Assessing the antiviral potential of modified exosomes against Dengue Virus (DENV)

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Interrogating complex biology with innovative molecular biotechnology

Introduction

Dengue virus (DENV) is a mosquito-borne viral pathogen in the *flaviviridae* family. *Flaviviridae* viruses, such as hepatitis C virus (HCV), manipulate the host cell's lipid metabolism through altered expression of genes, such as sterol regulatory element binding proteins (SREBPs) and peroxisome proliferation activated receptors (PPAR)[1], to facilitate viral entry and infection.

Exosomes are small extracellular vesicles (30–120 nm) containing genetic and protein components, and are important for cell-to-cell communication and shuttling biological cargo. Previous research has shown *Flaviviridae* viruses can utilise exosomes to enhance proliferation through the transfer of viral RNA and proteins to recipient cells[2]. However, exosomes can also act in an antiviral capacity through the transfer of miRNA and functional proteins which elicit an antiviral response, hindering viral proliferation[3].

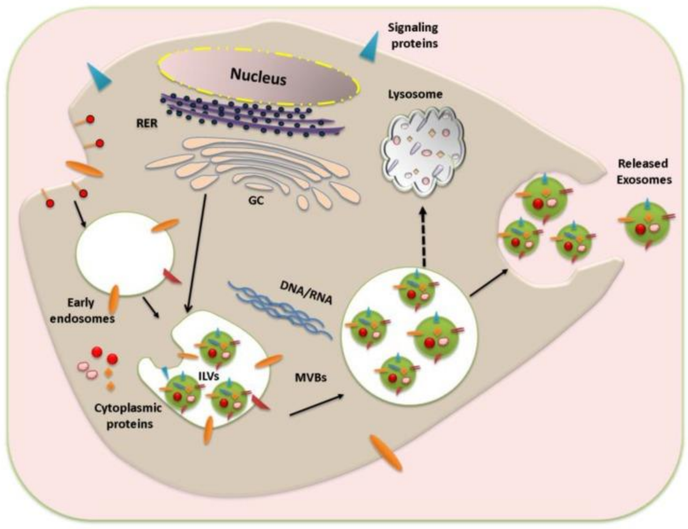


Figure 1: Exosome biogenesis and release from cell[2].

Our lab has demonstrated exosomes isolated from healthy cells treated with metabolic inhibitors, compounds "A" and "B", possess modified microRNA content which regulate genes involved in lipid metabolism, producing an antiviral effect on HCV.

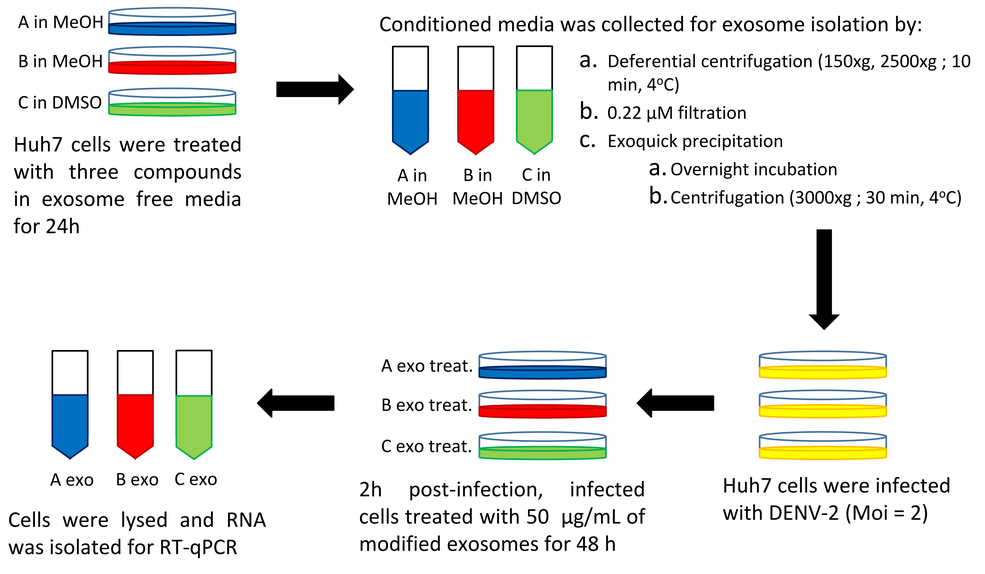
Hypothesis

Exosomes derived from healthy cells treated with compounds "A", "B" and "C" would display antiviral activity against DENV infection through alterations in their miRNA and protein cargo. Preferential changes will lower the expression of genes related to lipid metabolism.

Significance:

Agreement with results from previous studies would demonstrate pan-antiviral effects within the *flaviviridae* family.

Methodology



Results

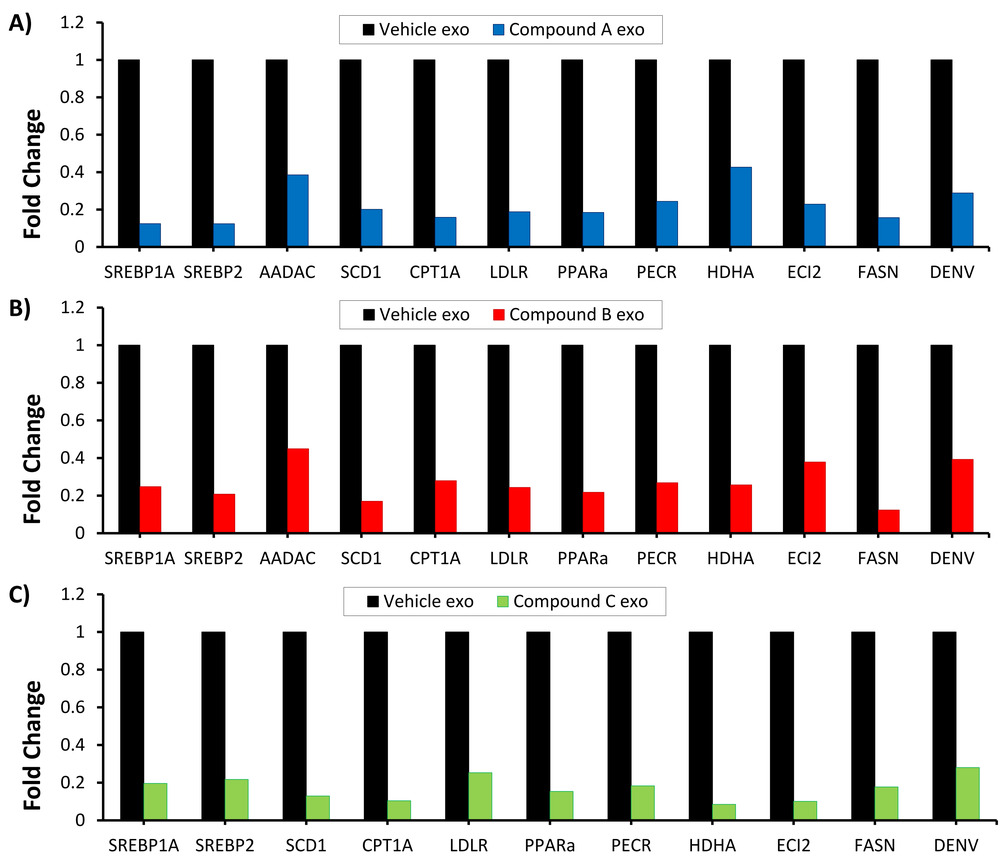


Figure 2: RNA expression of lipid metabolism genes in DENV infected cells treated with modified exosomes of compound A (A), compound B (B) and compound C (C).

Discussion

Exosomes from each condition decreased the expression of genes regulating lipid metabolic pathways and DENV RNA expression to different extents.

- **Compound A:** generated the greatest antiviral effect on DENV expression
  - most effective in downregulating genes (SREBP1A, SREBP2, AADAC, LDLR and PECR) related to lipid synthesis; important for viral replication and entry
- **Compound B**: most effective in downregulating FASN, a gene regulating fatty acid synthesis, important for viral replication
- **Compound C:** most effective in downregulation of genes (SCD1, CPT1A, PPARα, HDHA and ECI2) related to β-oxidation of lipids which produce energy required for viral replication

Conclusion

- Compound A, B and C modified exosomes possess pan-antiviral activity against DENV infection by downregulating genes involved in lipid metabolism
- Future steps will address the changes in exosome protein and miRNA content via immunoblotting and microarray analysis to identify factors responsible for the observed effects

References

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