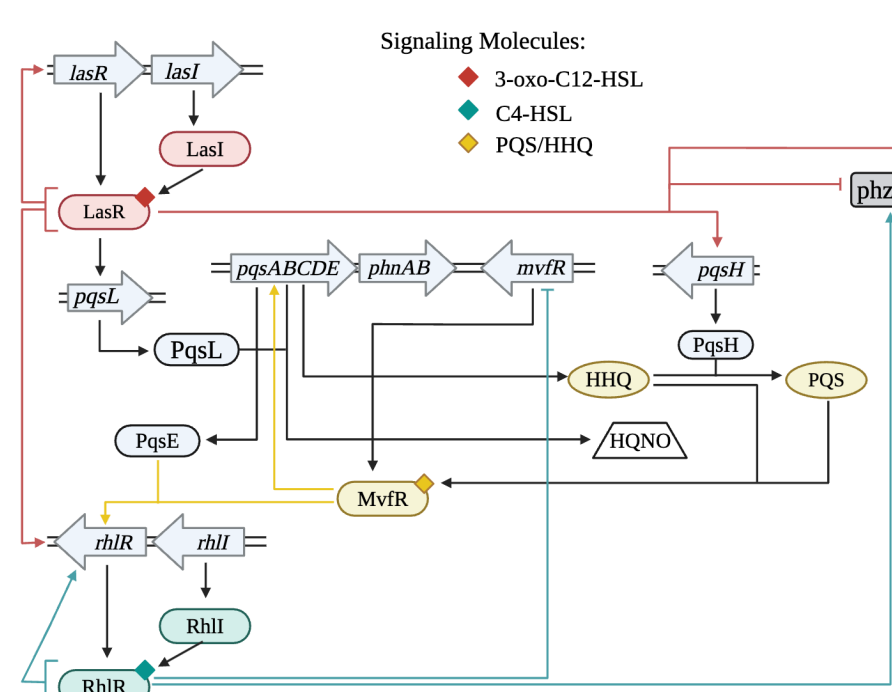
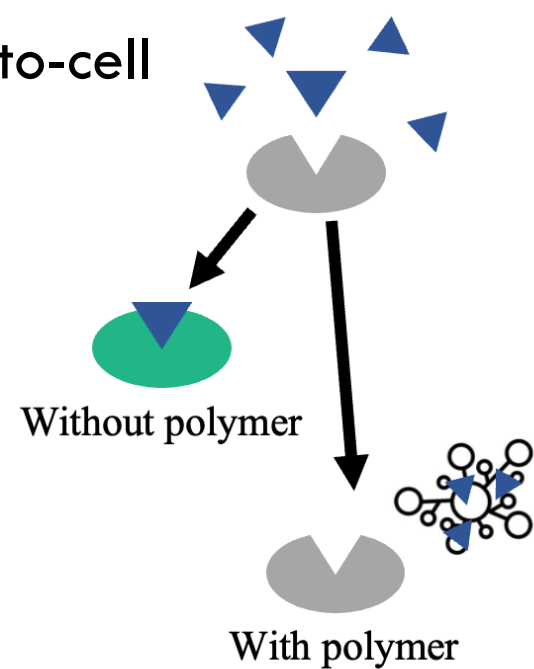


# Targeting signaling molecules of *P. aeruginosa* by using mucin as an anti-quorum sensing drug: A novel design to evaluate efficacy in the context of multidrug resistance

## Introduction

- Quorum Sensing (QS) is the process of cell-to-cell communication between bacteria to share information about cellular density
- Pathogenic bacteria synchronously express virulent traits, allowing for a magnified effect
- Bacteria bind to signaling molecules released by their local population
- Pseudomonas aeruginosa* is a gram-negative, opportunistic pathogen involved in many diseases such as cystic fibrosis
  - Biofilms protect bacteria from their surroundings and pyocyanin is a toxic phenazine



- Many polymers interfere with QS pathways
- As part of the immune system, mucins disperse cells in the environment and bind to invading pathogens.

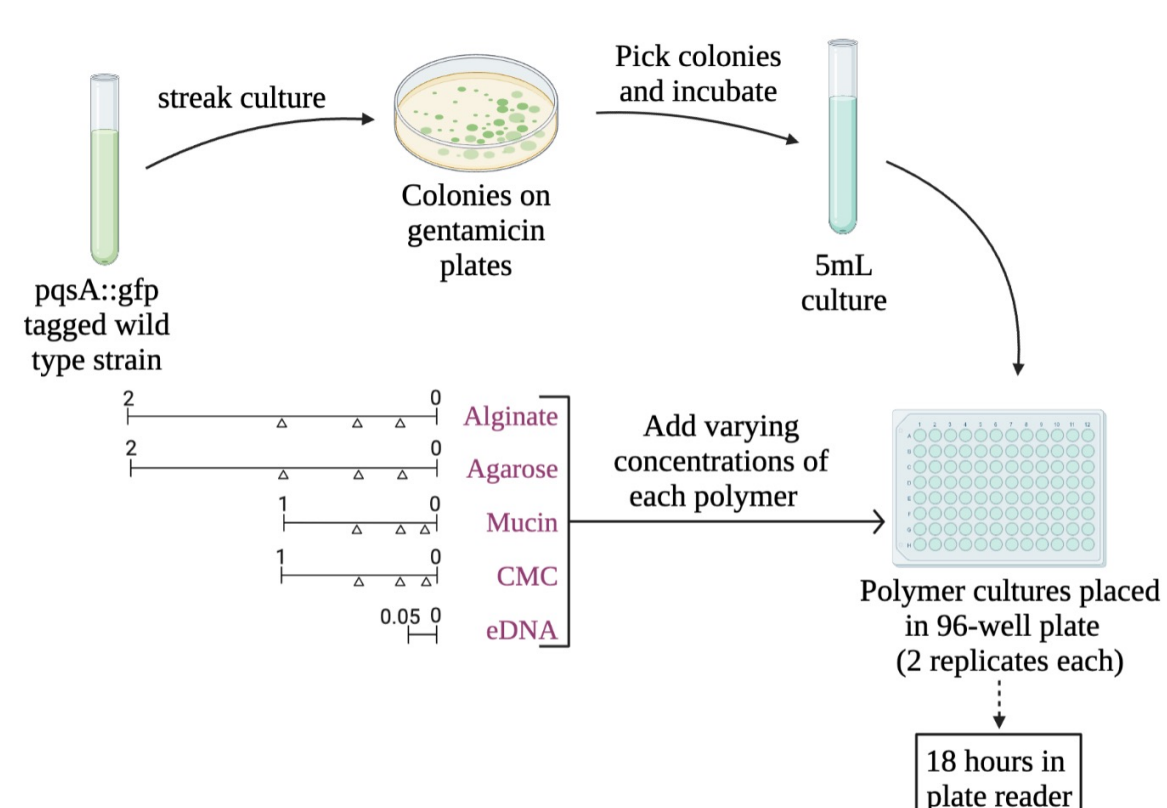
## Research Question

Can mucin serve as an anti-quorum sensing drug by interfering with the signaling molecules of *P. aeruginosa*?

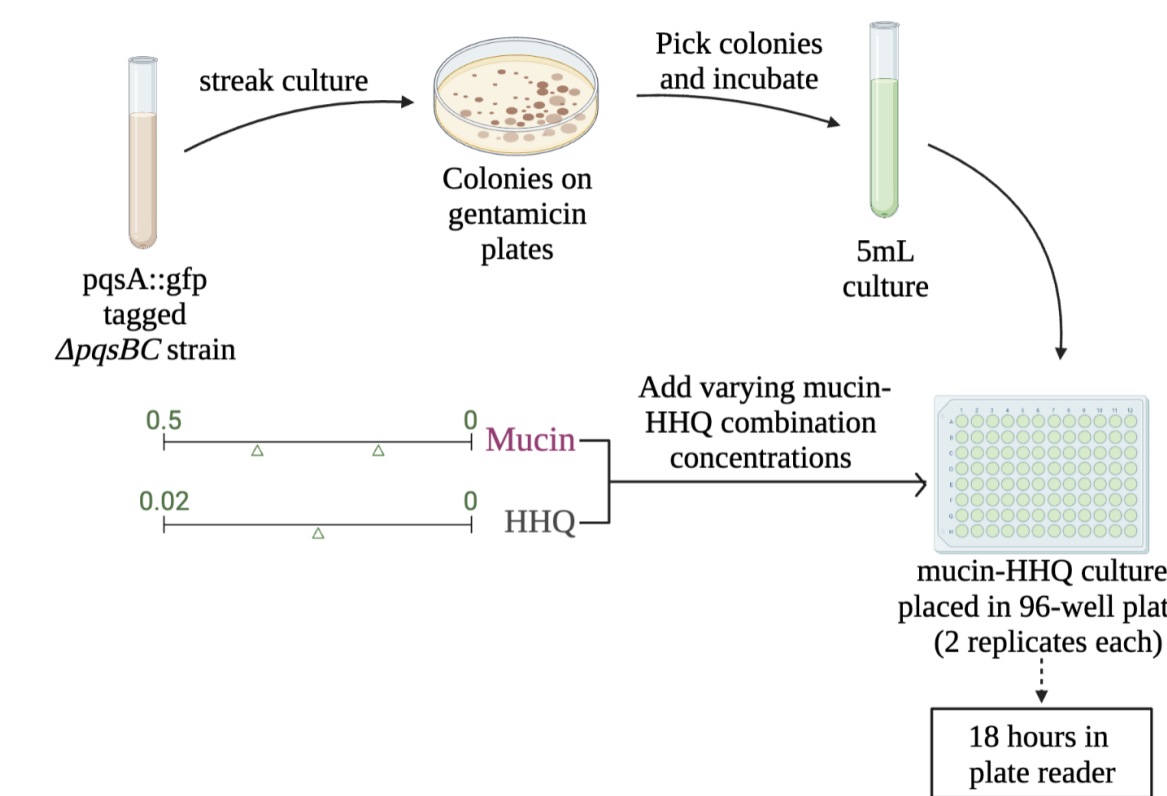
### Purpose:

- Curb virulent properties of pathogenic bacteria by using drugs to tame instead of kill bacteria in order to alleviate the multi-drug resistance crisis
- Evaluate the efficacy of targeting signaling molecules in downregulating quorum sensing (QS) activity of *P. aeruginosa* using multiple drugs
- Develop a statistical approach to model QS activity through time using fluorescence

## Methods

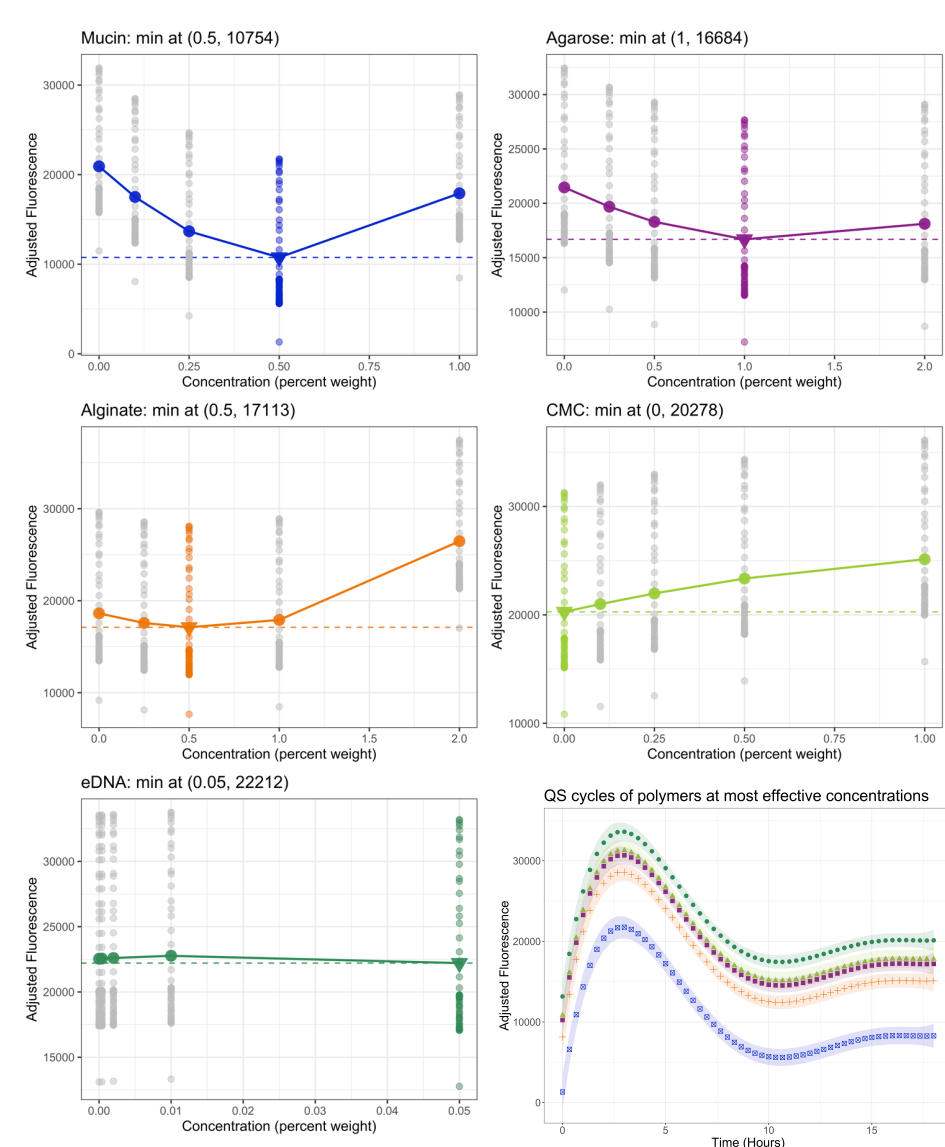


**Workstream 1:**  
Determine which polymer is most effective in suppressing QS activity



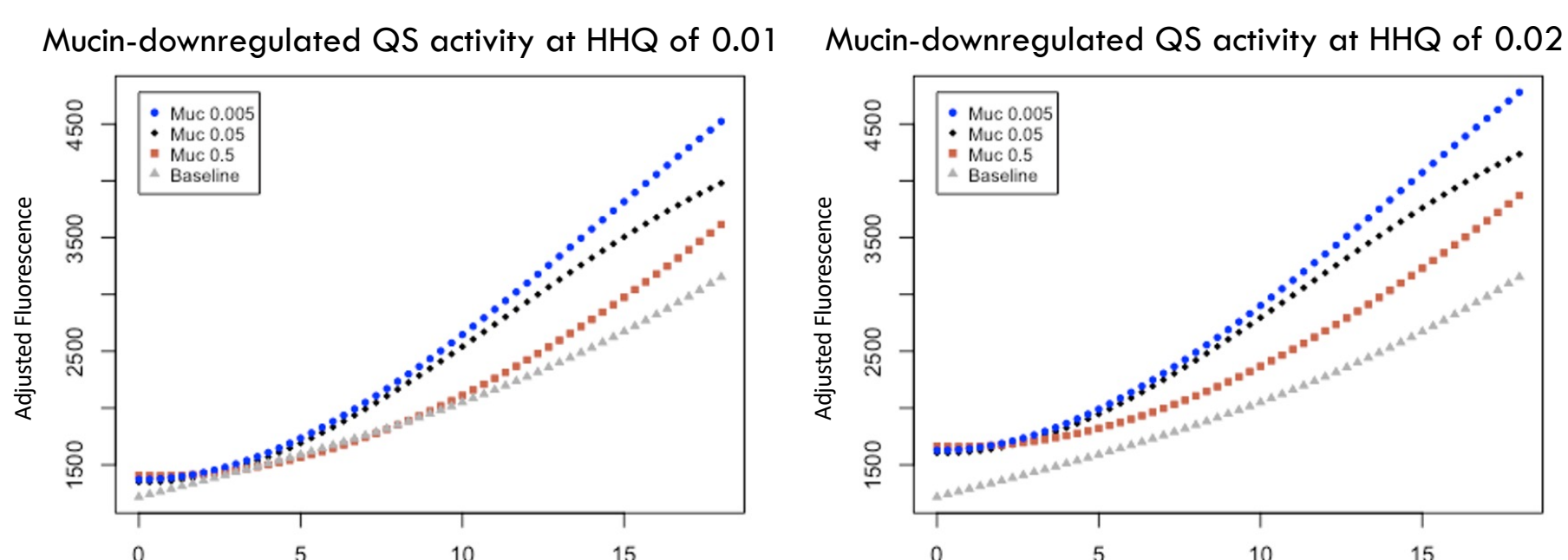
**Workstream 2:**  
Determine whether mucin is specifically targeting the signaling molecules of *P. aeruginosa*

## Results



### Workstream 1 Analysis:

- Mucin at 0.5% (wt) was the most effective polymer in suppressing QS activity.
- The non-linear trend of fluorescence across mucin concentrations confirms that mucin suppressed QS without impeding bacterial growth



### Workstream 2 Analysis:

Higher concentrations of HHQ at constant levels of mucin resulted in greater QS activity, indicating that mucin is targeting the signaling molecules of *P. aeruginosa*

## Conclusions

- A framework to attenuate QS by targeting signaling molecules and their pathways was developed
  - The approach evaluates the efficacy of the actual gene product on QS, which is more precise than measuring gene expression that may not always translate into protein
- Mucin neutralized the effect of HHQ signaling molecules
- Curbing virulence of pathogenic bacteria opens the door for the development of drugs with similar mechanisms of action in clinical setting
- Statistical adjustment of covariates led to more precise assessment of polymer effects through time

## Future Research

- Characterize the effects of the structural components of mucin on downregulating QS, for the purpose of developing efficient synthetic polymers as alternatives to antibiotics
- Capitalize on Biobank data to further investigate both the efficacy and safety of mucin against infectious human diseases by testing naturally-produced proteins such as mucins against thousands of diseases and health traits