THE SHORT ANSWER

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Chemical Genetics Reveals Environment-Specific Roles for Quorum Sensing Circuits in Pseudomonas aeruginosa

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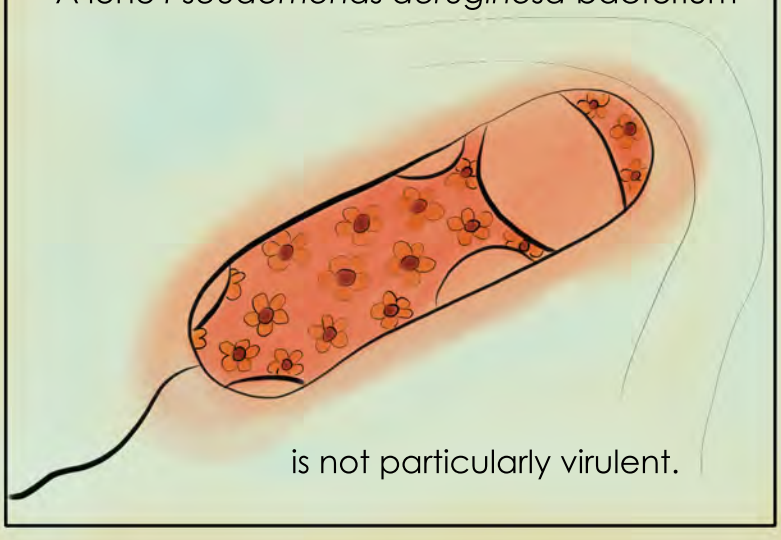
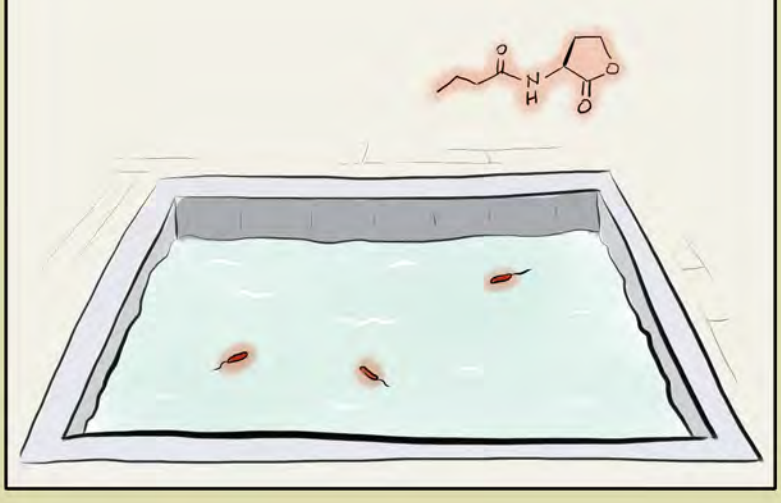
A lone *Pseudomonas aeruginosa* bacterium

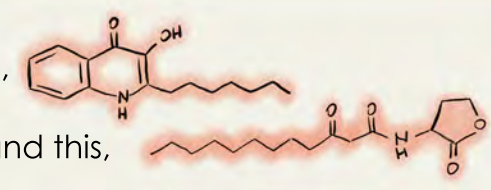


is not particularly virulent.

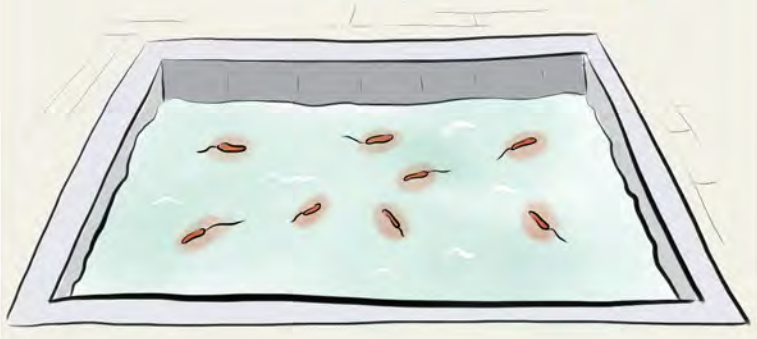
But it sends out signals, like this,



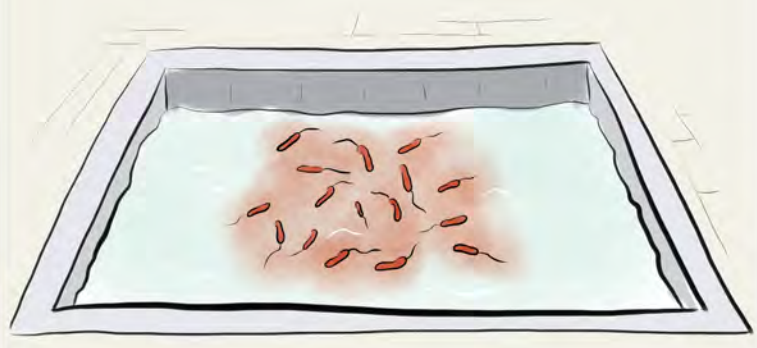
and this,



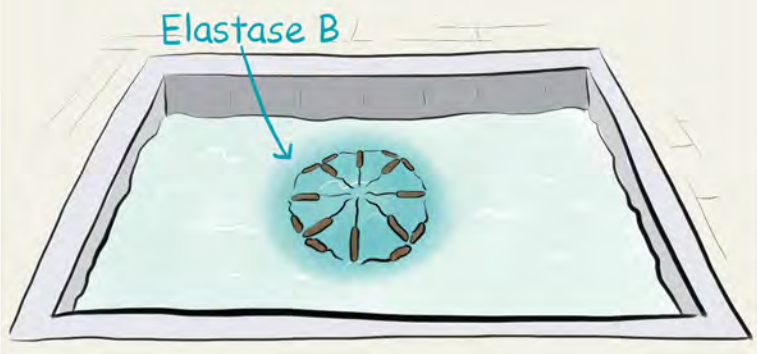
and this,



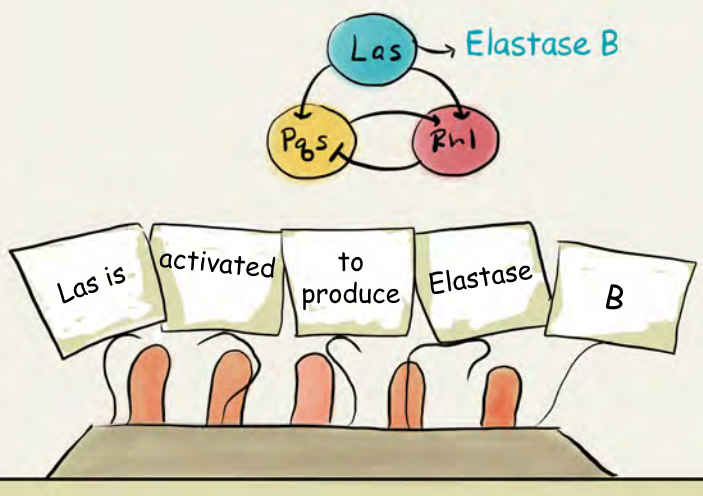
And when enough bacteria gather together with their signals, the compounds reach a threshold concentration,



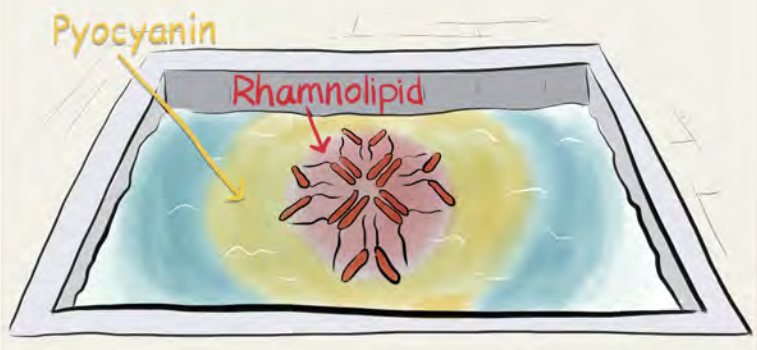
and the bacteria begin to work together, not unlike synchronized swimmers, in ways that are advantageous to the group. For instance, they produce virulence factors



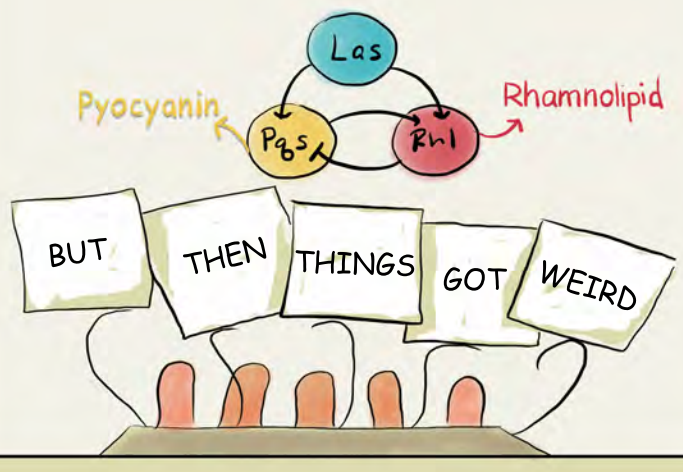
through activation of quorum sensing circuits



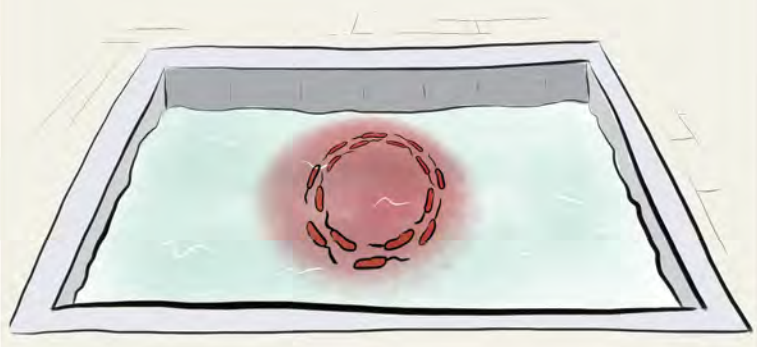
that until recently were thought to act in a stricty hierarchical manner, with Las activating the Rhl and Pqs circuits to produce more virulence factors,



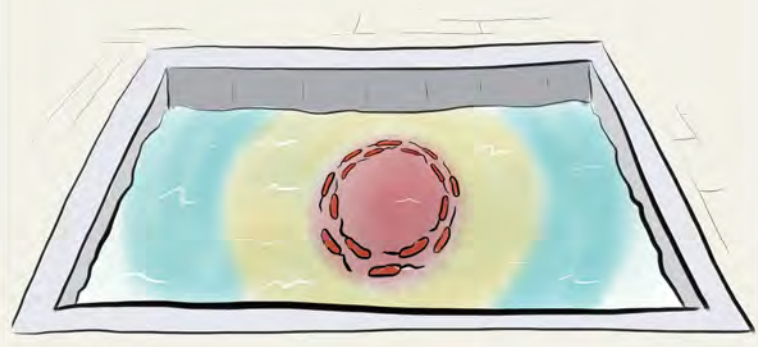
and with Pqs and Rhl activating and inhibiting each other, respectively.



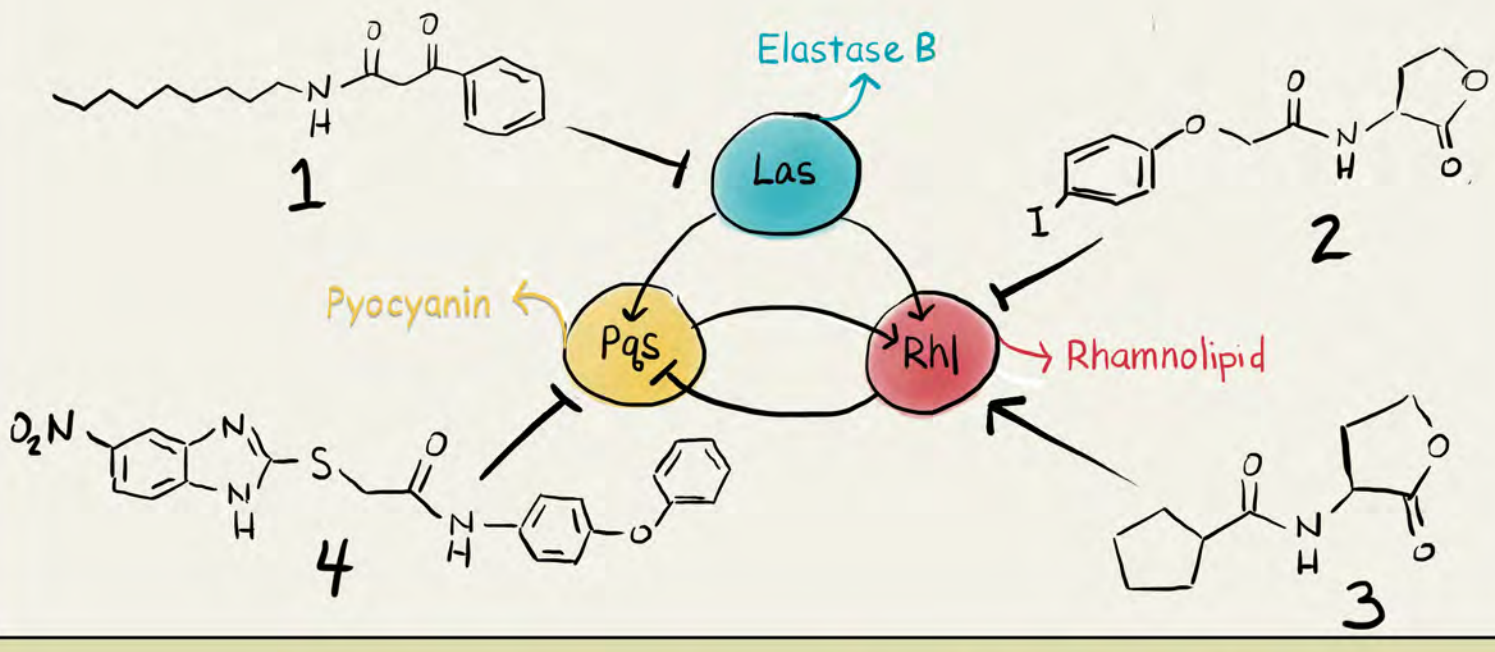
Turns out, if you inhibit the Las circuit, you see a loss of Elastase B and pyocyanin, which makes sense.

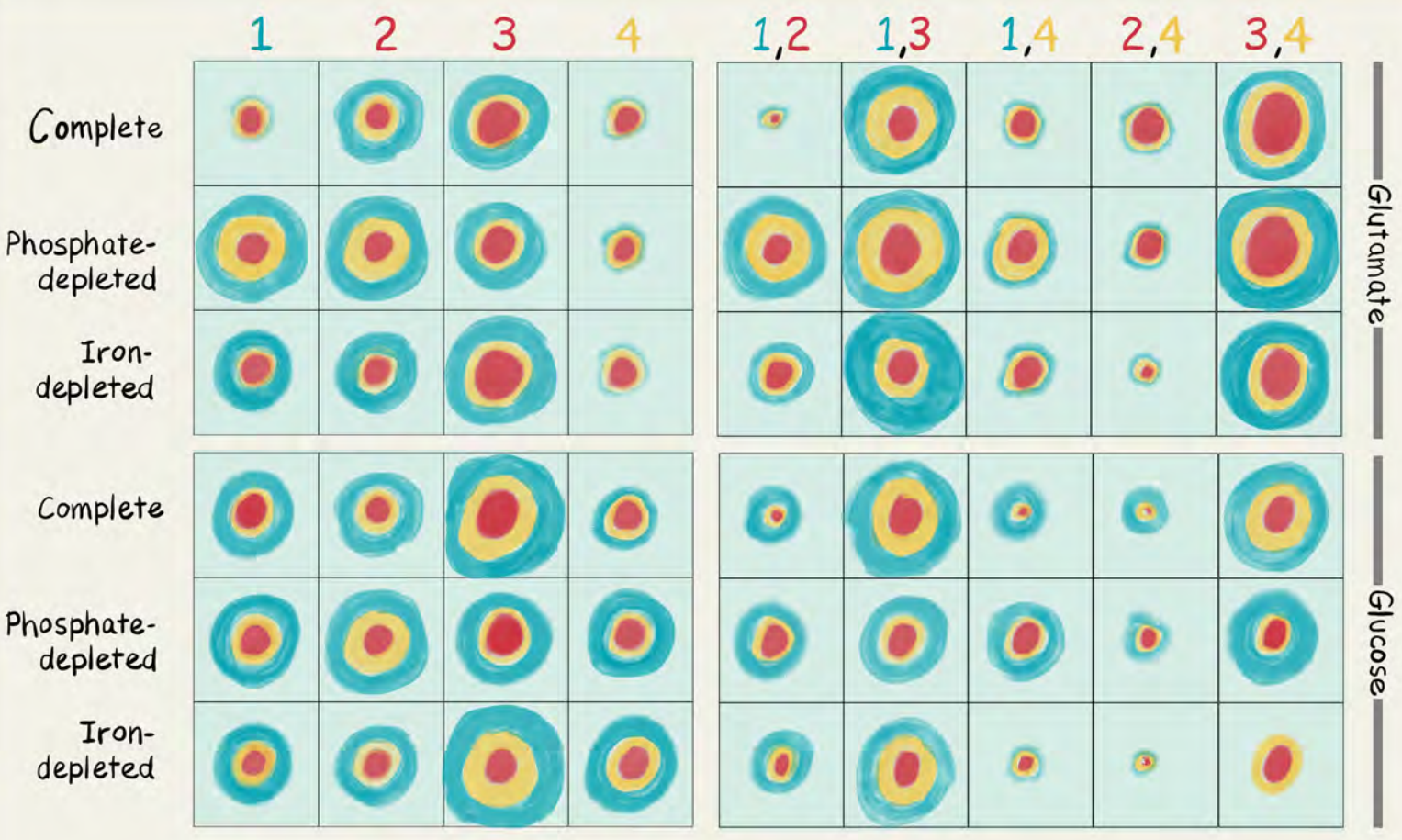


But if you try it again in low-phosphate medium, you see all three virulence factors.



This was a game changer because it showed that the environment can play a huge role in how *Pseudomonas aeruginosa* responds to potential anti-bacterial drugs that target quorom sensing circuits. And these are important targets because they are less likely to lead to resistance than anti-bacterials that kill the cells. So, Welsh and Blackwell used compounds they developed in the lab to tease out the relative contributions of the three interconnected quorum sensing circuits under a range of conditions.





A fairly loose but relatively true representation of the data showing the results of treatment of *Pseudomonas aeruginosa* with the compounds shown above on the production of the virulence factors rhamnolipid (red), pyocyanin (yellow), and Elastase B (blue).

For all of the promise of targeting Las (the protein LasR specifically), it seems that the Pqs circuit may be a better target overall, and combining Pqs and Rhl inhibitors seems to achieve the greatest anti-virulence effect in the broadest range of conditions. This work provides a treasure trove of information that may actually raise as many questions as it answers, which is great. Every time I look at it I see something new that is interesting. Makes you wonder what other conditions could be relevant. Looking forward to more on this.