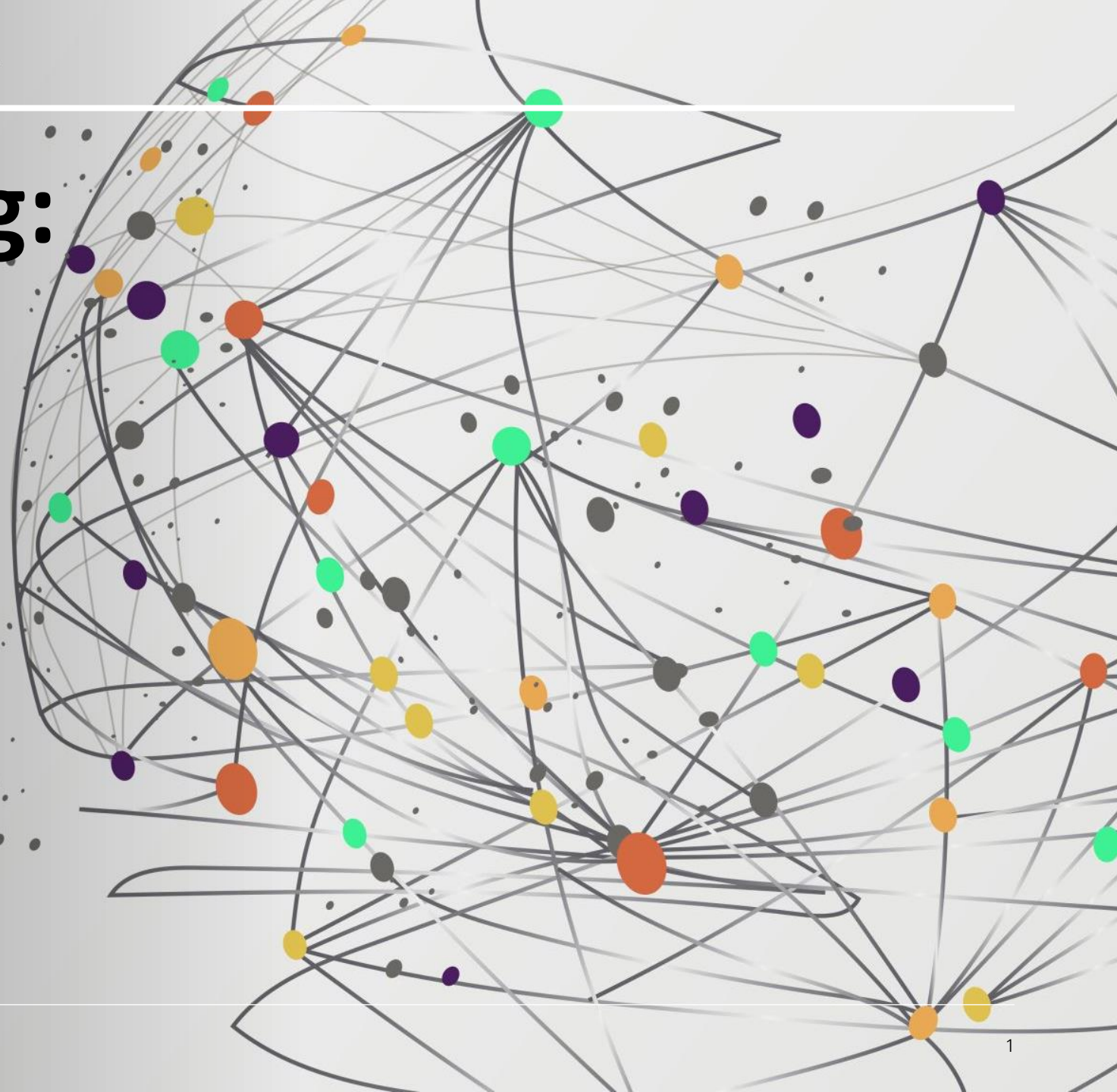

Quorum Sensing: Harnessing the Power of Collective Intelligence

Joint Graduate Student Seminar

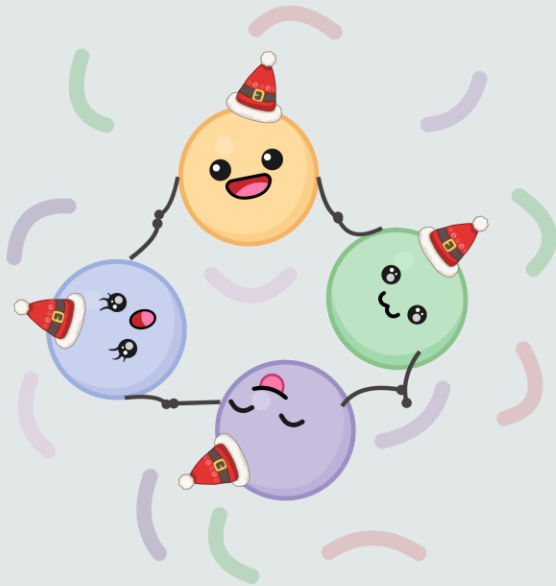
Jiayi Qu

Year 1 PhD student

Supervisor: Prof Xiao Yang



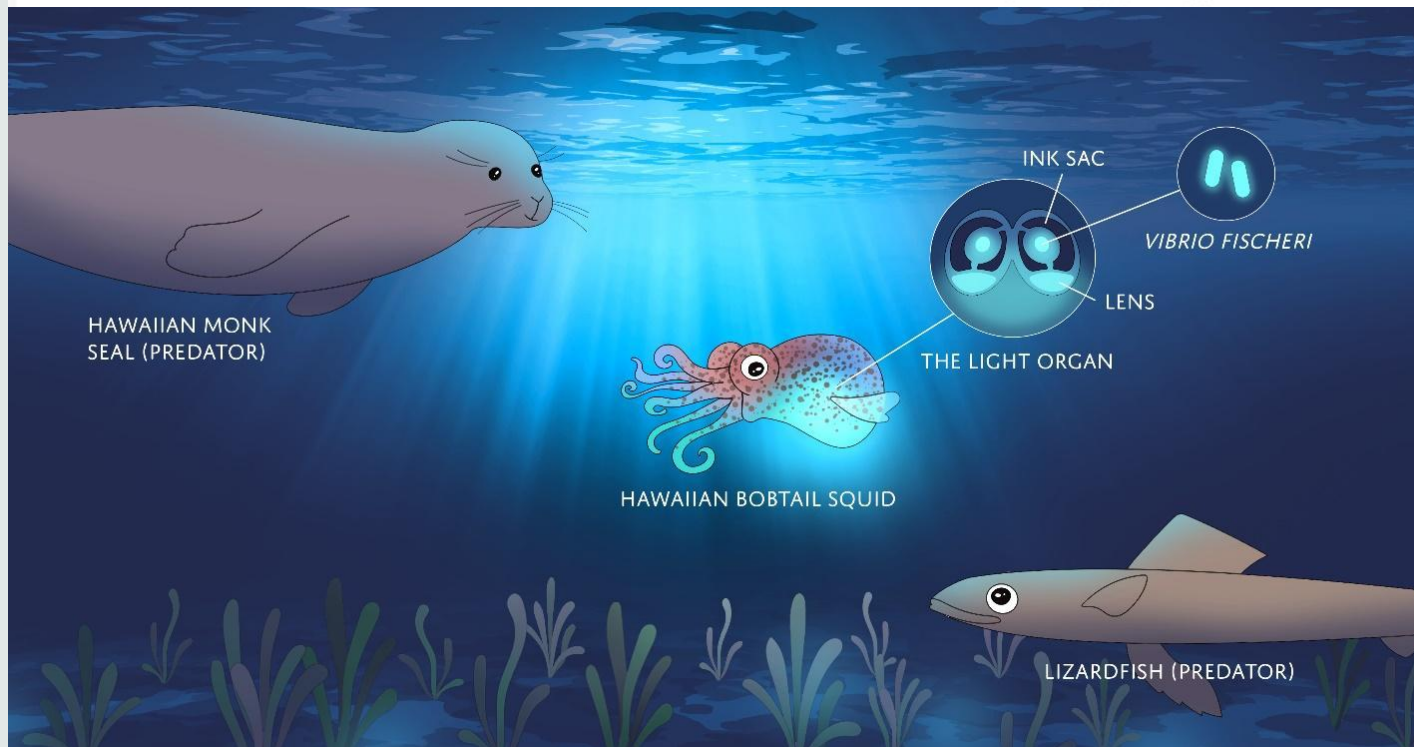
Outline



- Introduction of quorum sensing (QS)
- QS in infection
- QS and antibiotic resistance
- Conclusion

What is Quorum Sensing (QS)?

Cellular Control of the Synthesis and Activity of the Bacterial Luminescent System¹



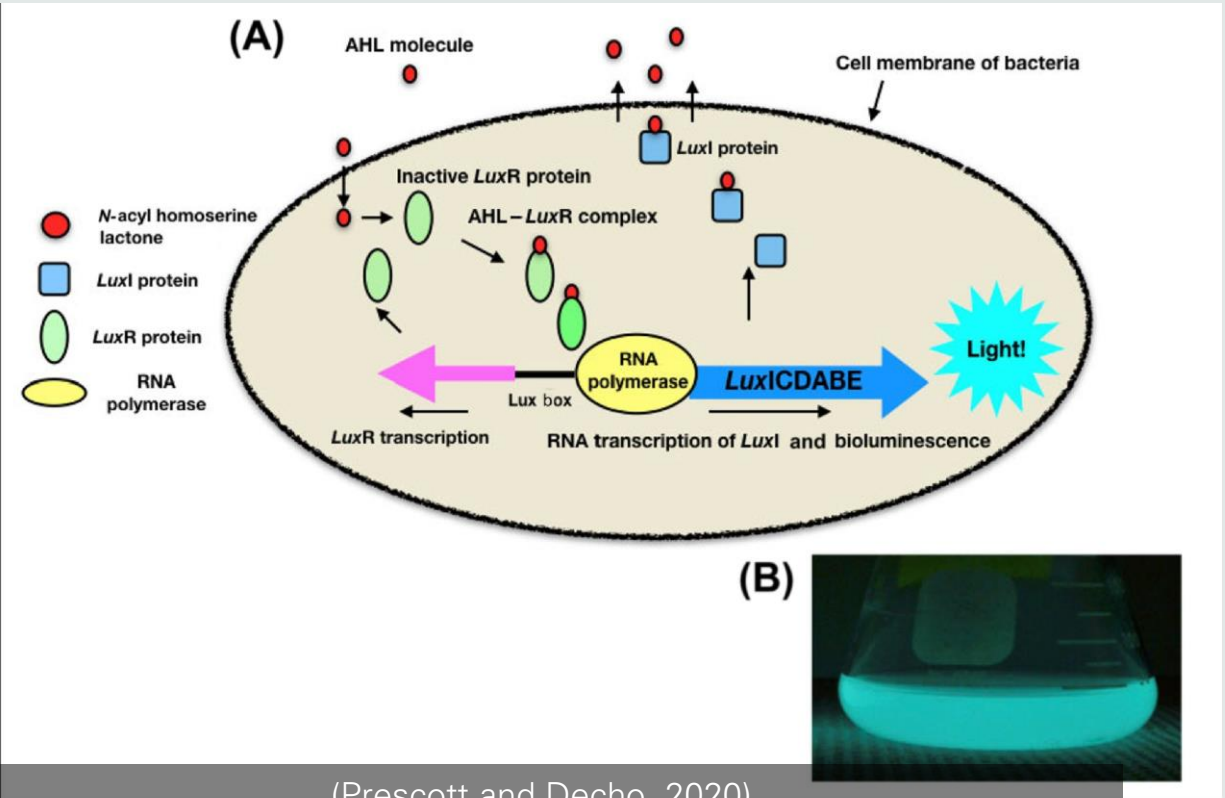
- A luminous marine bacterial species, *Vibrio fischeri* (Nealson et al., 1970)
- Cell density-dependent process, But “more than just a numbers game” (Xavier and Bassler, 2003)

Hawaiian bobtail squid



QS mechanism of *V. fischeri*

- The luminescence gene(*lux*) found in 1980s (Engebrecht et al., 1983)(Engebrecht and Silverman, 1984)
 1. Highly conservative ***LuxI*** gene, which encoded to produce acyl-homoserine lactone (AHL) autoinducer
 2. Highly variable receptor ***LuxR*** protein among species
- The *luxCDABE* genes of *V. fischeri*, encoded LuxICDABE operon transcribes luciferase enzyme



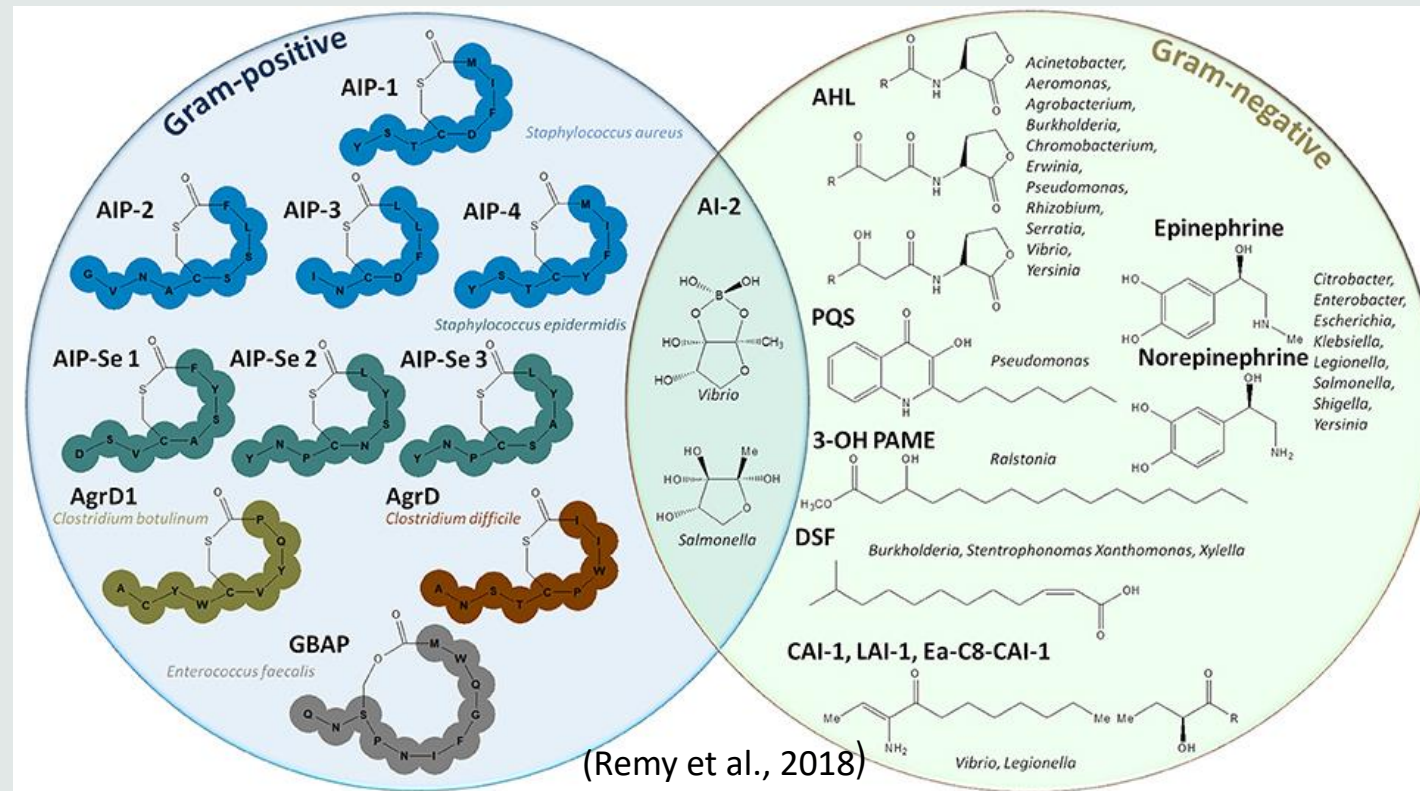
(Prescott and Decho, 2020)

Trends in Microbiology

Autoinducers

Gram-positive

Made of **peptide (AIP)** for actively transported through peptidoglycan cell wall via the ABC transporter system

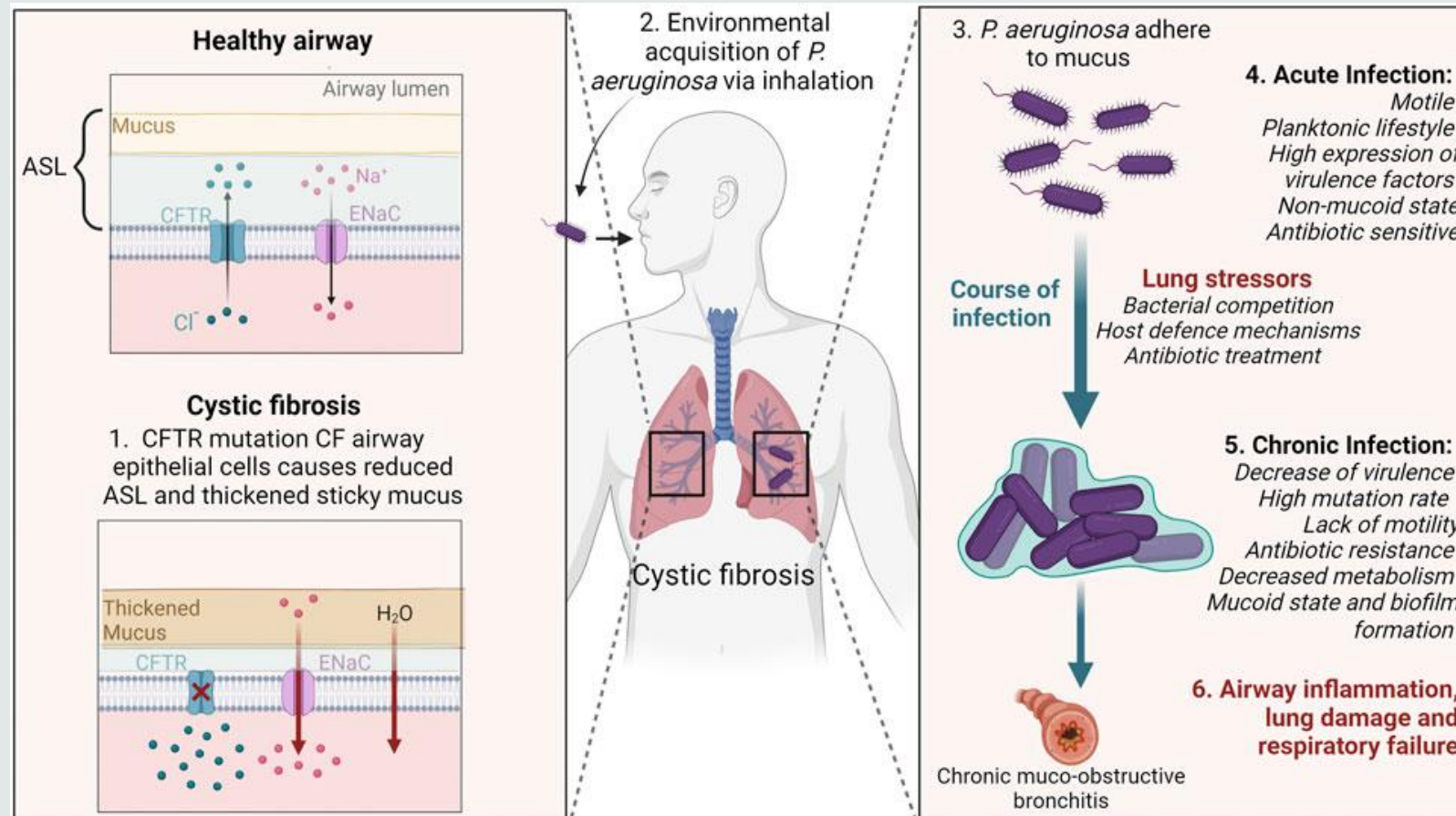


Gram-negative

Consist of acyl-homoserine lactones **(AHLs)** for passive diffusion through the cell wall

Quorum Sensing in infection

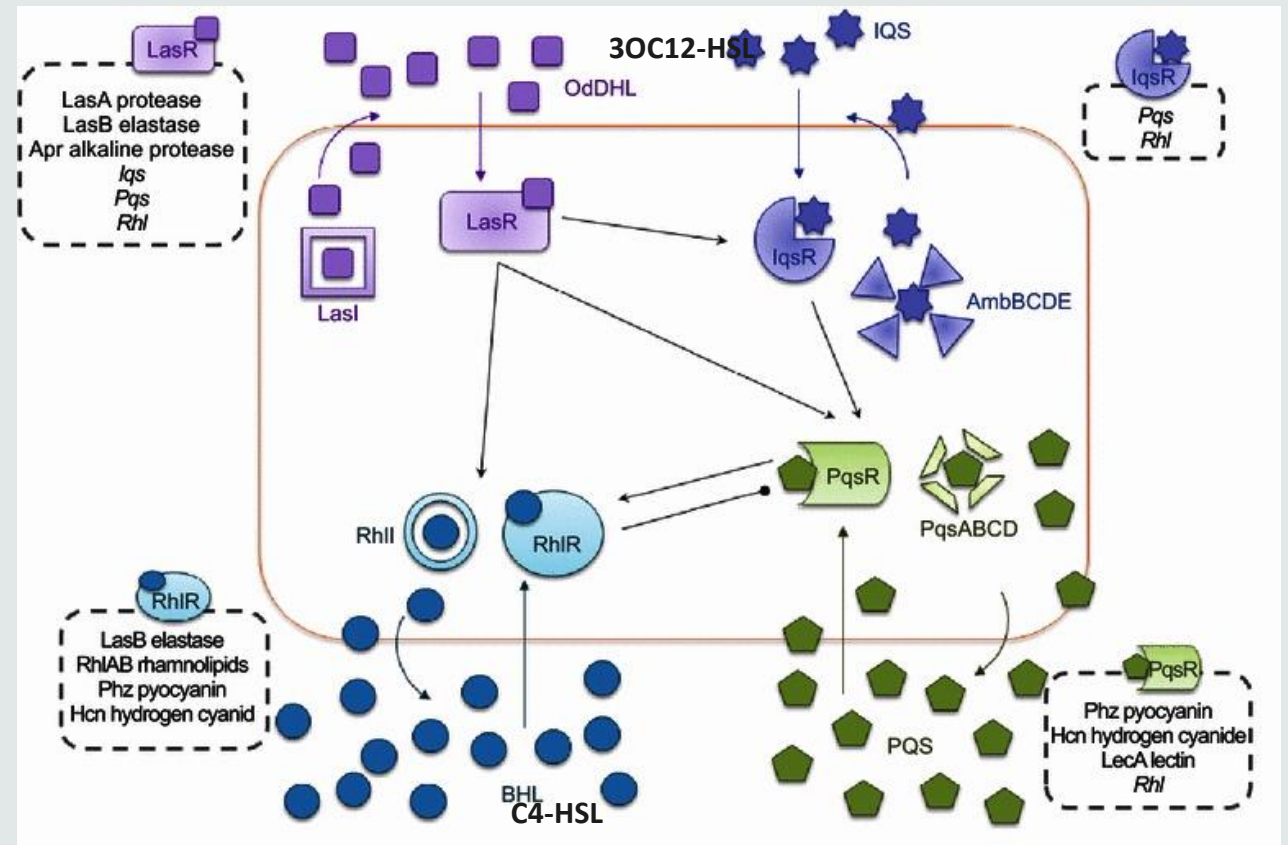
Cystic Fibrosis and *P. aeruginosa*



(Reyne et al., 2023)

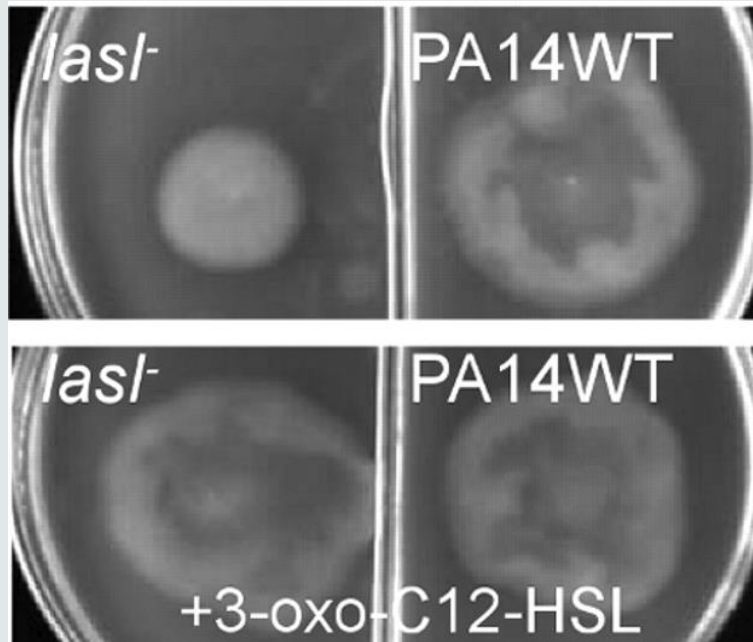
QS Circuitry

- The *las* and *rhl* are interconnected hierarchically
- The *las*- and *rhl*-encoded regulons regulate genes to produce major virulence factors, such as LasB elastase and rhamnolipids, which promote early infiltration of primary human airway epithelia
- **PQS system** relates to the lung tissue damage

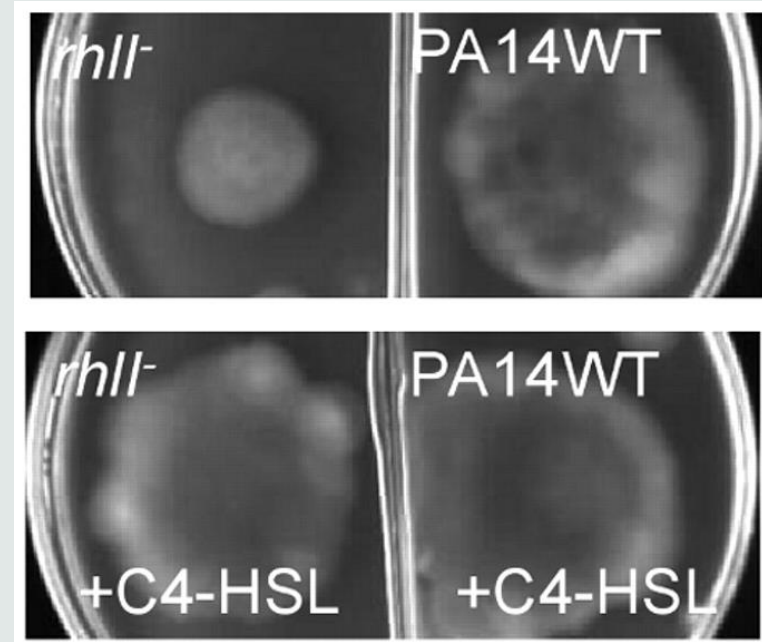


(Lee and Zhang, 2015)

las mutated *P. aeruginosa*



rhII mutated *P. aeruginosa*

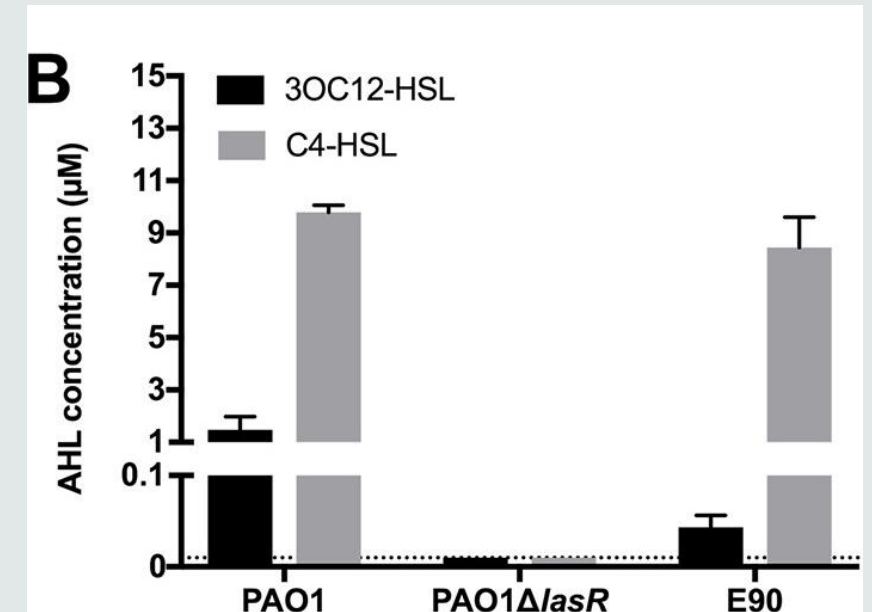
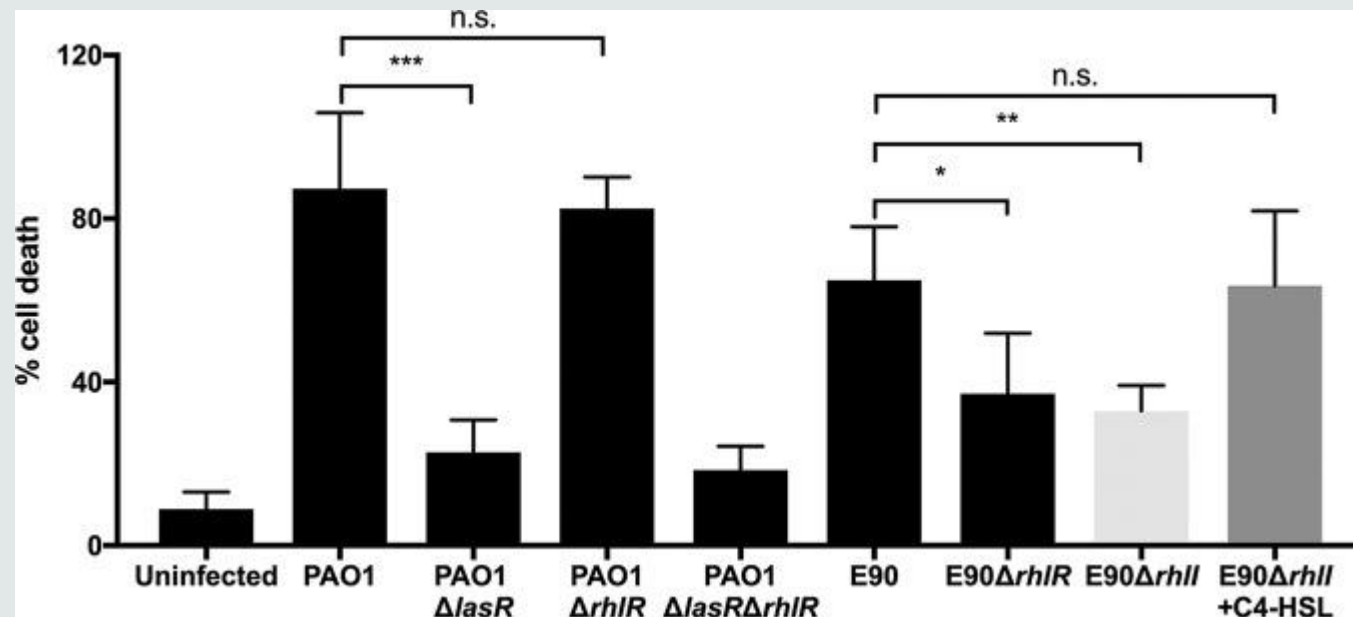


The addition of the AHLs restored the surface motility zones (Yeung et al., 2012)

Social Cheater Hypothesis

- Evolutionary theory predicts that the cost of performing cooperative behavior leaves a population vulnerable to social cheating (Diggle et al., 2007).
- Social cheaters use the resources made by the QS wild-type without contributing to the generation of public goods

- *P. aeruginosa* E90, a LasR-null, RhIR-active chronic infection isolate from cystic fibrosis patients



- RhIR act independently of LasR regulation, remaining active in the QS system
- In E90, RhIR but not LasR is the critical determinant of cytotoxicity

(Cruz et al., 2020)

Quorum Sensing and Antibiotic Resistance

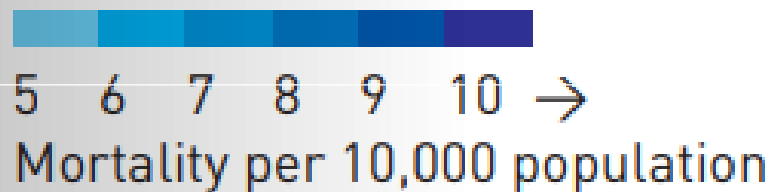
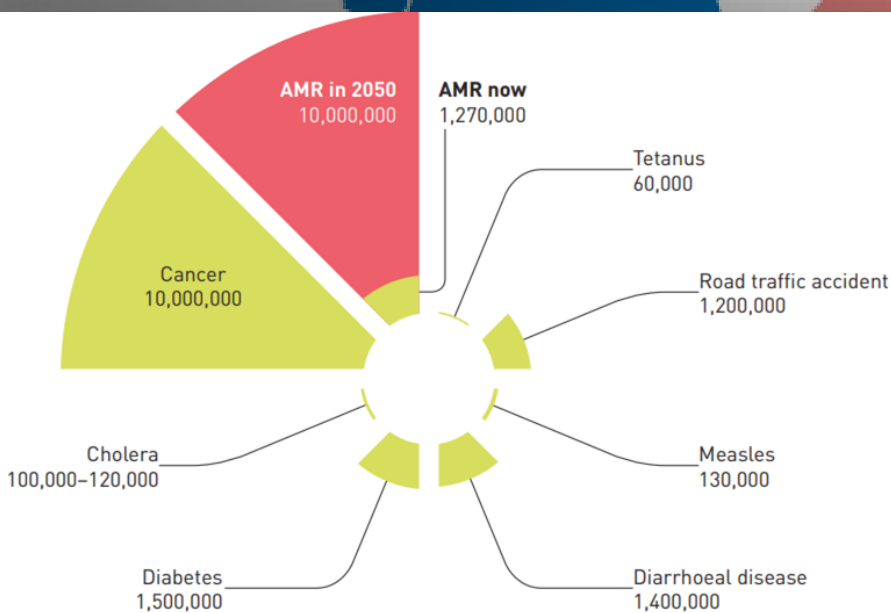
Urgent crisis of AMR

Europe
390,000

Asia
4,730,000

Africa
4,150,000

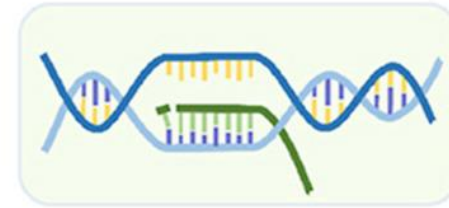
Oceania
22,000



Increase
drug efflux

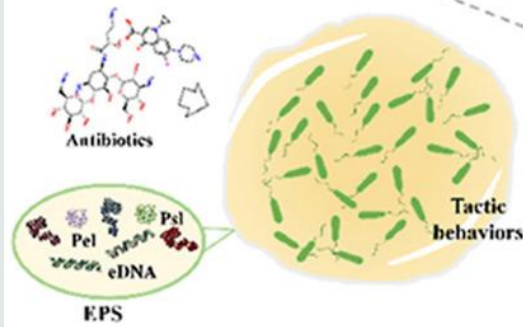


Cell membrane

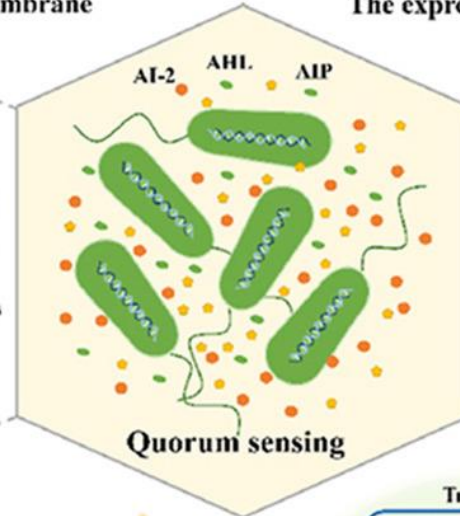


The expression of ARGs

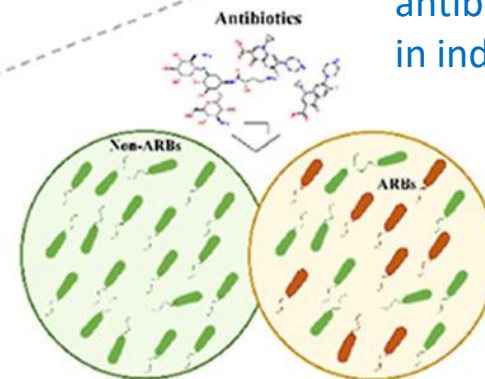
Evolving under
antibiotic treatment
in individual



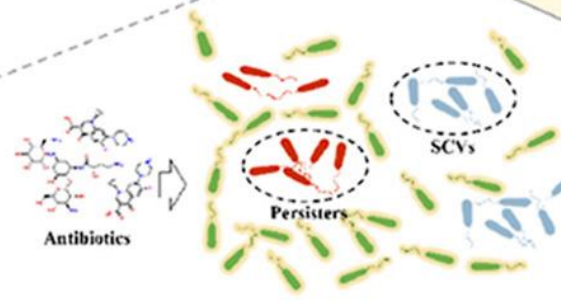
Biofilm formation



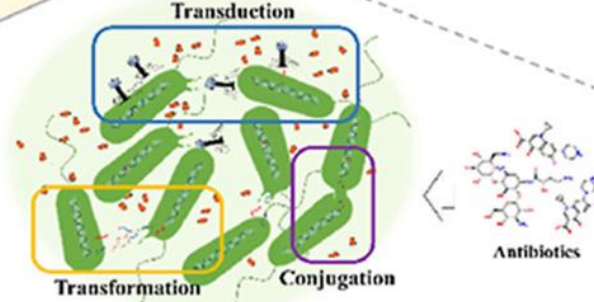
Quorum sensing



The evolution of AMR



Persister formation



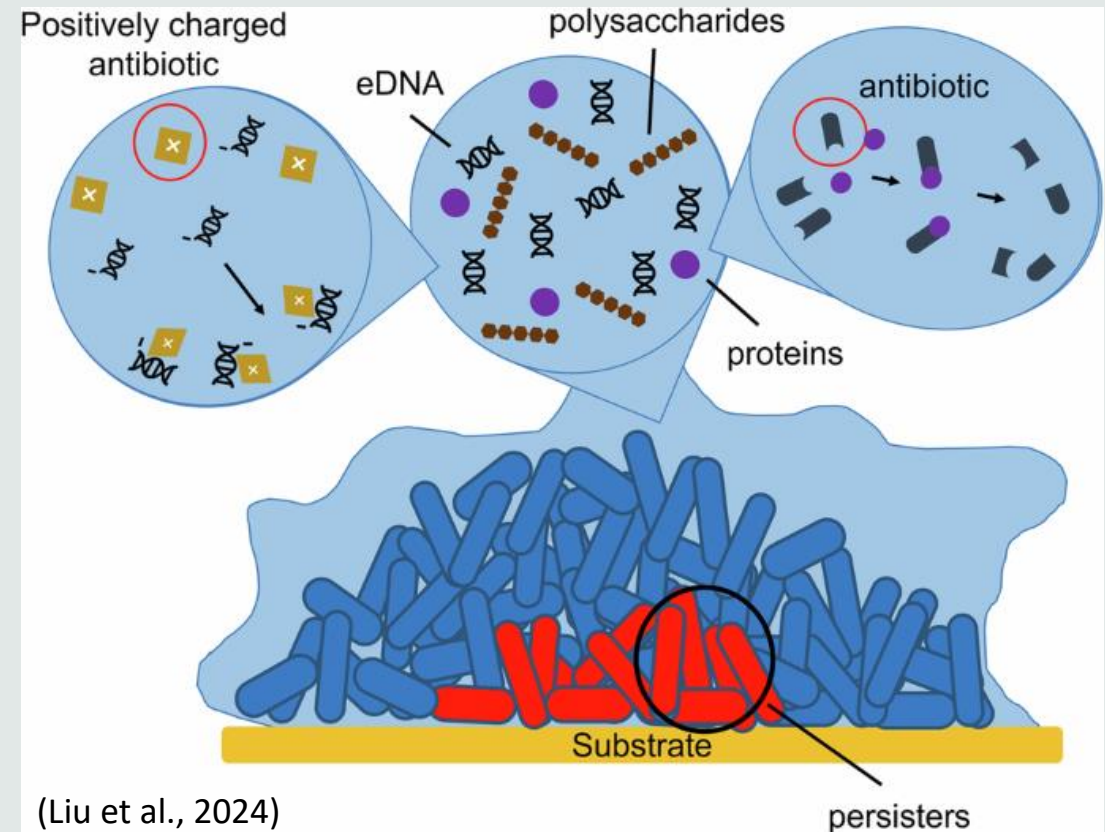
Horizontal gene transfer (HGT)

(Wang et al., 2023)

Biofilm and Persisters

- The extracellular polymeric substance (EPS) promotes mechanical stability, adhesion and cohesive bonding between the bacterial networks

- I. Polysaccharides (alginate, Pel and Psl)
- II. Proteins
- III. Extracellular DNA (eDNA)
- IV. lipids



New antibiotic target?

> J Appl Microbiol. 2016 Apr;120(4):966-74. doi: 10.1111/jam.13073. Epub 2016 Mar 7.

Quercetin is an effective inhibitor of quorum sensing, biofilm formation and virulence factors in *Pseudomonas aeruginosa*

J Ouyang¹, F Sun¹, W Feng¹, Y Sun¹, X Qiu¹, L Xiong¹, Y Liu¹, Y Chen¹
Mol Plant Microbe Interact. 2016 Jun;13(6):637-46. doi: 10.1094/mpm.2016.13.6.637.

Plants secrete substances that mimic bacterial N-acyl homoserine lactone signal activities and affect population density-dependent behaviors in associated bacteria

Article | [Open access](#) | Published: 29 August 2017

A broad range quorum sensing inhibitor working through sRNA inhibition

Tim H. Jakobsen[✉], Anders N. Warming, Rebecca M. Vejborg, Joana A. Moscoso, Marc Stegger, Frederik Lorenzen, Morten Rybtke, Jens B. Andersen, Rico Petersen, Paal Skytt Andersen, Thomas E. Nielsen, Tim Tolker-Nielsen, Alain Filloux, Hanne Ingmer & Michael Givskov

[Scientific Reports](#) **7**, Article number: 9857 (2017) | [Cite this article](#)

Synectic effect?

> J Med Chem. 2022 Jan 13;65(1):688-709. doi: 10.1021/acs.jmedchem.1c01781. Epub 2021 Dec 24.

New *Pqs* Quorum Sensing System Inhibitor as an Antibacterial Synergist against Multidrug-Resistant *Pseudomonas aeruginosa*

Jun Liu¹, Jin-Song Hou¹, Yi-Qun Chang², Li-Jun Peng¹, Xiao-Yi Zhang¹, Zhi-Ying Miao¹, Ping-Hua Sun¹, Jing Lin¹, Wei-Min Chen¹

Affiliations + expand

PMID: 34951310 DOI: [10.1021/acs.jmedchem.1c01781](#)

Research Article | 22 November 2017



Pharmacological Inhibition of the *Pseudomonas aeruginosa* MvfR Quorum-Sensing System Interferes with Biofilm Formation and Potentiates Antibiotic-Mediated Biofilm Disruption

Authors: [Damien Maura](#), [Laurence G. Rahme](#) | [AUTHORS INFO & AFFILIATIONS](#)

<https://doi.org/10.1128/aac.01362-17> • [Check for updates](#)

Summary

- Quorum-sensing is a cell density-dependent behaviour, that collectively works to enhance survival and Pathogenicity
- *V. fischeri* utilises QS to behave symbiotically with the Hawaiian bobtail squid
- *P. aeruginosa* exhibits various virulence factors regulated via QS, which induces a higher mortality rate and chronic infection in CF patients
- Quorum sensing (QS) plays a significant role in the development and expression of antibiotic resistance in bacteria

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**Thank you for
your listening**

