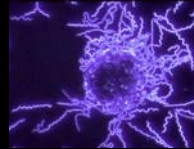
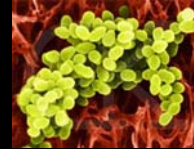


tiny conspiracies

A Potpourri of Personalities



Lyme Disease



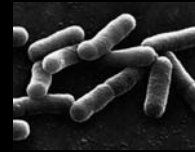
Toxic Shock



Food Poisoning



Food Digestion
Immune Defense

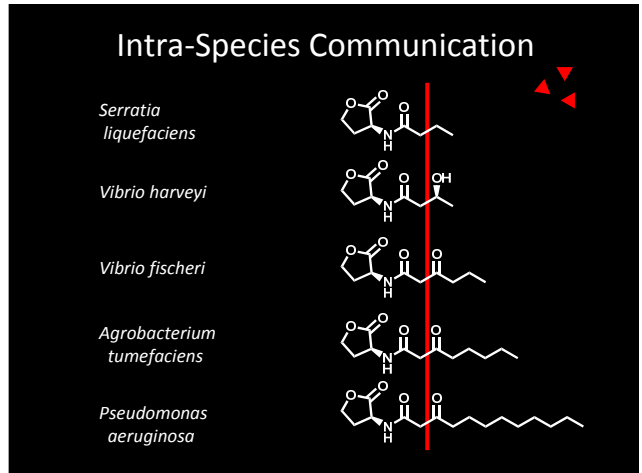
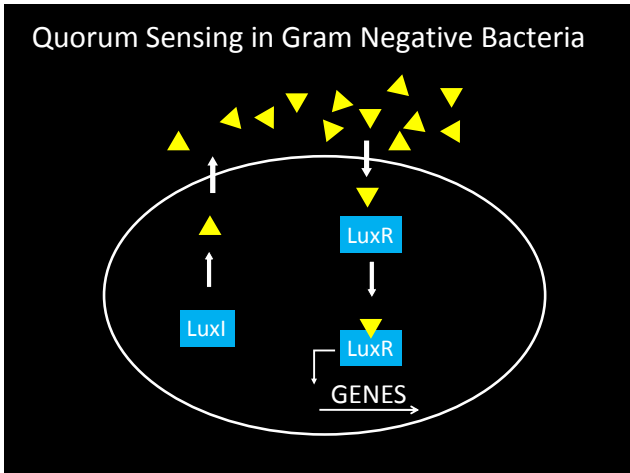
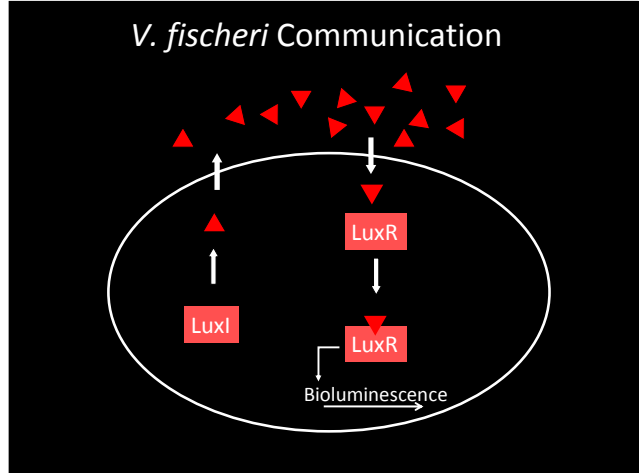
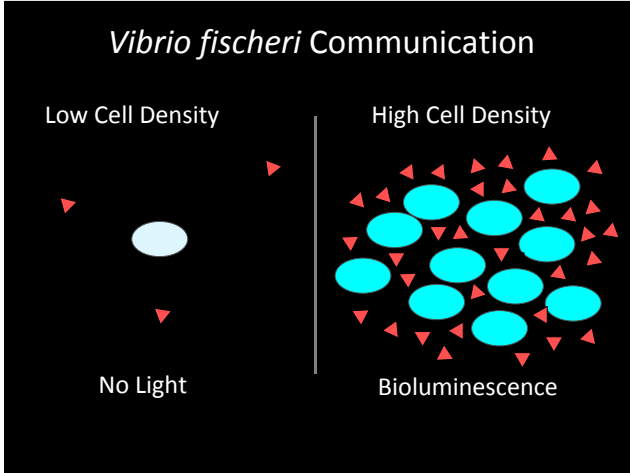


Provides Vitamin K

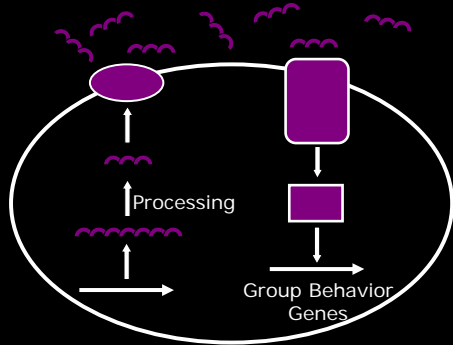


HHMI and Margaret McFall-Ngai

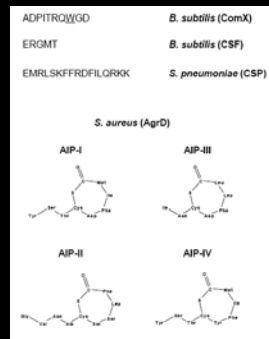




Quorum Sensing Gram-Positive Bacteria



Peptide Autoinducers

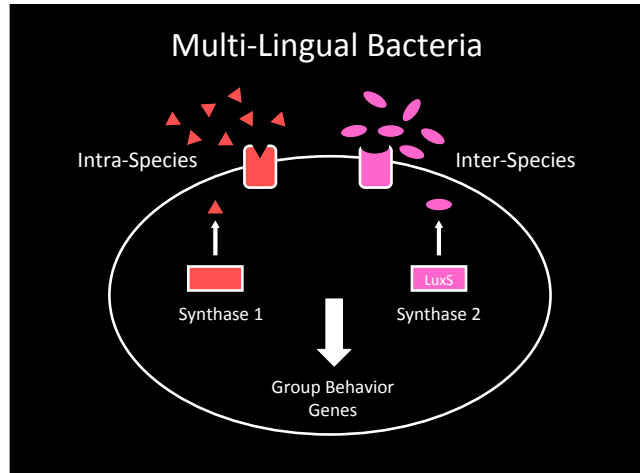
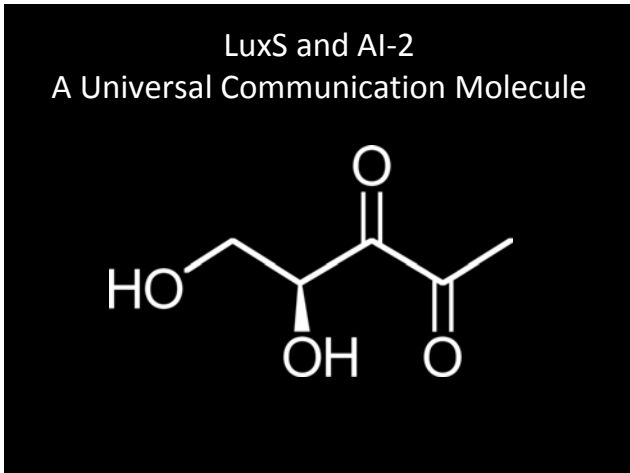
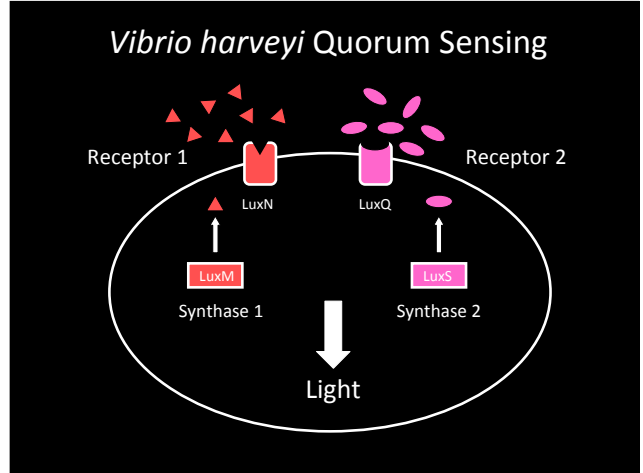


Quorum-Sensing Behaviors

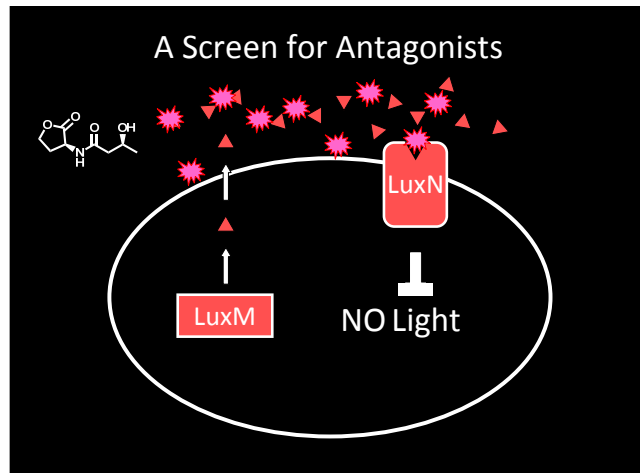
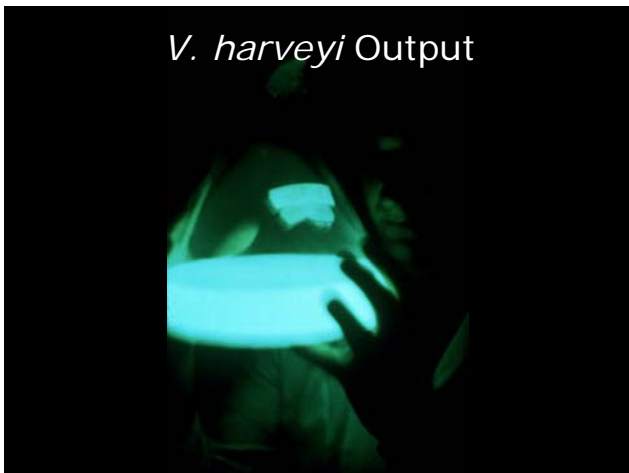
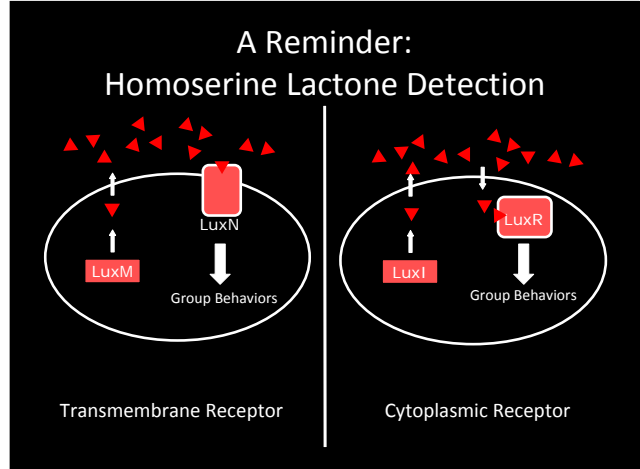
<i>V. fischeri</i>	Bioluminescence
<i>P. aeruginosa</i>	Virulence Factors, Biofilms
<i>S. aureus</i>	Virulence Factors
<i>E. carotovora</i>	Virulence Factors, Antibiotics

Bacterial Communities

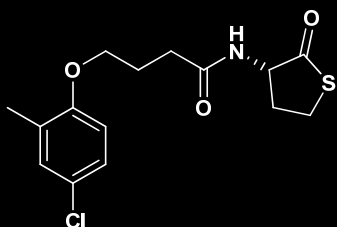




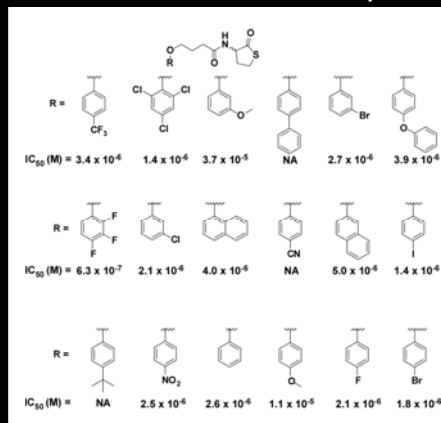
Manipulating Quorum Sensing to Control Bacterial Pathogenicity?



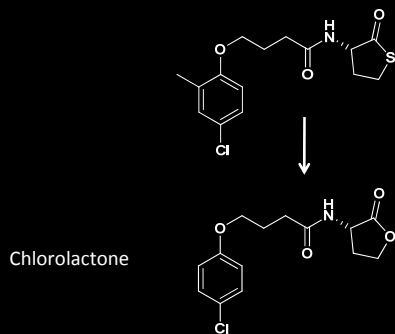
A Potent Antagonist



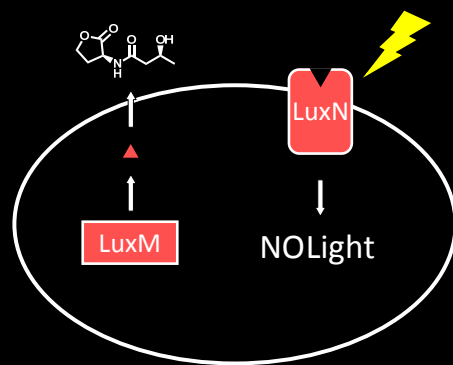
Structure Function Analysis



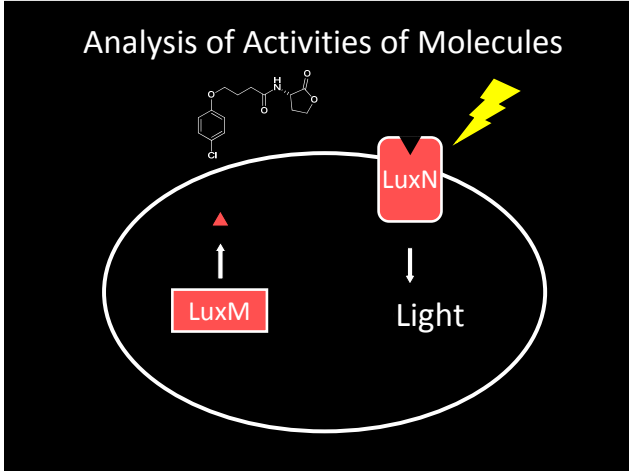
A 10-Fold More Potent Molecule



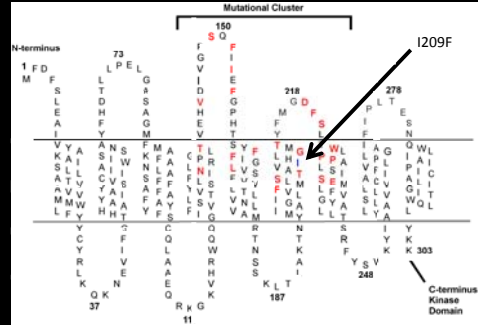
Analysis of Activities of Molecules



Analysis of Activities of Molecules

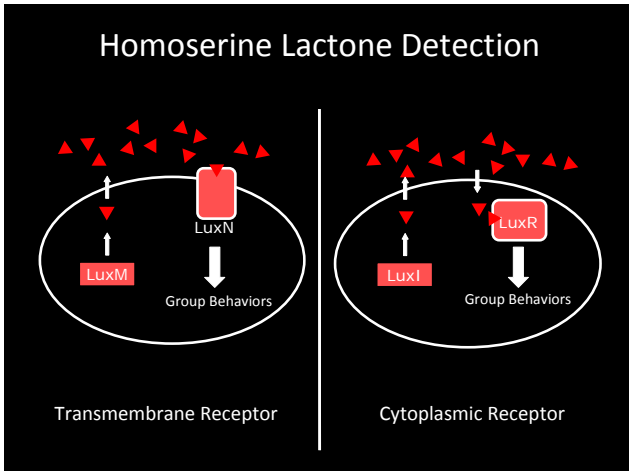


LuxN Mutational Analysis

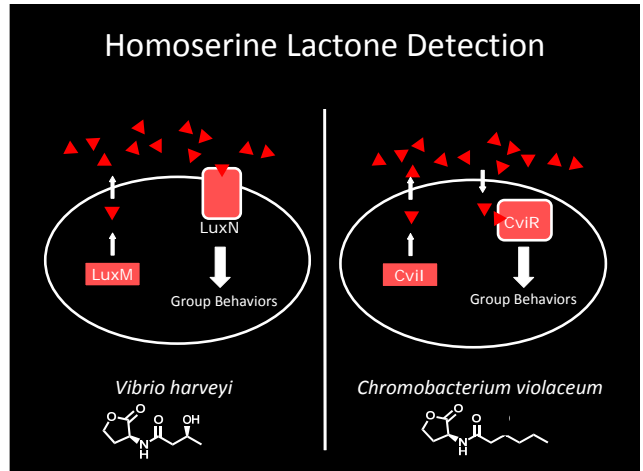


I209F = No Antagonism/Reacts fine to the native signal

Homoserine Lactone Detection



Homoserine Lactone Detection



C. violaceum Output

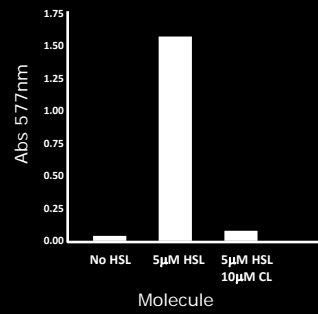


WT

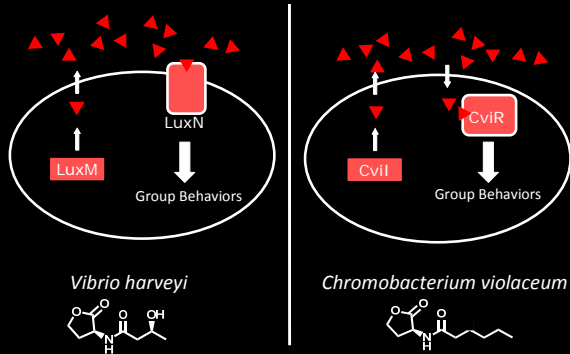
Receptor⁻

Synthase⁻

Cross-Antagonism



Homoserine Lactone Detection



The Inhibited Structure



Domain-swapped conformation

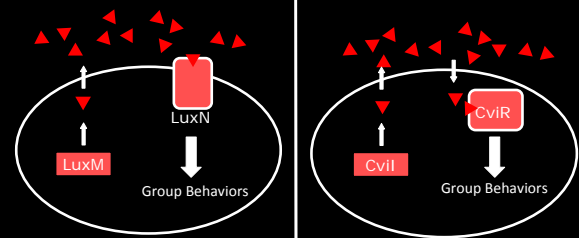
The DNA-Bound Structure



Vannini et al., EMBO J. 2002 Sep 2;21(17):4393-401

Increasing Antagonist Potency

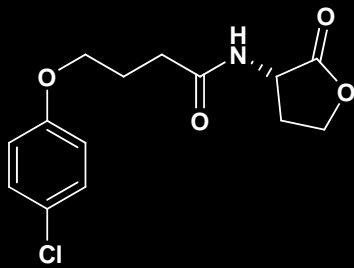
Homoserine Lactone Detection



Transmembrane Receptor

Cytoplasmic Receptor

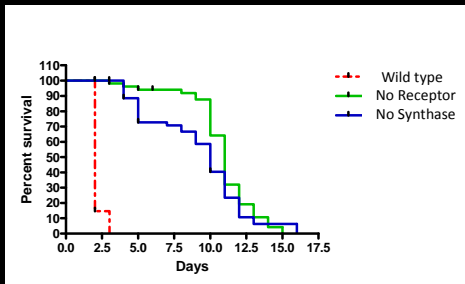
A Therapeutic?



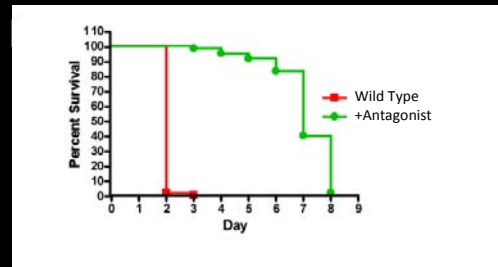
A Therapeutic?



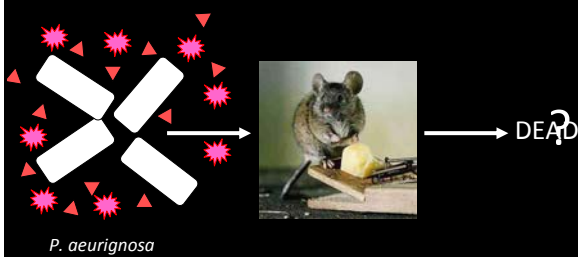
Quorum-Sensing-Mediated Killing of *C. elegans*



Saving *C. elegans*



Our Current Experiment



Quorum Sensing In Bacteria

Bacteria talk to each other

Bacteria are multi-cellular

Bacteria can distinguish self from other

Develop strategies to impede/improve quorum sensing

Natural anti- and pro-quorum sensing strategies already exist

Lee and Danielle Swem



Structure: Fred Hughson and Joe Chen Chemistry: Martin Semmelhack and Lark Perez

Thanks

