An *in vitro* exposure platform for investigating bacterial and epithelial cell responses to aerosolized phage challenge.

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INTRODUCTION

Pseudomonas aeruginosa is a bacterial pathogen responsible for chronic respiratory infections in cystic fibrosis (CF) patients.[1] Bacteriophages (also known as phages) are viruses that infect bacteria. Phages are promising alternatives to antibiotics for treating drug resistant bacterial infections.[1,2] Investigations with aerosolized phage are limited and primarily focus on proof-of-concept demonstrations with animal models.[2] We have developed a **platform for conducting phage aerosol exposure studies using *in vitro* cultures of bacterial and airway epithelial cells.**

AIM

To determine if our platform is suitable for probing cellular responses to aerosolized phage challenge we investigated:

1. Bacterial responses to aerosolized phage.
2. Calu-3 airway epithelial cell responses to aerosolized phage.
3. Bacterial and epithelial cell responses to airflow exposure within the aerosol platform.

MATERIALS

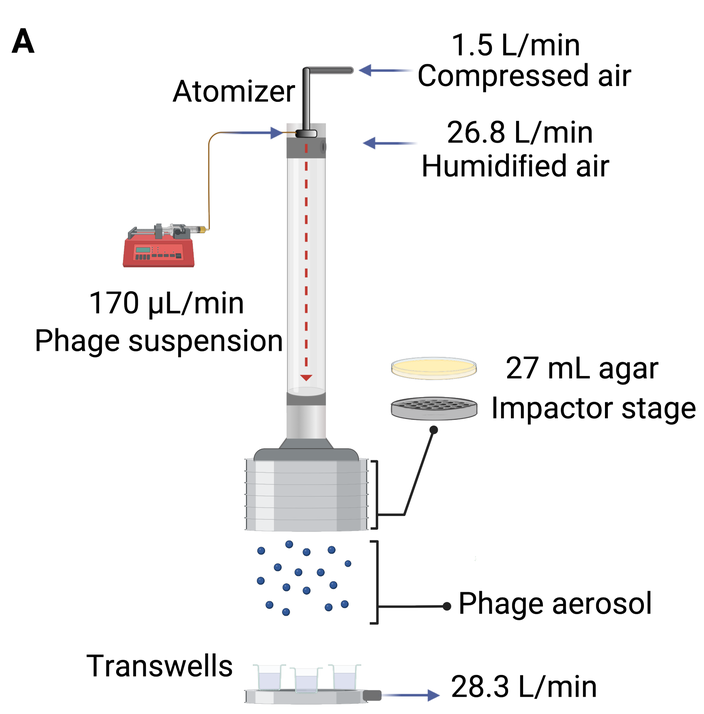
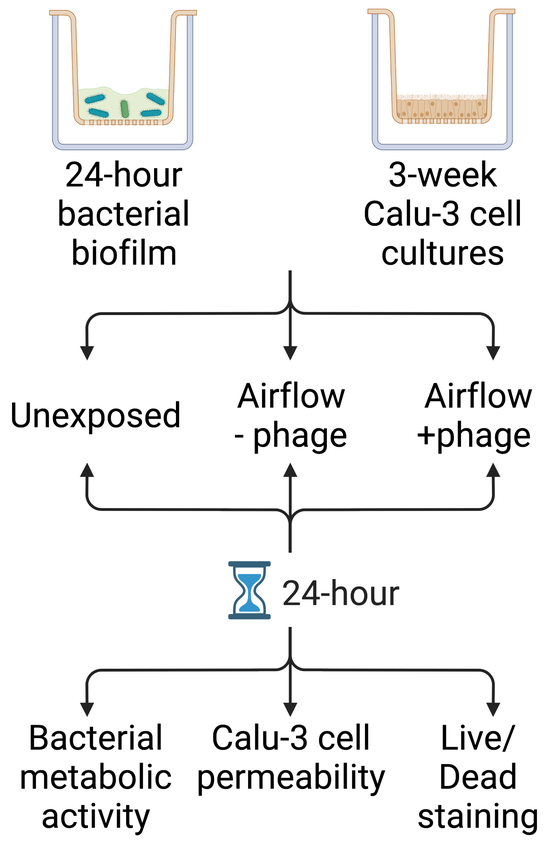


Figure 1 – (A) Aerosol platform; (B) Calu-3 cells; (C) Bacterial cells; (D) Phage virion.

METHODS



RESULTS

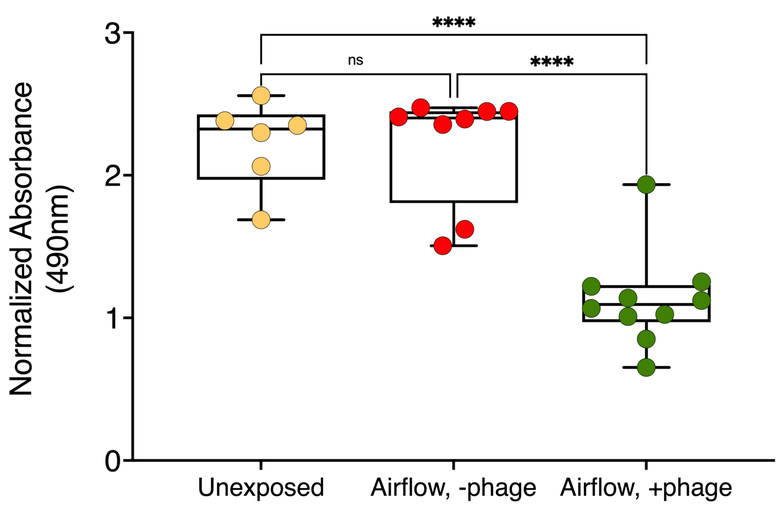


Figure 2 – Absorbance value reflects the number of viable bacterial cells. Airflow exposure alone did not alter bacterial viability. However, phage exposure significantly reduced bacterial viability.

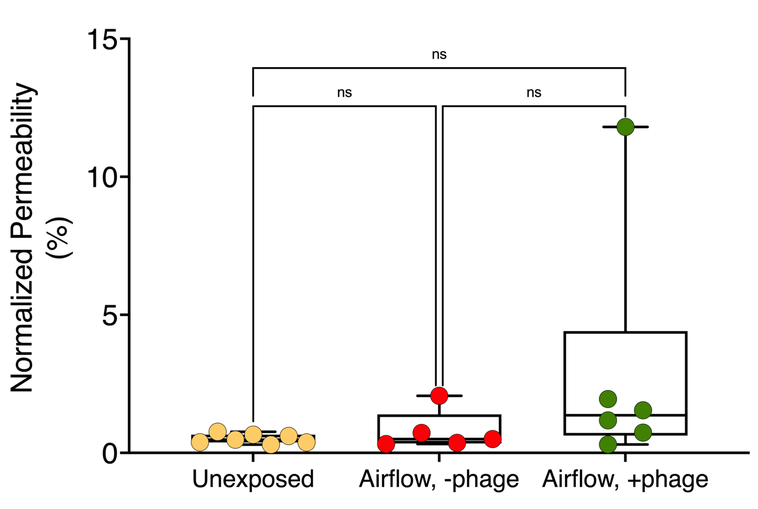


Figure 3 – FITC-dextran leakage from transwells was used as an indicator of permeability. Epithelial cell permeability values were not altered by airflow or airflow + phage exposure conditions.

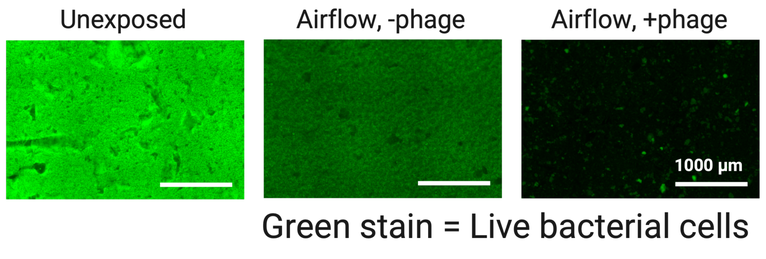


Figure 4 – Bacterial cells were stained with equal parts Syto9 (Live) and propidium iodide (Dead). Live cell density following phage exposure is significantly reduced, indicative of phage-mediated lysis.

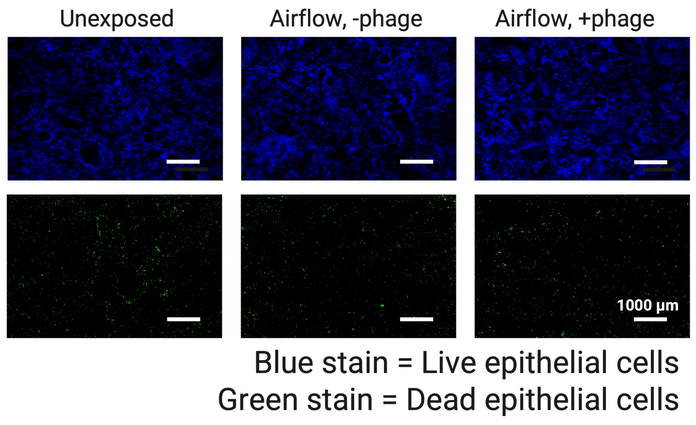


Figure 5 – Airway epithelial cells were stained with equal parts DAPI (Live) and NucGreen™ (Dead). Airflow and phage exposure did not alter the viability of epithelial cells.

SUMMARY

1. Bacterial viability was significantly reduced following phage exposure.
2. Epithelial cell barrier integrity and viability was not altered by phage exposure.
3. Airflow exposure had negligible effects on bacterial and epithelial cell cultures.

CONCLUSION

Our platform can be used to evaluate bacterial and epithelial cell responses to aerosolized phage challenge.

REFERENCES

1. Hassett, Daniel J., et al. *Expert Opin. Ther. Targets,* 2010.
2. Morello, Eric, et al. *PloS one,* 2011.
3. Thirugnanasampanthar, Mathura, et al. *DDL Conference*, 2022.

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