LDs

Hypothesis

- Based on the literature on other dsRNA viruses, we hypothesize that ARV and IBDV infection would induce LD formation, and that LD upregulation would be pro-viral

Results

Figure 1. ARV infection increased the number of LDs per nucleus while IBDV infection had a less significant effect.

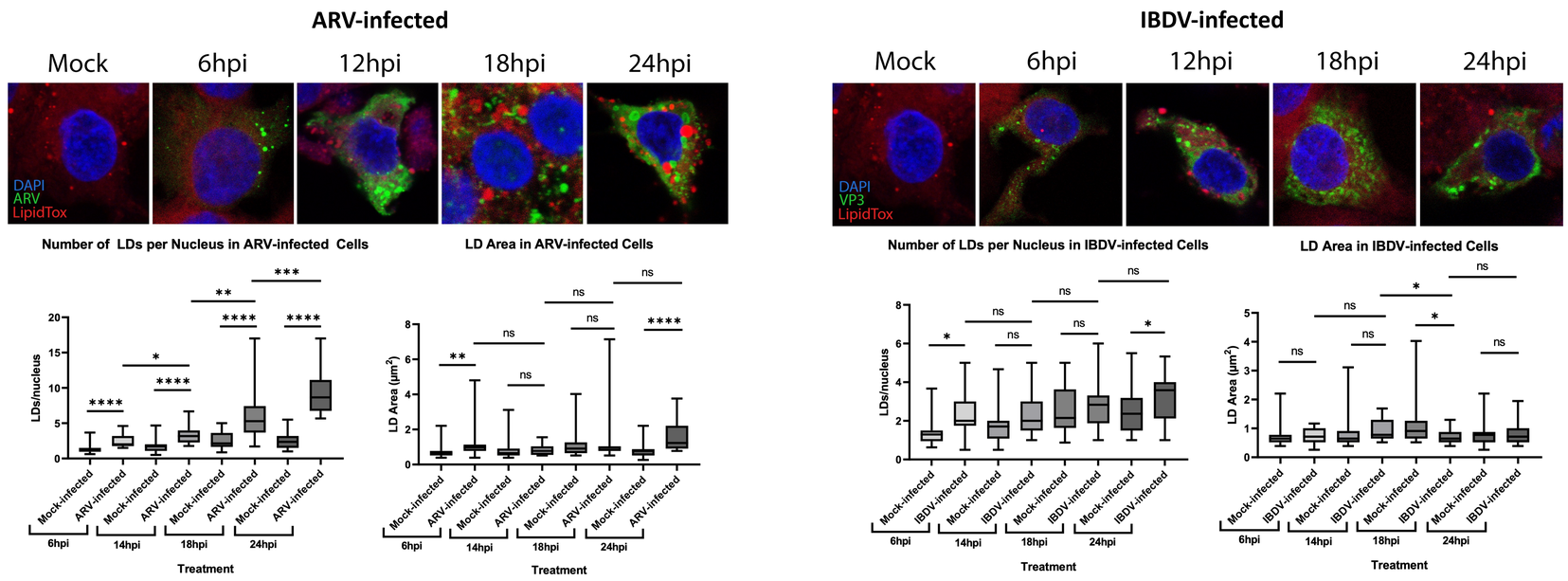


Figure 2. ARV infection decreased the expression of some genes involved in lipogenesis while IBDV did not.

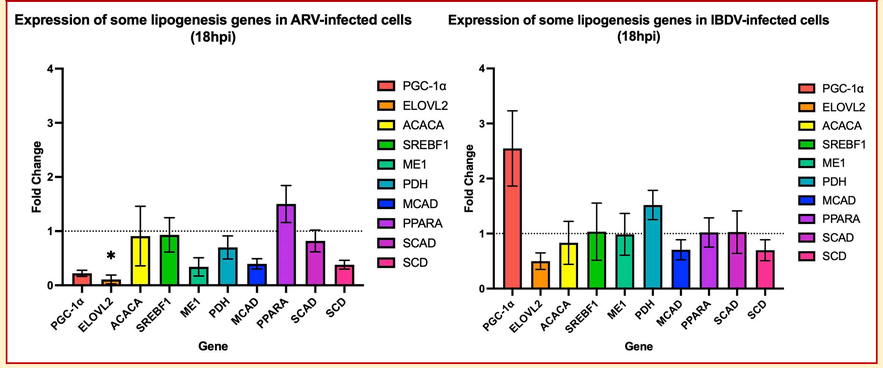
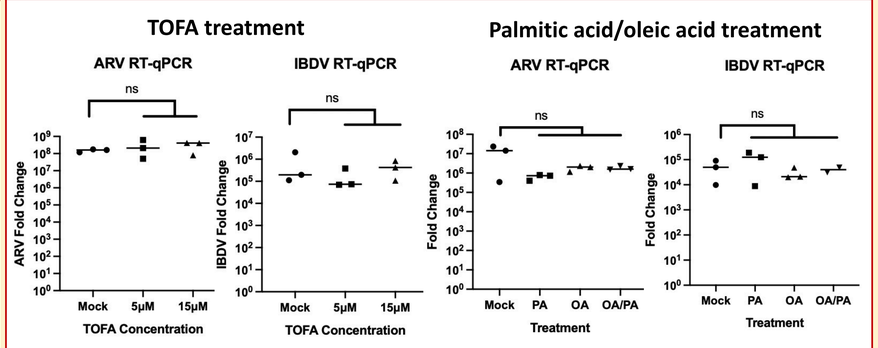


Figure 3. Both inhibition and upregulation of *de novo* lipogenesis did not affect viral replication.



Conclusions

- ARV infection upregulated LD formation and changed lipogenesis gene expression while IBDV did not. This suggests that ARV and IBDV affect cellular lipid metabolism differently.
- ARV-infected cells showed decreased expression of PGC-1α and ELOVL2 at 18hpi. Previous research has shown that decreased PGC-1α or ELOVL5 expression lead to lipid accumulation and hepatic steatosis in mice. Therefore, ARV infection may upregulate LDs by decreasing PGC-1α and ELOVL2 expression in infected cells.
- TOFA inhibition of *de novo* lipogenesis decreased but did not completely prevent ARV-mediated upregulation of LDs in infected cells. This suggests that ARV induces LD formation in part through enhancing the *de novo* lipogenesis pathway, but other LD synthesis pathways that involve the uptake of exogenous fatty acids into the cell may be involved as well.
- Both inhibition of *de novo* lipogenesis through TOFA treatment and upregulation of lipogenesis through fatty acid treatment does not affect ARV and IBDV viral replication. Thus, it is unknown whether LD upregulation is pro-viral, anti-viral, or neutral in terms of viral replication.

References

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