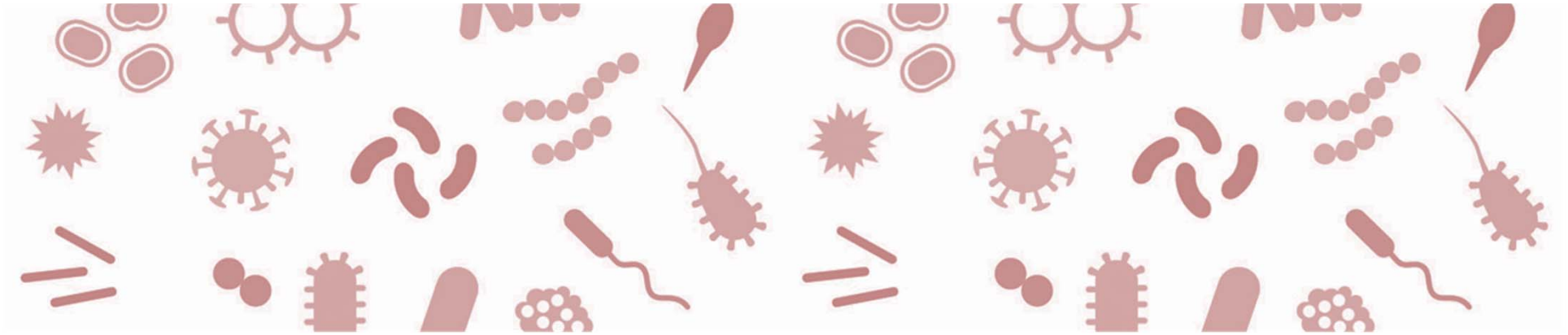

Quorum Sensing in the Gut Microbiome and its Applications

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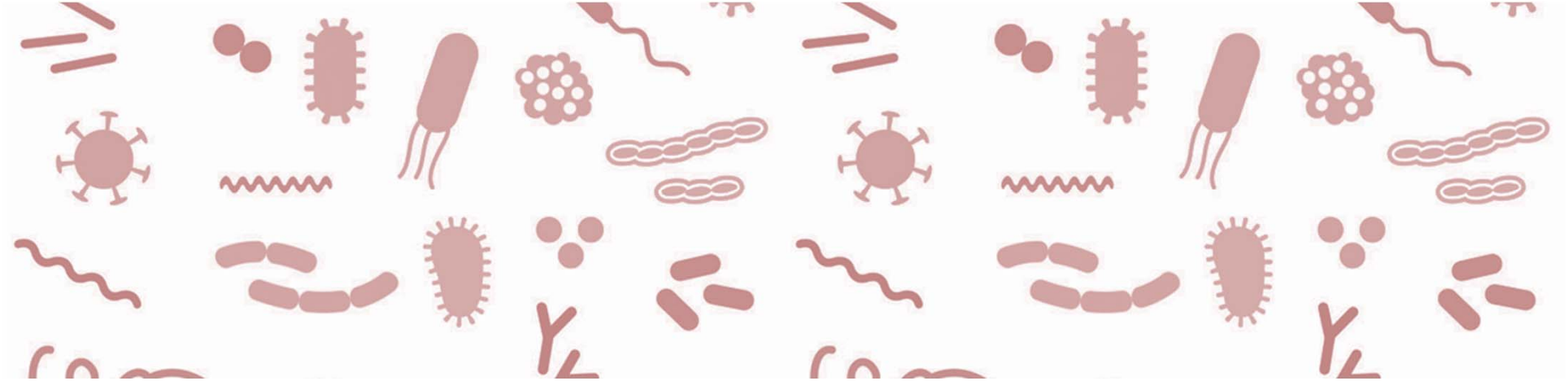
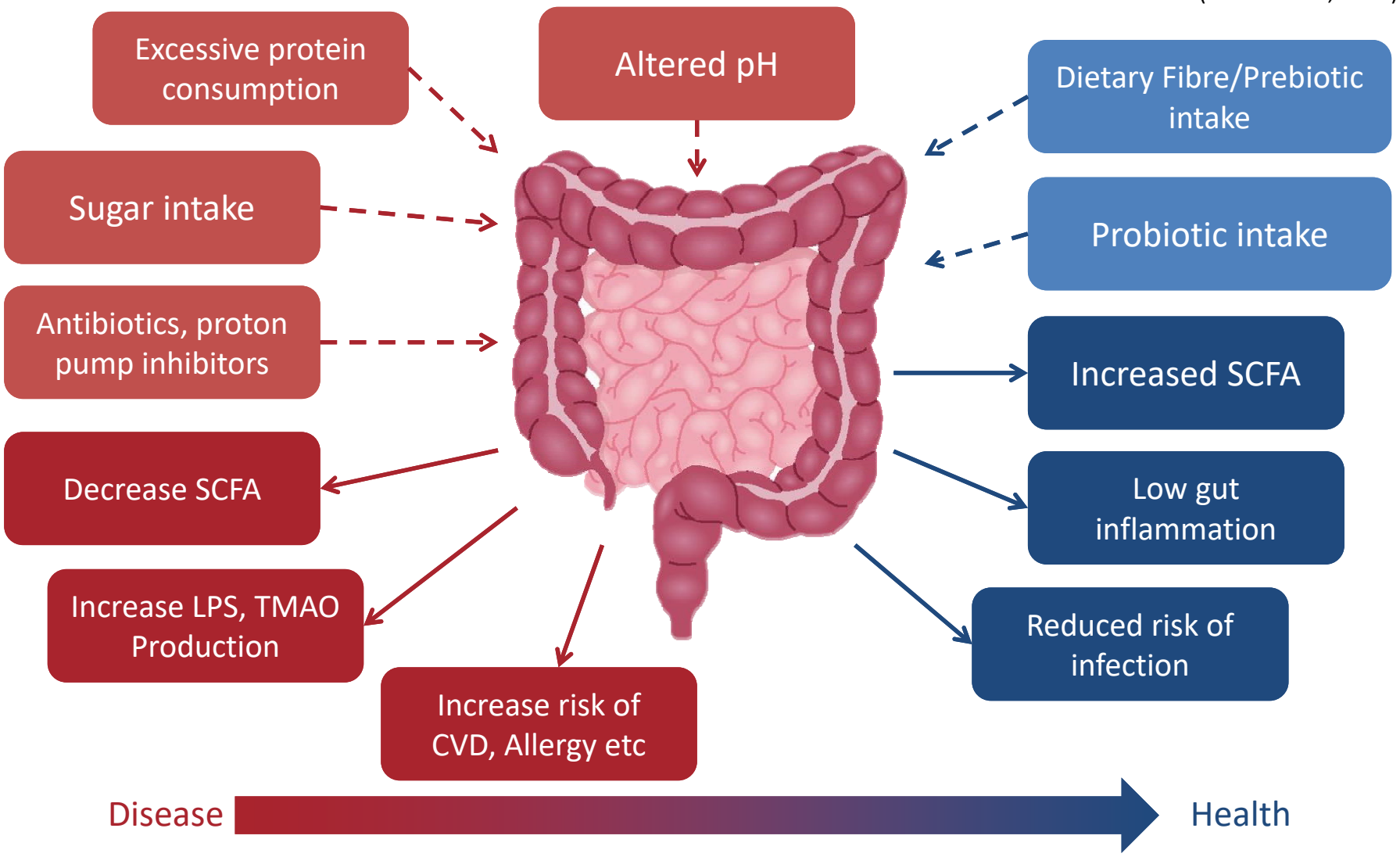


Overview

- Gut Microbiome
- Quorum Sensing and Quorum Quenching
- Application of QS
- Benefits and potential application
- Conclusion

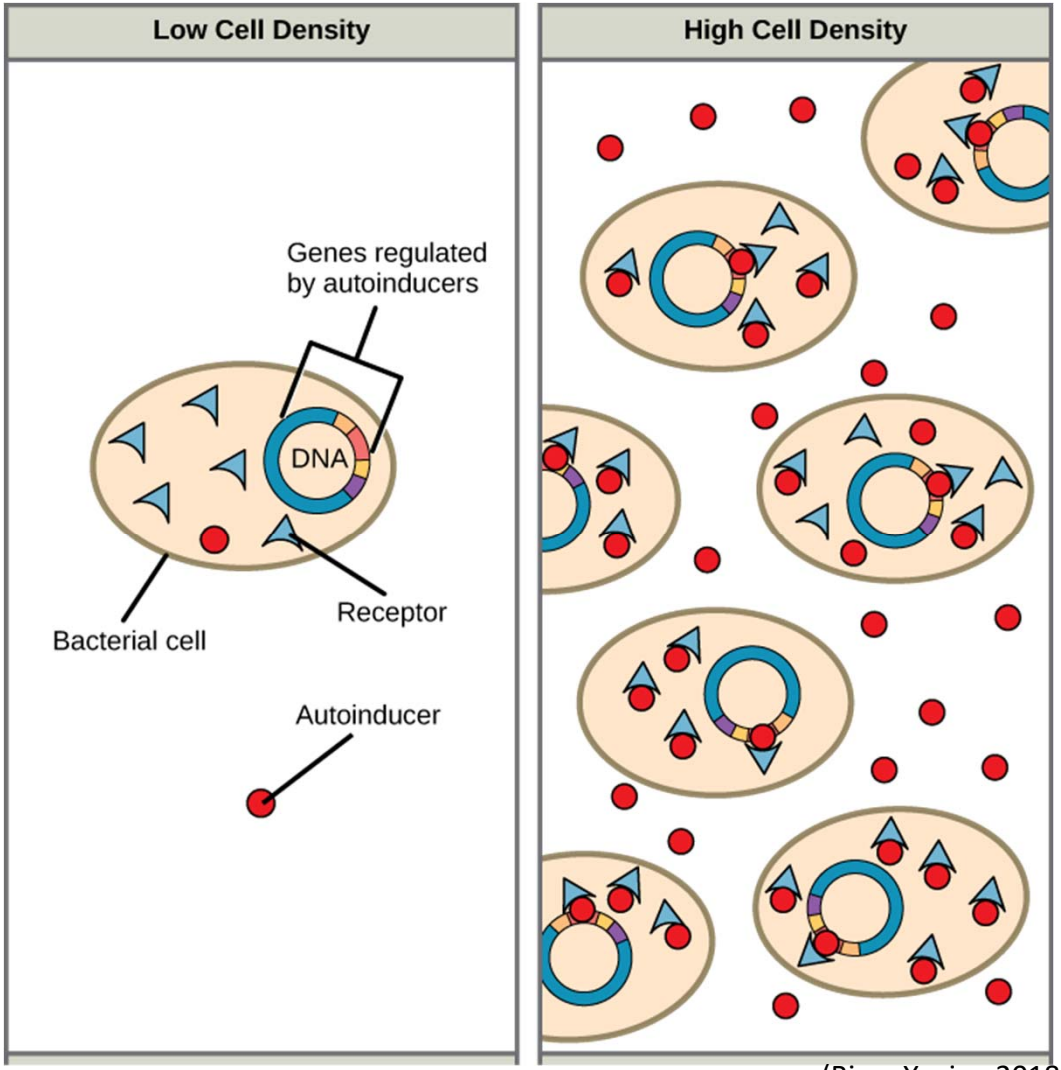
Gut Microbiome

(Valdes et al., 2018)



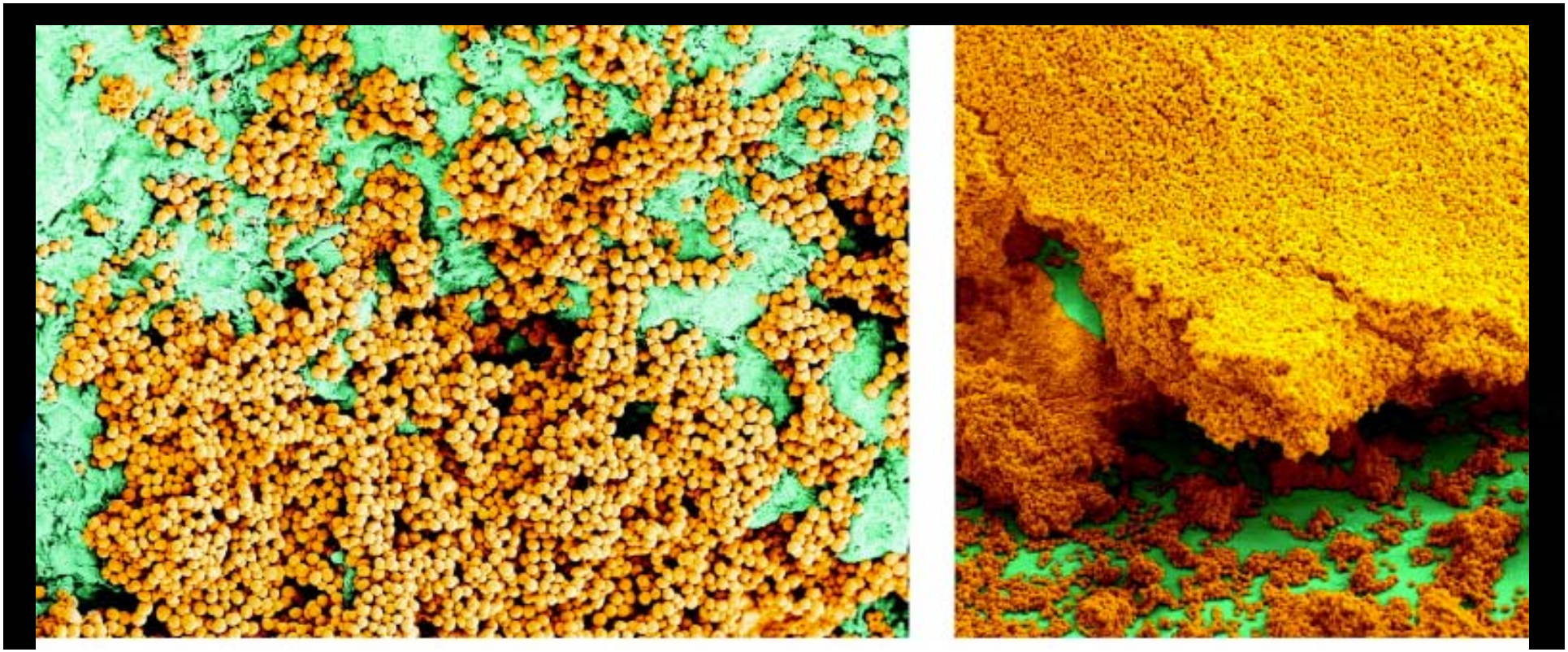
Quorum Sensing

1. production of small signaling molecules
2. release of the signal molecules (active/passive)
3. Recognition of the signal molecules at threshold
4. Change in gene regulation



(Bivar Xavier, 2018)

Quorum Sensing in gram –ve and +ve

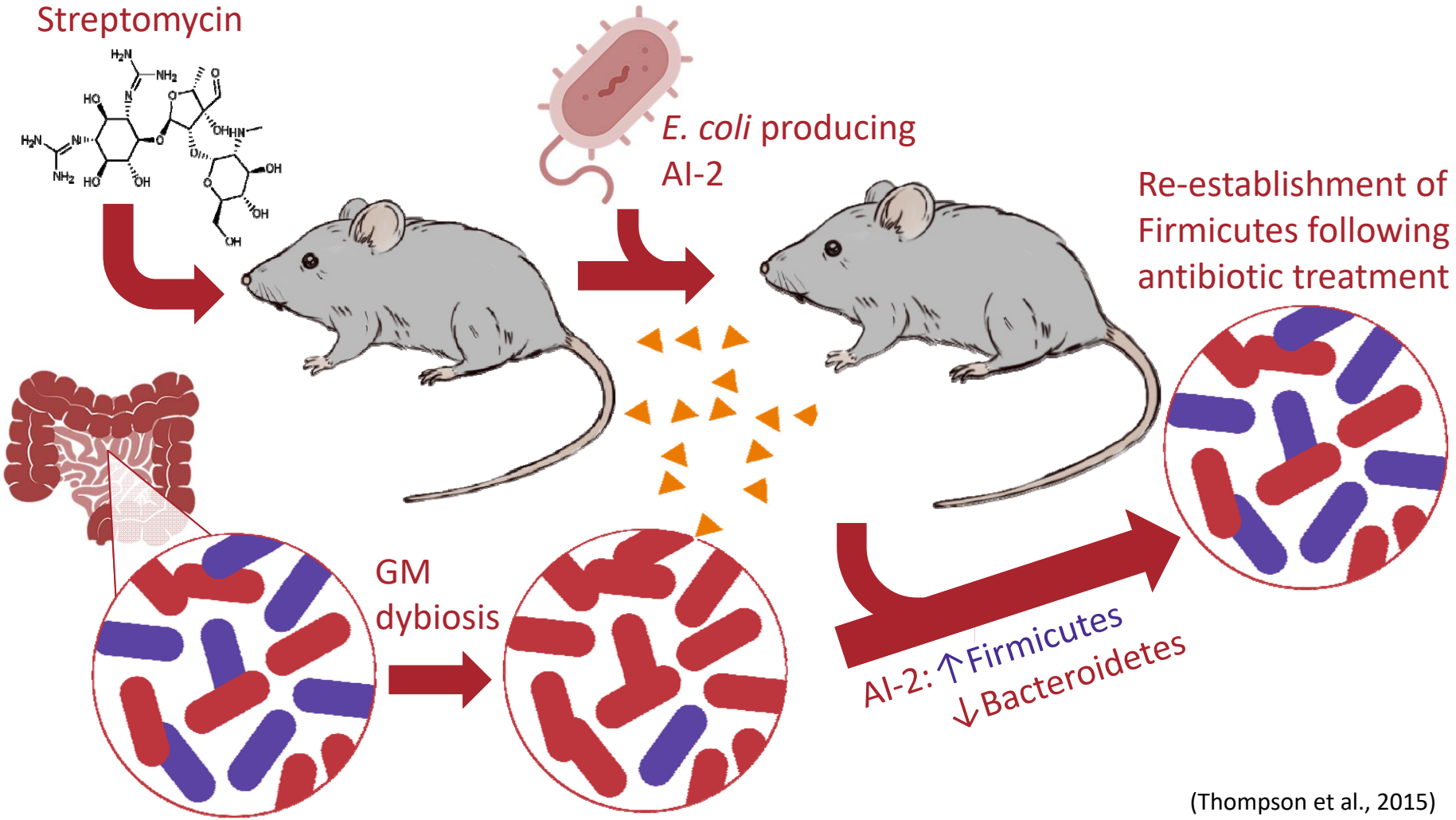


(Boles and Horswill, 2011; “Glowing Bacteria Control Squid Hosts – National Geographic Blog,” n.d.; Hsiao et al., 2008)

Shaping the Gut Microbiome using QS

Challenges faced by GM	Resolution by QS
Antibiotic treatment Wide spectrum antibiotics will kill members of GM	• Extracellular polymers in bioflms dilutes Antb • Competence • Conjugation
Host immune system Modulates members of GM	• Evasion of host IS via biolfim formation, sporulation, alternative gene expression
Gut Motility Remaining in the gut during peristalsis, food passing down the gut	• Biofilm formation

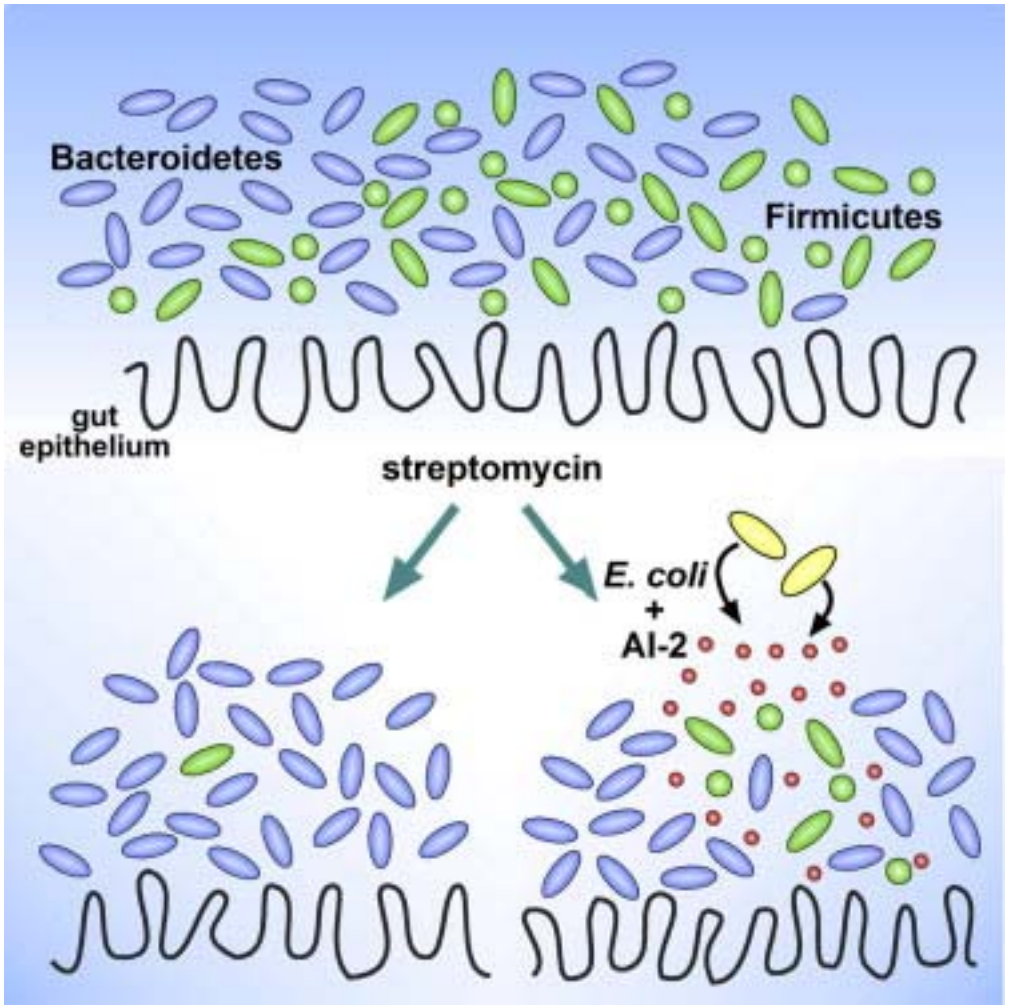
E. coli AI-2 influencing species composition following antibiotic treatment



(Thompson et al., 2015)

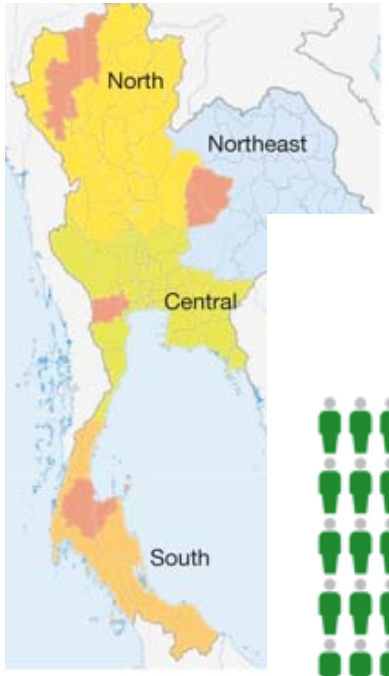
E. coli AI-2 influencing species composition following antibiotic treatment

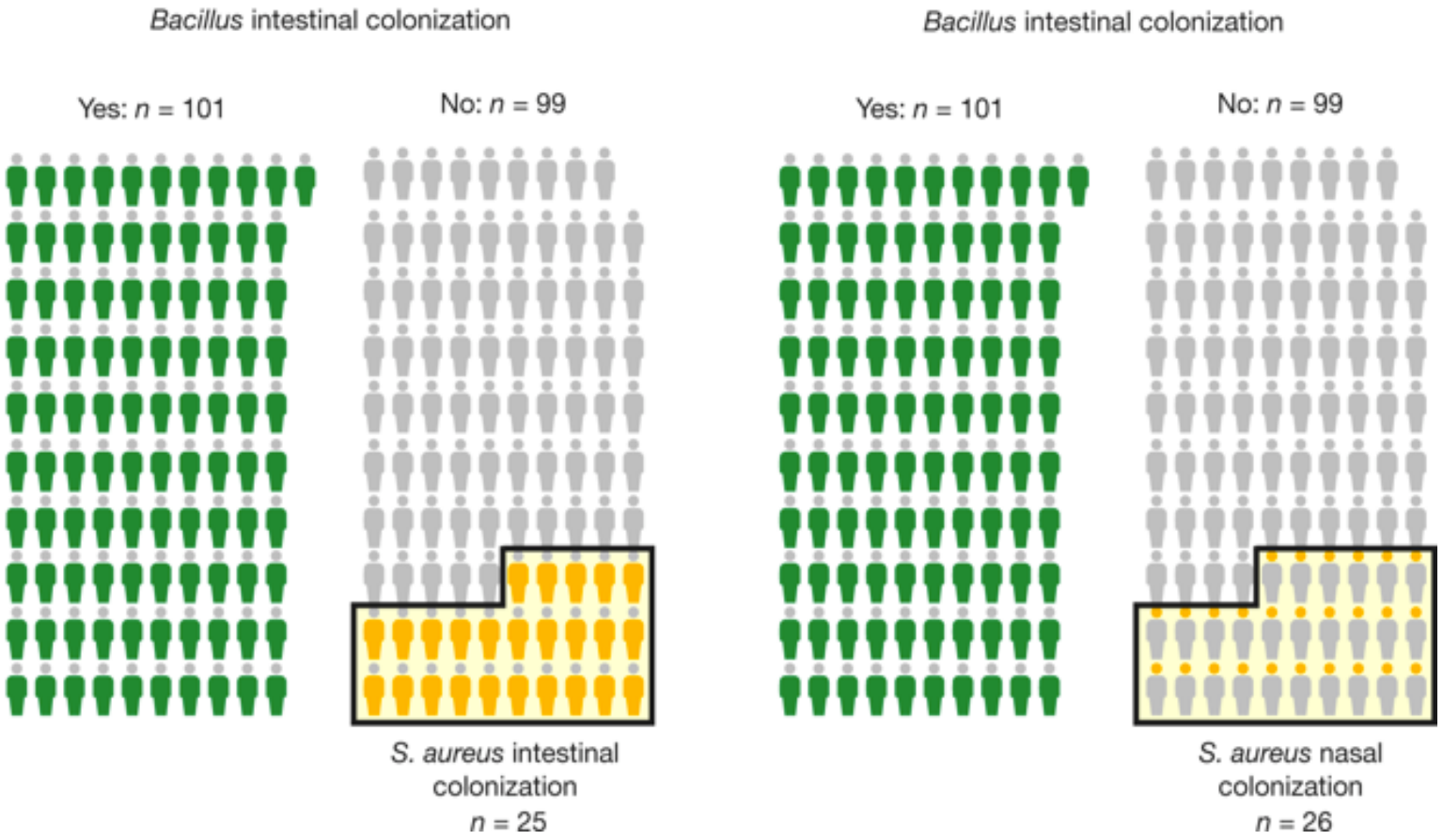
- AI-2 can shape the microbiota composition
  - Engineer bacteria to express QS molecules/peptides
- QS can reconstitute GM following dybiosis
- Applicable in real GM?



(Thompson et al., 2015)

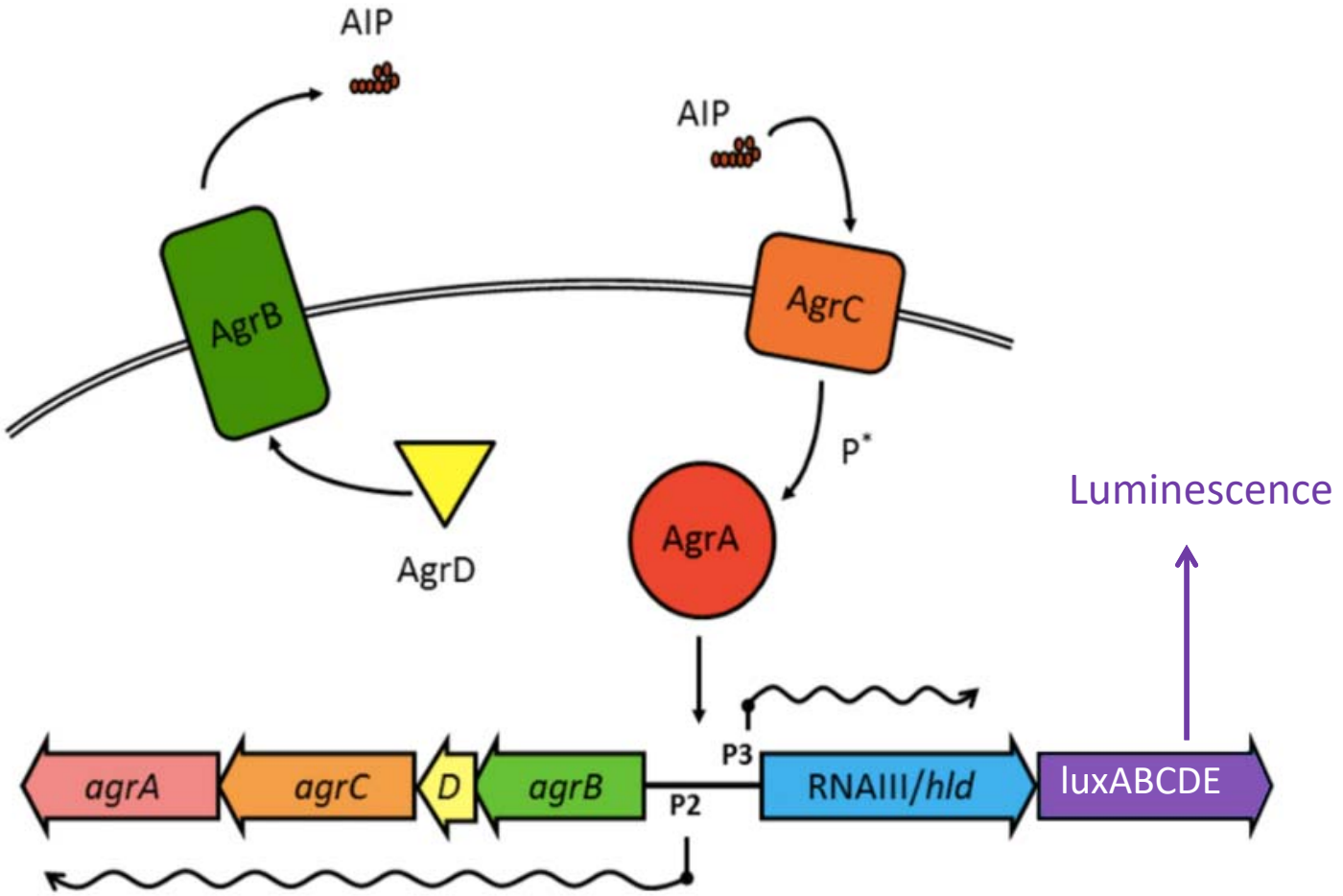
Probiotic *Bacillus* vs *Staphylcoccus aureus*





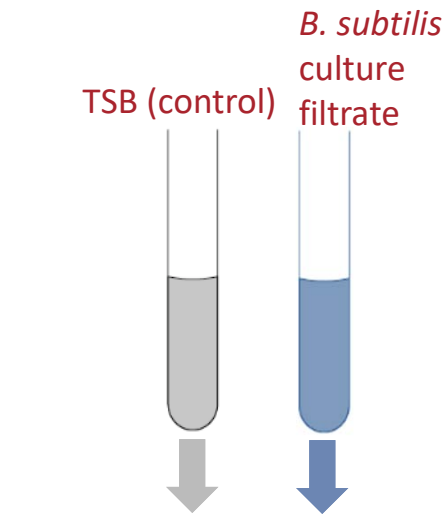
(Piewngam et al., 2018)

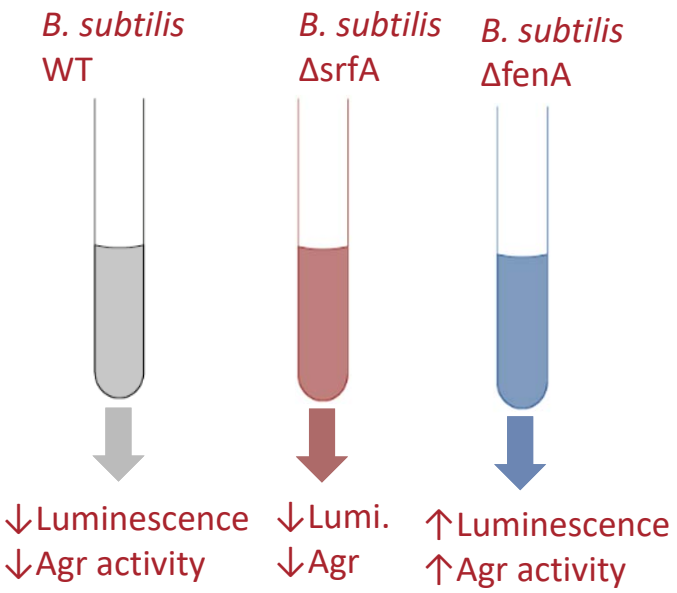
Inhibition of *Staphylcoccus aureus* QS

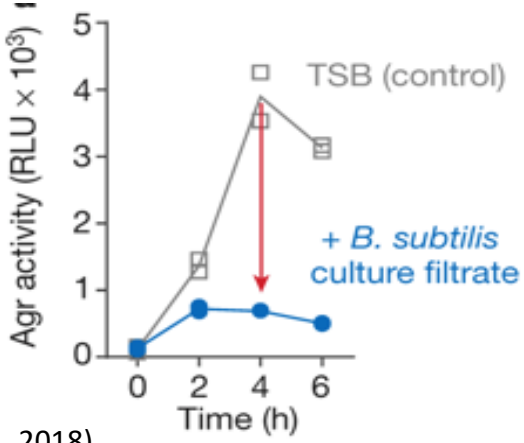


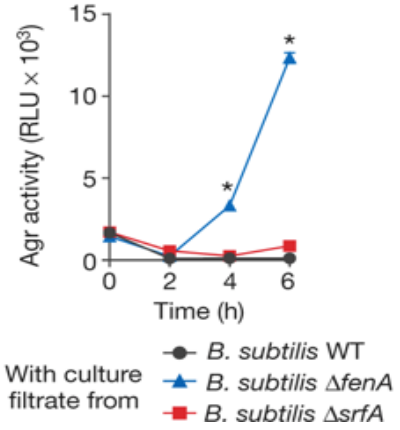
(Baldry, 2016)

Inhibition of *Staphylcoccus aureus* QS









(Piewngam et al., 2018)

Probiotic *Bacillus* vs *Staphylcoccus aureus*

Oral gavage
2 x 10^7 S. aureus

Fecal collection

Euthanasia
Intestine Collection

Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7

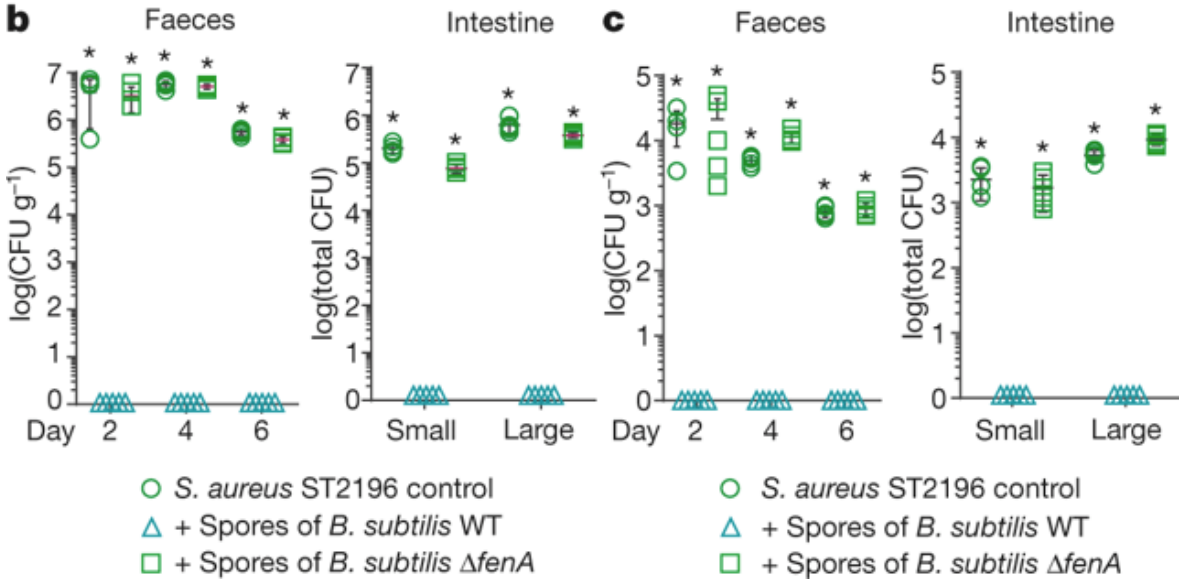
Oral gavage
B. Subtilis spores

Oral gavage
B. Subtilis spores

Oral gavage
B. Subtilis spores

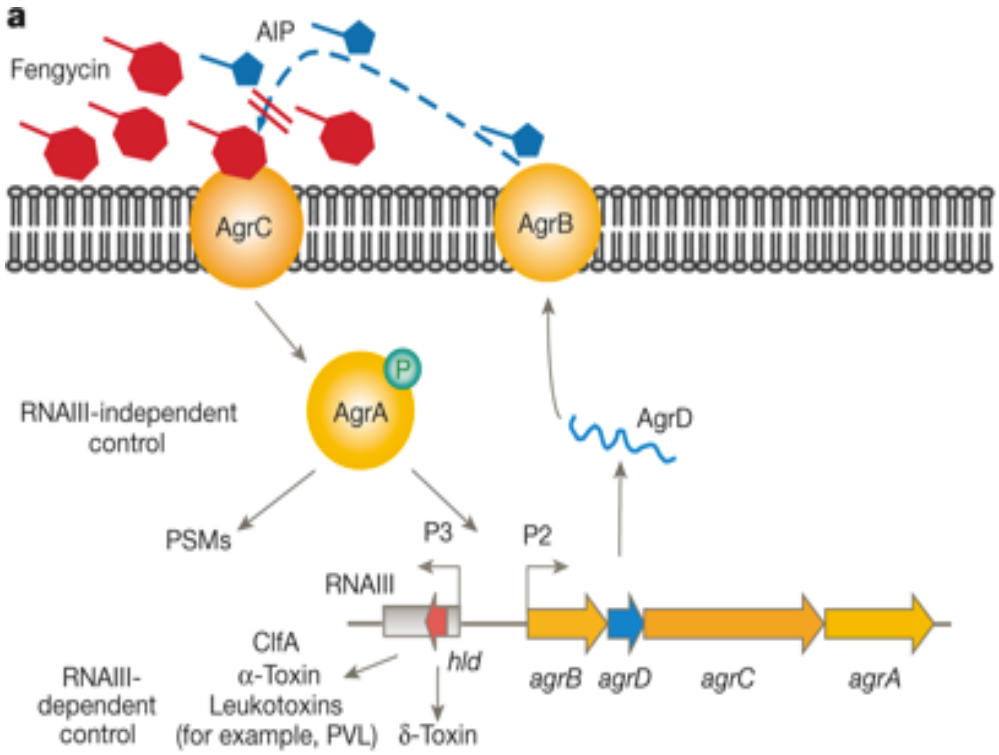
7 day antibiotic pretreatment

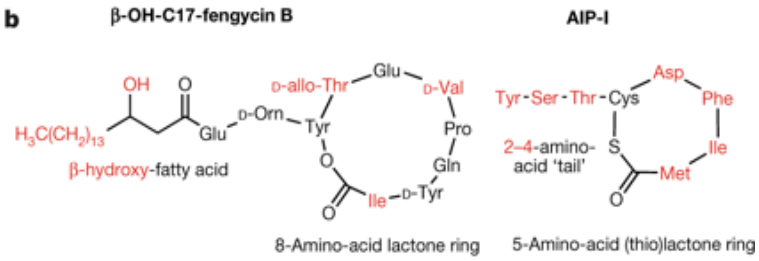
+1 day without antbiotics



(Piewngam et al., 2018)

Competitive Inhibition of *Staphylcoccus aureus* QS via *Bacillus* fengycin

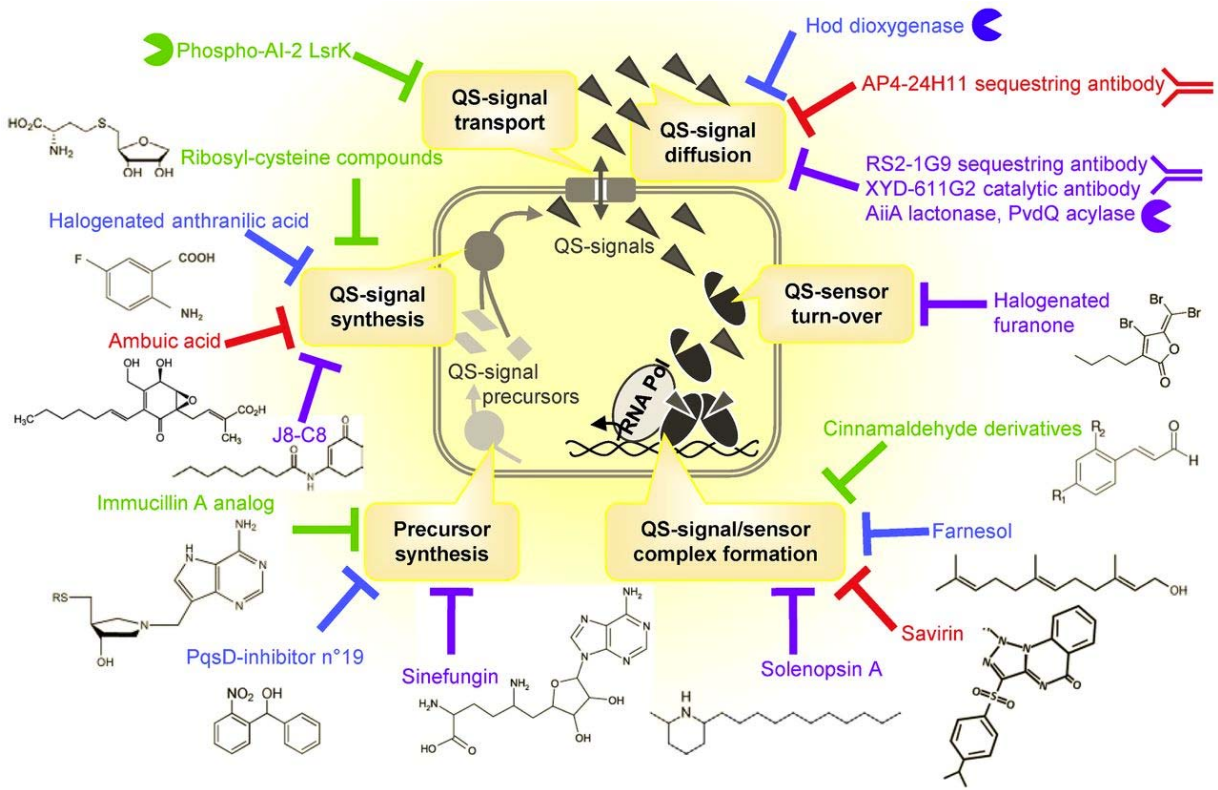




(Piewngam et al., 2018)

Benefits of using Quorum Sensing

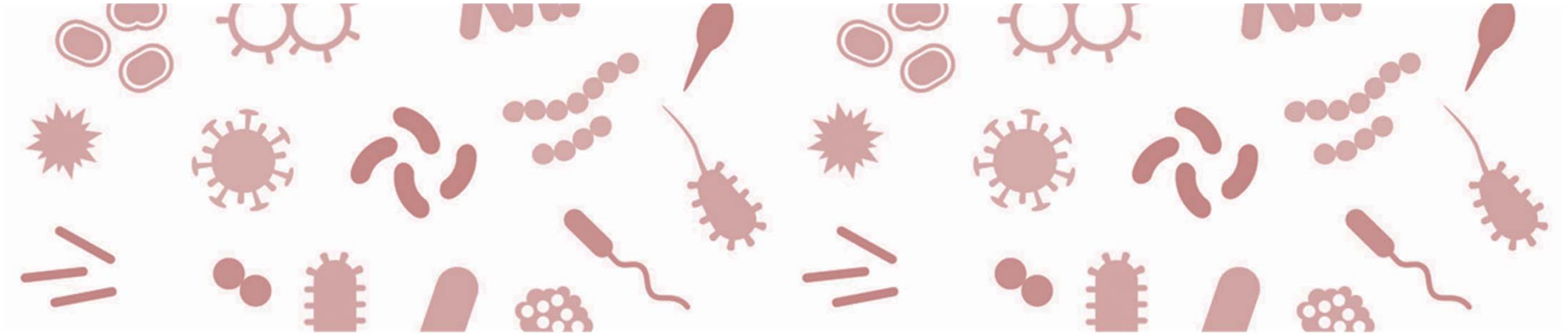
- Low selective pressure = Low resistance
- Many targets
- Combined therapy



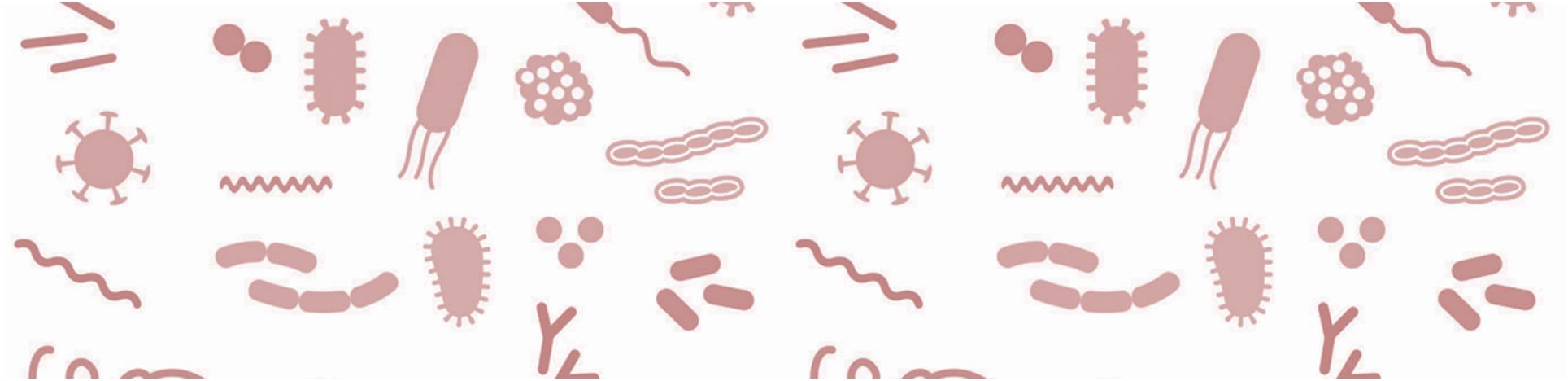
(Grandclément et al., 2016)

Conclusion

- New, rapidly growing research area
- Applicable in the lab and real life
- Many potential applications and uses

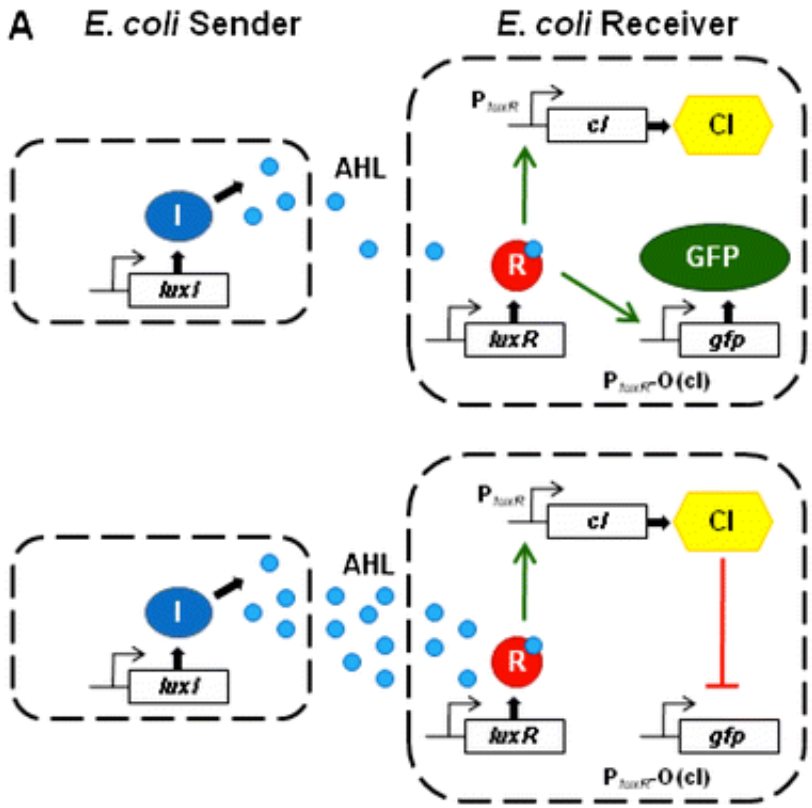


Thank you for listening.
Any questions?



Extra information

- Other potential applications of QS and QQ?
  - Aquaculture
  - Agriculture
  - Anti-biofouling
  - Biosensors
  - Tissue engineering
  - Biomaterials
  - Dentistry
  - etc



Extra information

- 1:1 ratio of human:microbial cells?
  - "Revised Estimates for the Number of Human and Bacteria Cells in the Body" Sender et al., 2016

population segment	body weight [kg]	age [y]	blood volume [L]	RBC count [10^{12}/L]	colon content [g]	bac. conc. [10^{11}/ g wet] (1)	total human cells [10^{12}] (2)	total bacteria [10^{12}]	B:H
ref. man	70	20–30	4.9	5.0	420	0.92	30	38	**1.3**
ref. woman	63		3.9	4.5	480	0.92	21	44	**2.2**
young infant	4.4	4 weeks	0.4	3.8	48	0.92	1.9	4.4	**2.3**
infant	9.6	1	0.8	4.5	80	0.92	4	7	**1.7**
elder	70	66	3.8 (3)	4.8	420	0.92	22	38	**1.8**
obese	140		6.7	5.0(4)	610(5)	0.92	40	56	**1.4**

(1) No significant change in bacteria concentrations in relation to high variation for the reference man [40,43].

(2) Assuming RBCs account for 84% of the total host cells as observed for the reference man.

(3) Decrease of 24% in the blood volume, according to [44].

(4) No significant change in the hematocrit in obesity [45].

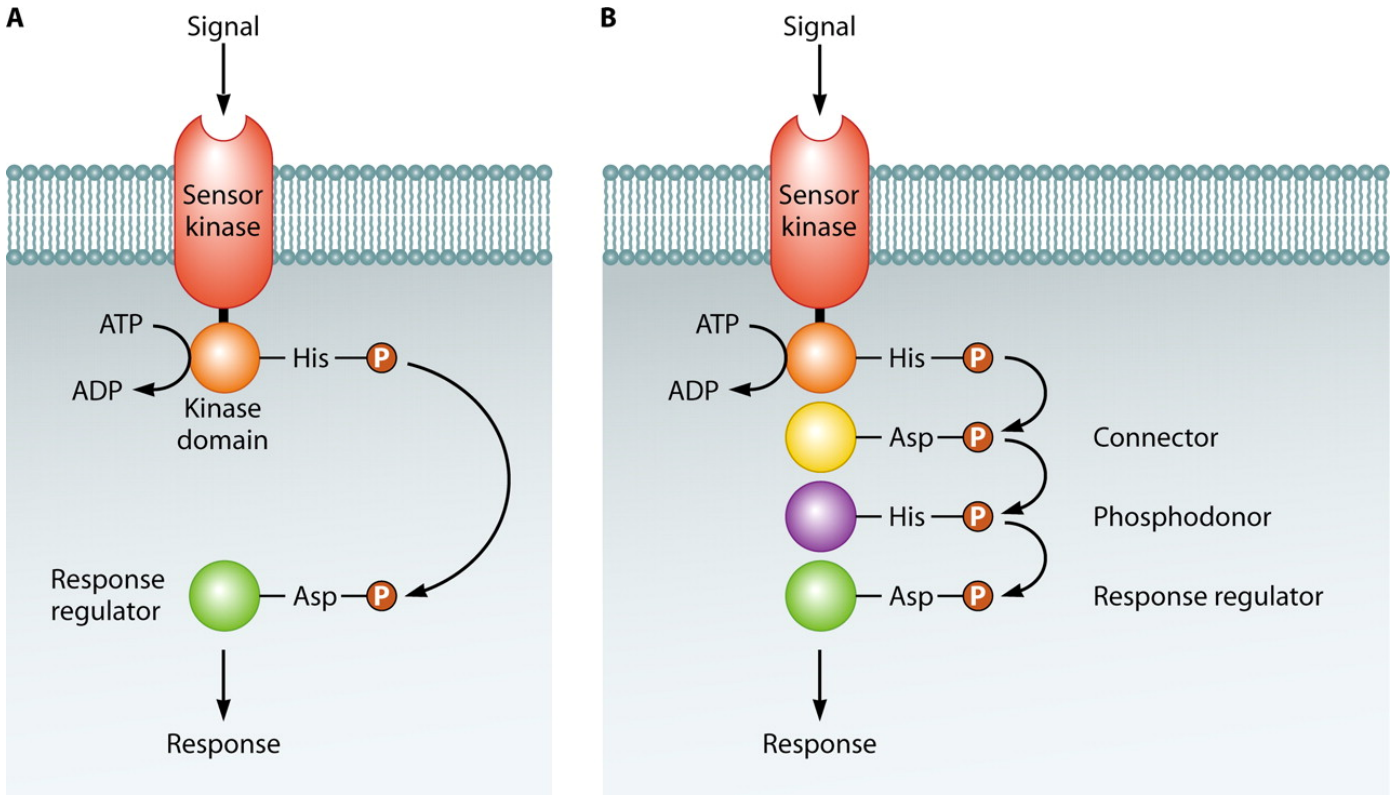
(5) We could not find any direct measurements of the colonic volume for obese individuals in the literature, yet from an indirect analysis the volume increases with weight and plateaus at about 600 mL [46].

doi:10.1371/journal.pbio.1002533.t003

(Sender et al., 2016)

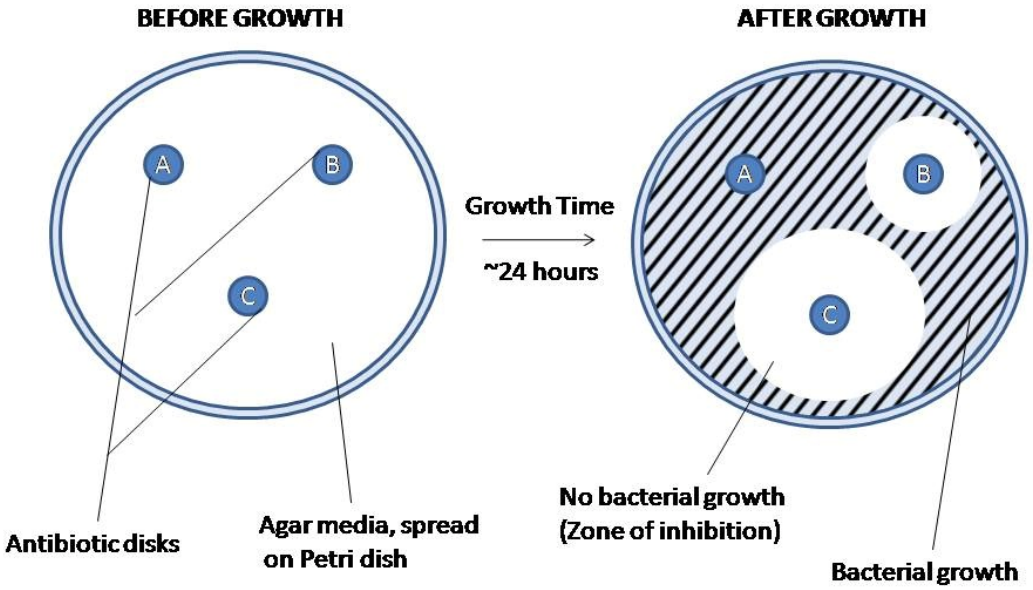
Extra information

- What is a two component system?
  - membrane-bound histidine kinase, and;
  - a response regulator (changes gene expression)



Extra information

- How did they rule out bacteriocin effect of Bacillus?
  - Growth inhibition agar method
  - 6 times concentration
  - 6 out of 105 inhibited growth (v minimal effect)



Extra infomation

- How do biofilms induce antibiotic resistance?
  - 10 to 1000 times increase in antibiotic resistance
  - Spread of antibiotic resistance and virulence genes