PERMEABILITY OF QUORUM SENSING SIGNAL MOLECULES THROUGH A MUCUS MODEL: AN LC-MS/MS QUANTITATIVE ANALYSIS

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INTRODUCTION

The microbiota plays a key role in the regulation of human health. Accumulating evidence focus current research on identifying the microbiota-derived small molecules as the main characters of the crosstalk between microbiota and human body. Particularly, the spotlight is set on Quorum sensing (QS), one of the major density-dependent bacterial communication systems. QS molecules are involved in regulation of gene expression and virulence factors. of many pathogen, such as *Pseudomonas aeruginosa.*

In literature, QS system of *P. aeruginosa,* is increasingly being documented. Understanding microbiota metabolites may provide opportunities to investigate the unknown etiologies of many diseases and display promise in diseases diagnosis.

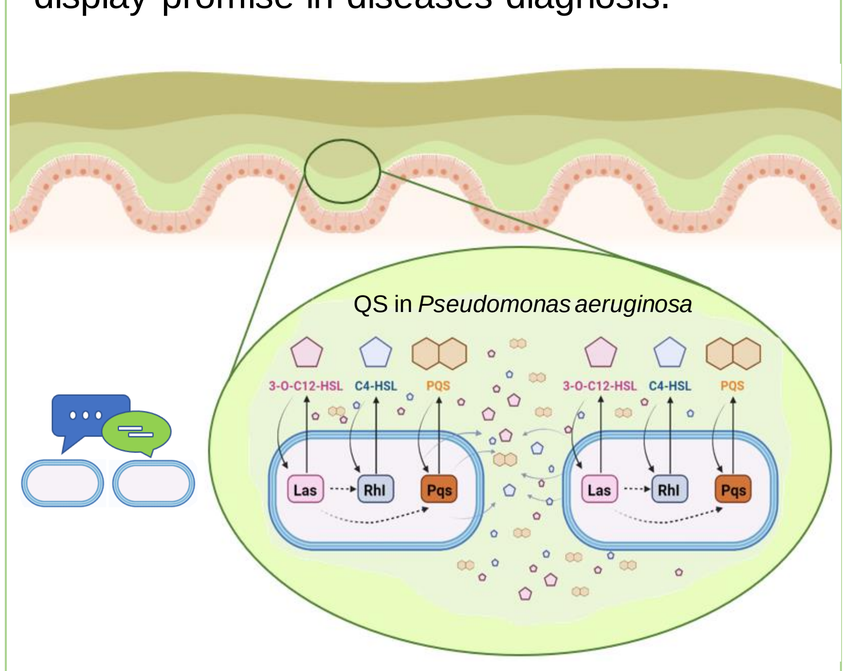

Figure 1: Quorum sensing of *P.aeruginosa*

THE NEED

- How does mucus interfere on diffusion of QS?
- Up to the present time there are no systematic studies of diffusion of microbial small molecules trough the mucus

EXPERIMENTAL PART

- **The diffusion of standard QS small molecules (Figure 3) was studied by LC-MS/MS [1]**
- **The PAMPA model**, a high throughput permeability assay, **was coupled with mucus**
- **The mucus model [2] mimics the physico-chemical properties of cystic fibrosis mucus (figure 4)**

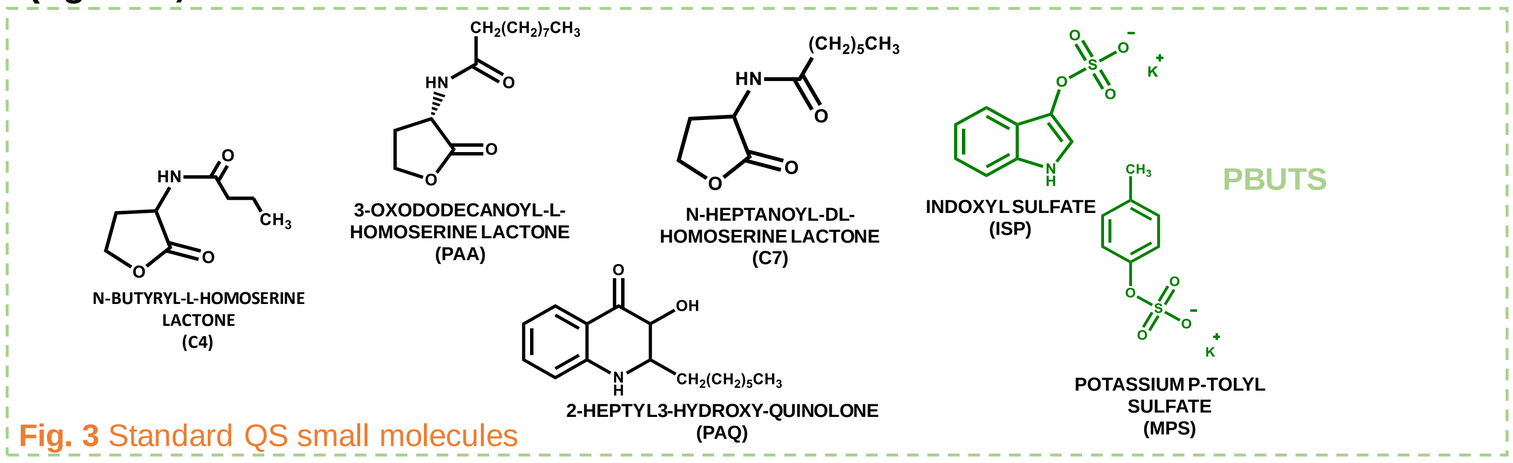

Fig. 3 Standard QS small molecules

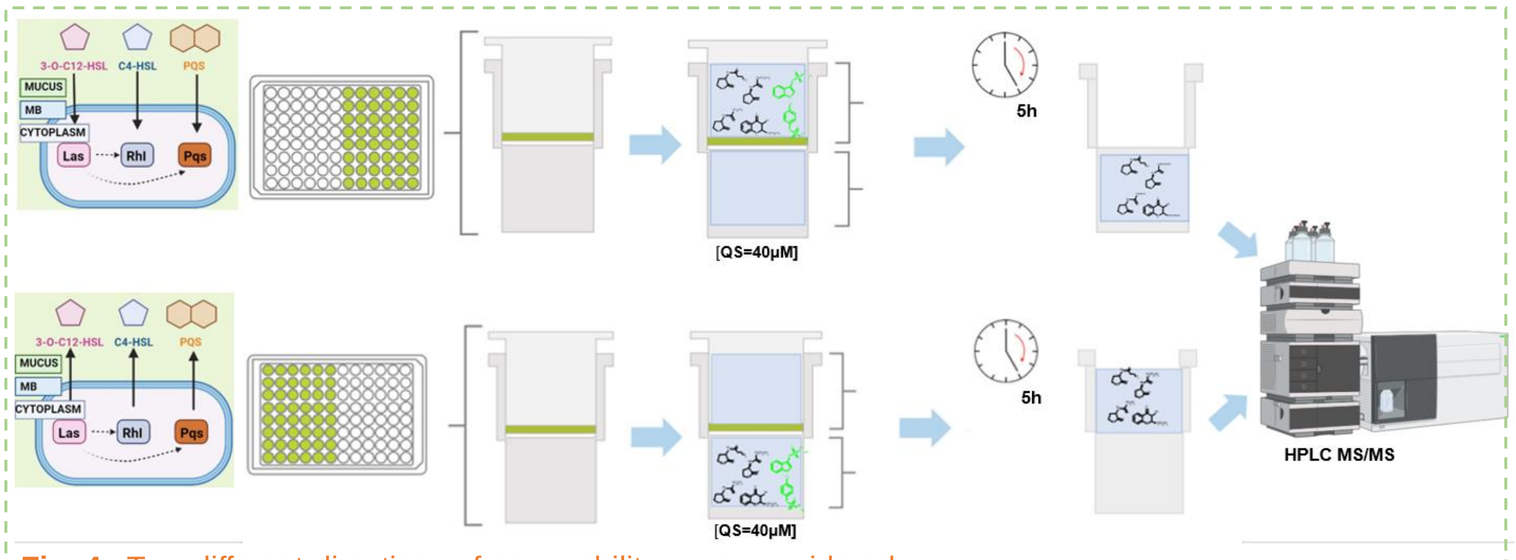

Fig. 4 : Two different directions of permeability were considered

RESULTS AND DISCUSSION

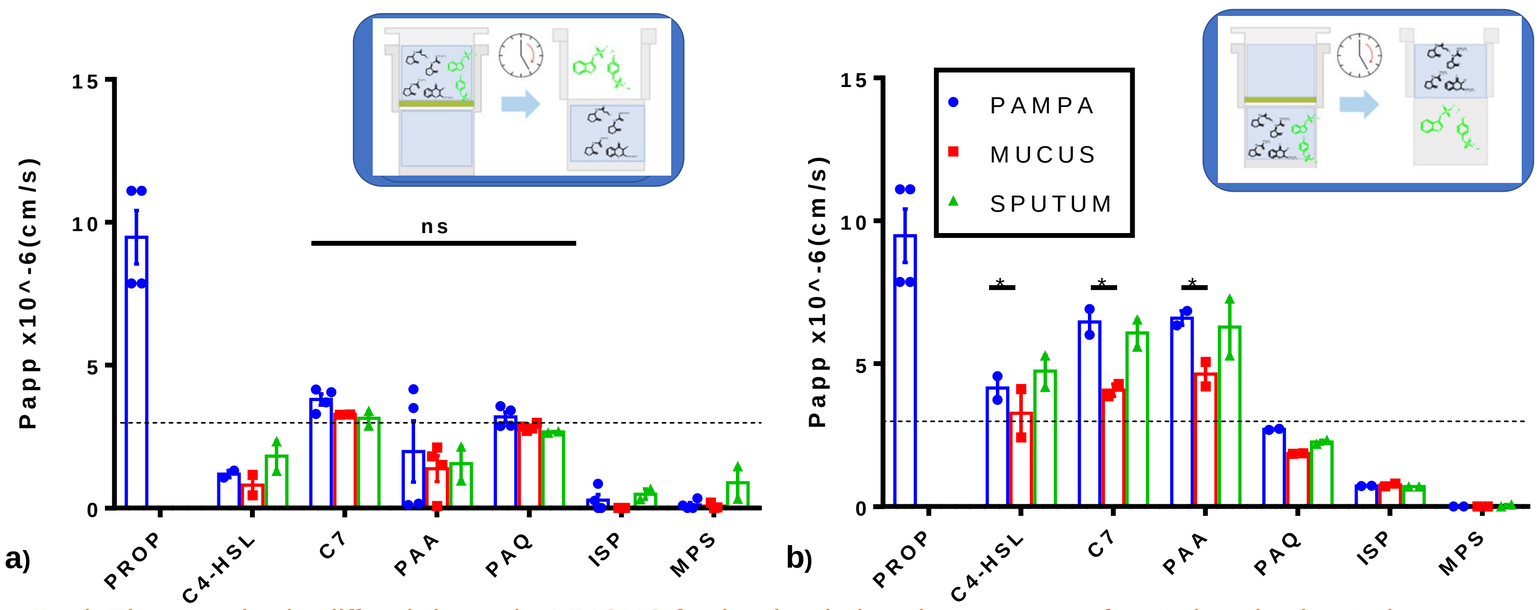

Fig. 5: **a**) The standards diffond through: MUCUS→mb, simulating the process of entering the bacteria; **b)** The standards diffond through. Mb→ Mucus simulating the exit from the bacteria

Quantification of standard QS permeability by LC-MS/MS:

- **PBUTS**→ No diffusion, because their charge
- **QS** of *P.aeruginosa*→ difference in % of diffusion, reflect their way to cross the mb
- **QS** through mucus→ ↓ % of diffusion (compared to PAMPA)

TAKE HOME MESSAGE

➢QS is a cell-to-cell communication

➢Studying the diffusion through mucus can aid to develop strategies against the circuits of QS

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[2] Pacheco D. P.; Butnarasu C. S.; Briatico Vangosa F.; Pastorino L.; Visai .; Visentin S.; Petrini P. *J Mater Chem B.* 2019 Aug; 7(32):4940-4952

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