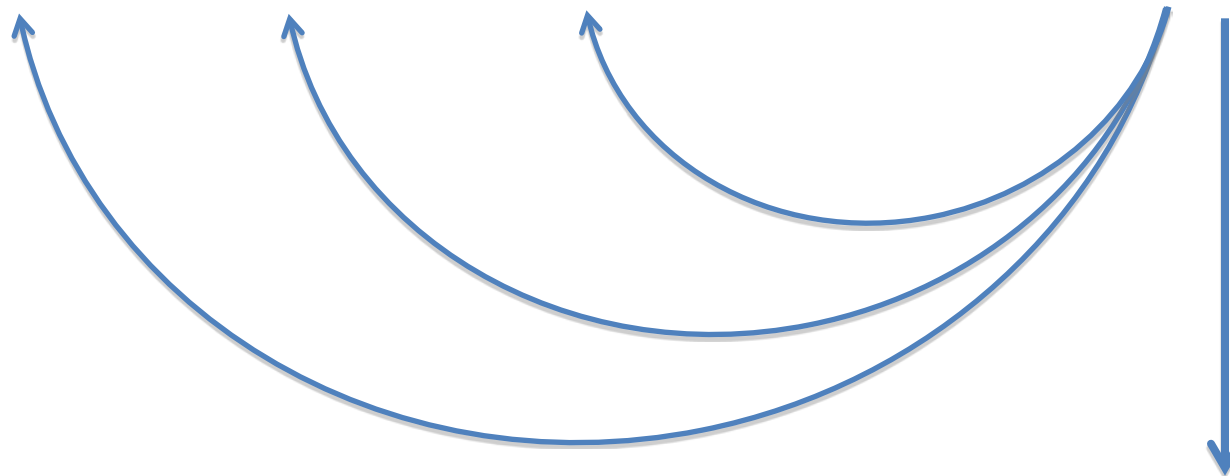


# The "New" Central Dogma

(GENOME)      (TRANSCRIPTOME)      (PROTEOME)      (PARVOME)\*  
DNA ↔ RNA → Protein → Natural Products



MANY FUNCTIONS

\*par- small (Greek), -ome- group (Latin)

# Some Useful Numbers

Weight of Bacteria in the Universe:  $5 \times 10^{17}$ g

Number of Bacteria in the Universe:  $5 \times 10^{30}$

Number of bioactive small molecules:  $1 \times 10^{32}$

US National Debt:  $\$14 \times 10^{11}$

# Using the *lux* operon to probe and find new bioactive molecules



**(XXX)**

*luxC*

*luxD*

*luxA*

*luxB*

*luxE*

Insert defined promoters  
or random DNA fragments



Light production when  
transcription is activated  
(functional promoter  
sequence and bioactive  
molecule)

# Plate assays for bioactive compounds (and their sources) using *lux* gene expression

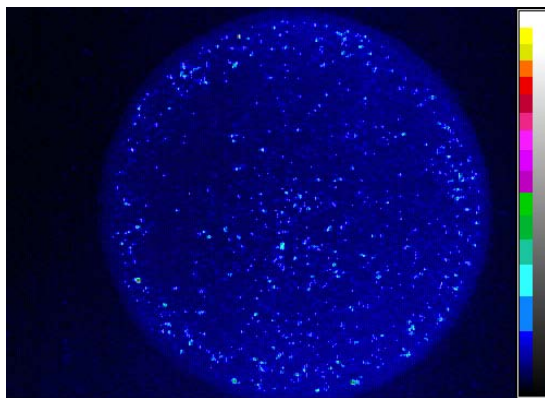
1. RESUSPEND SAMPLE (SOIL, etc.)
2. DILUTE IN SOFT AGAR
3. POUR ON PLATE
4. INCUBATE 15-30 hr
5. RECORD WITH CCD CAMERA
6. PICK ACTIVE CLONES



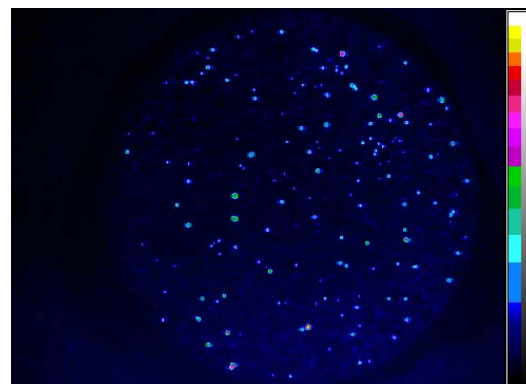
A. Soft agar containing lux reporter,  
with/without sample

B. Sample dispersed in agar

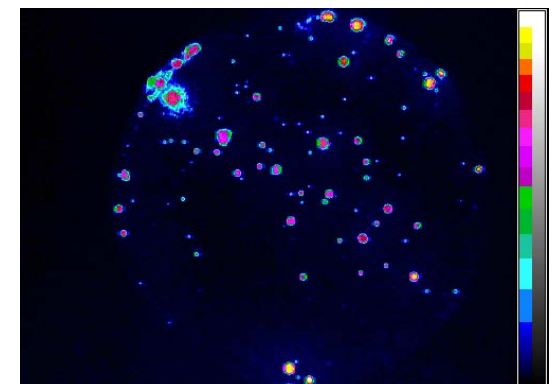
C. Nutrient agar



SOIL

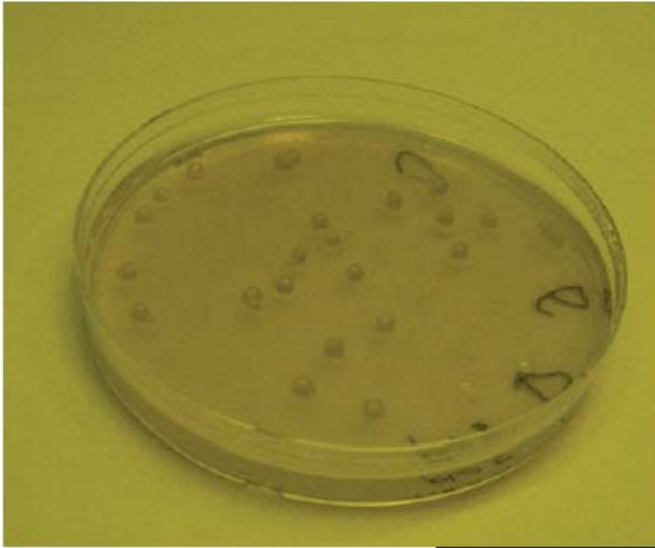


SKIN



SEDIMENT

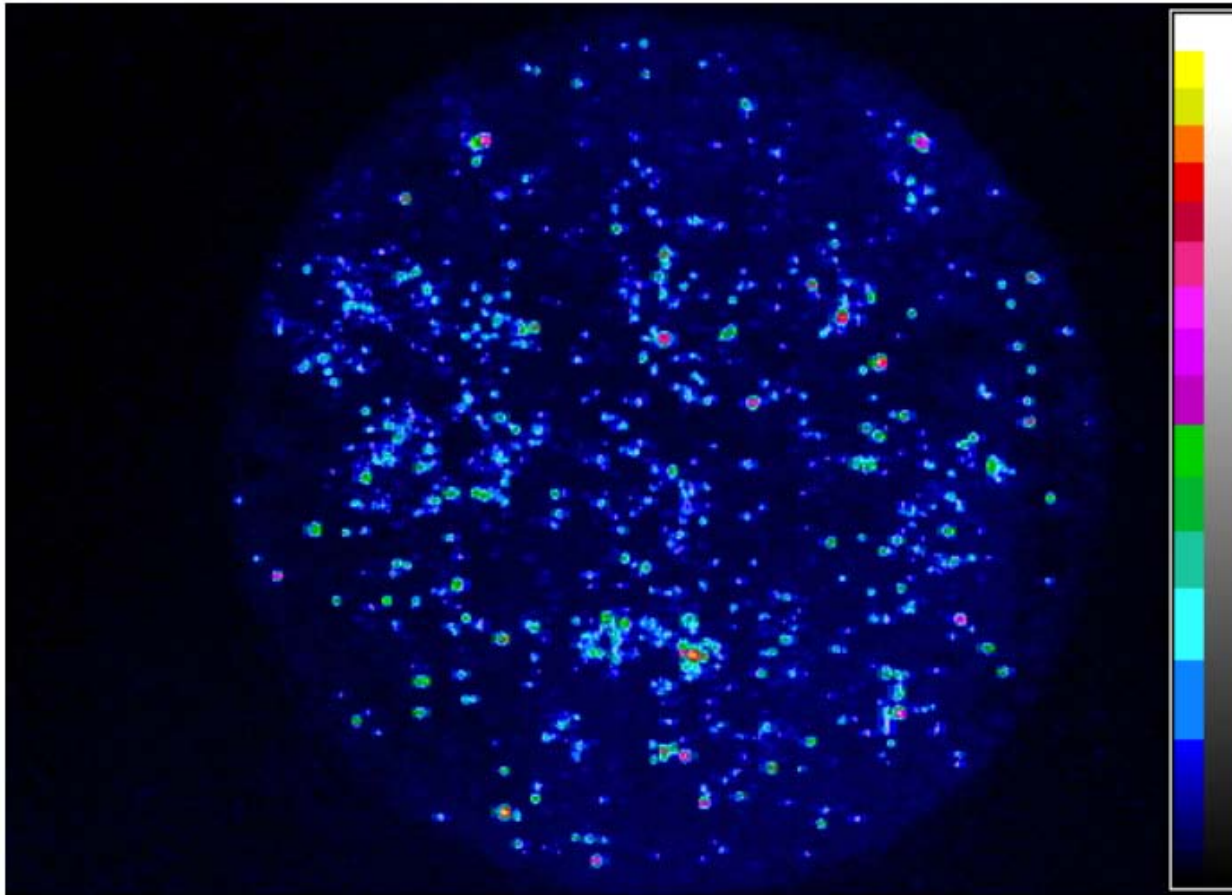
# ALGINATE MACRODROPLETS



An approach to single bacteria sequencing?

# Detecting bioactive compounds made by bacteria *in situ*

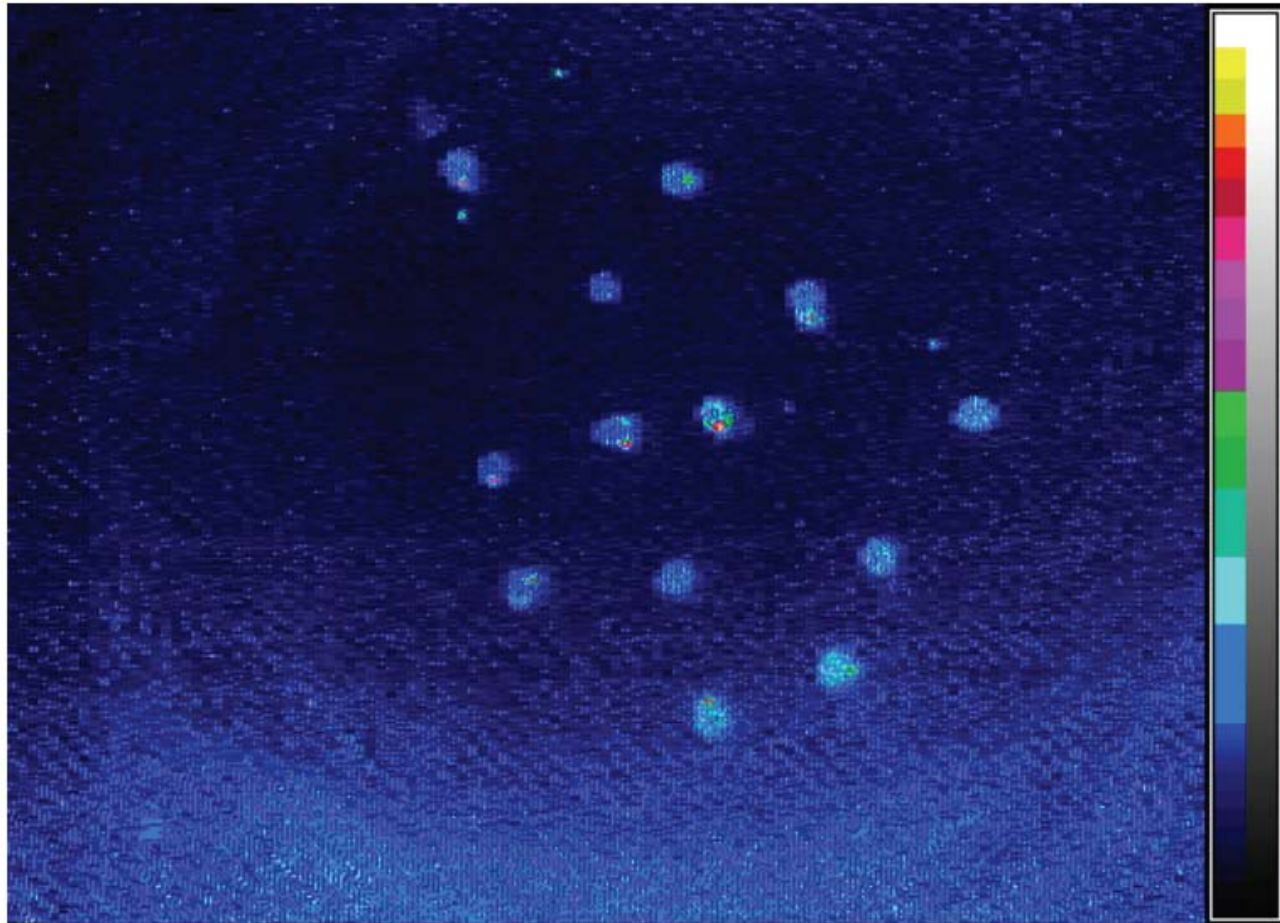
(How many have antibiotic activity?)



A soil sample containing about  $10^8$  bacteria in contact with a *lux* reporter strain



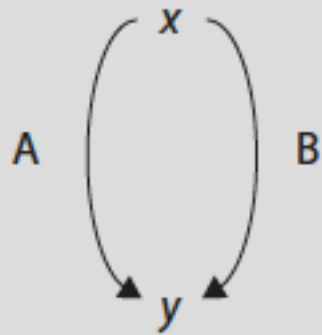
## Lux reporter assays in alginate beads



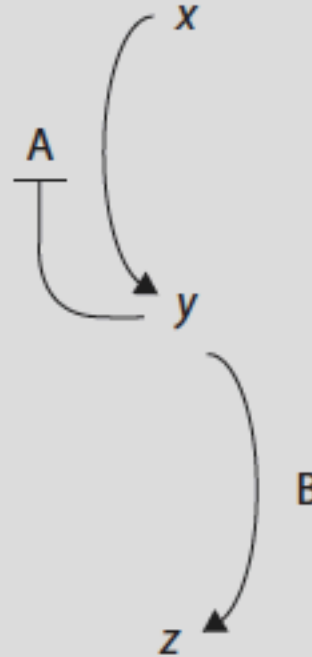
Are these diffusible signals?



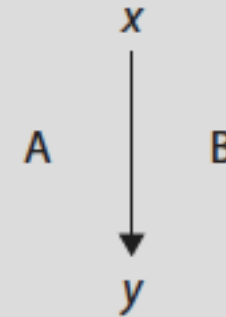
# Signaling Interactions between Cells (Communication, Cues, Competition, Cooperation)



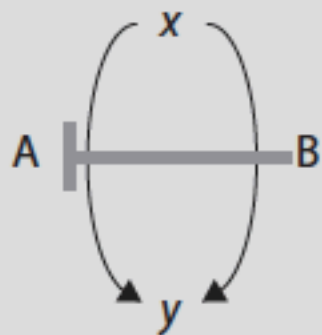
**a** *Passive competition*



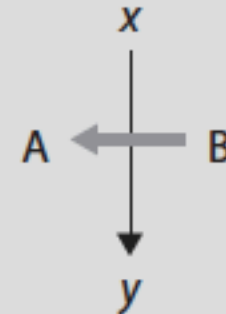
**c** *Syntrophic interactions*



**d** *Passive cooperation*



**b** *Active competition*



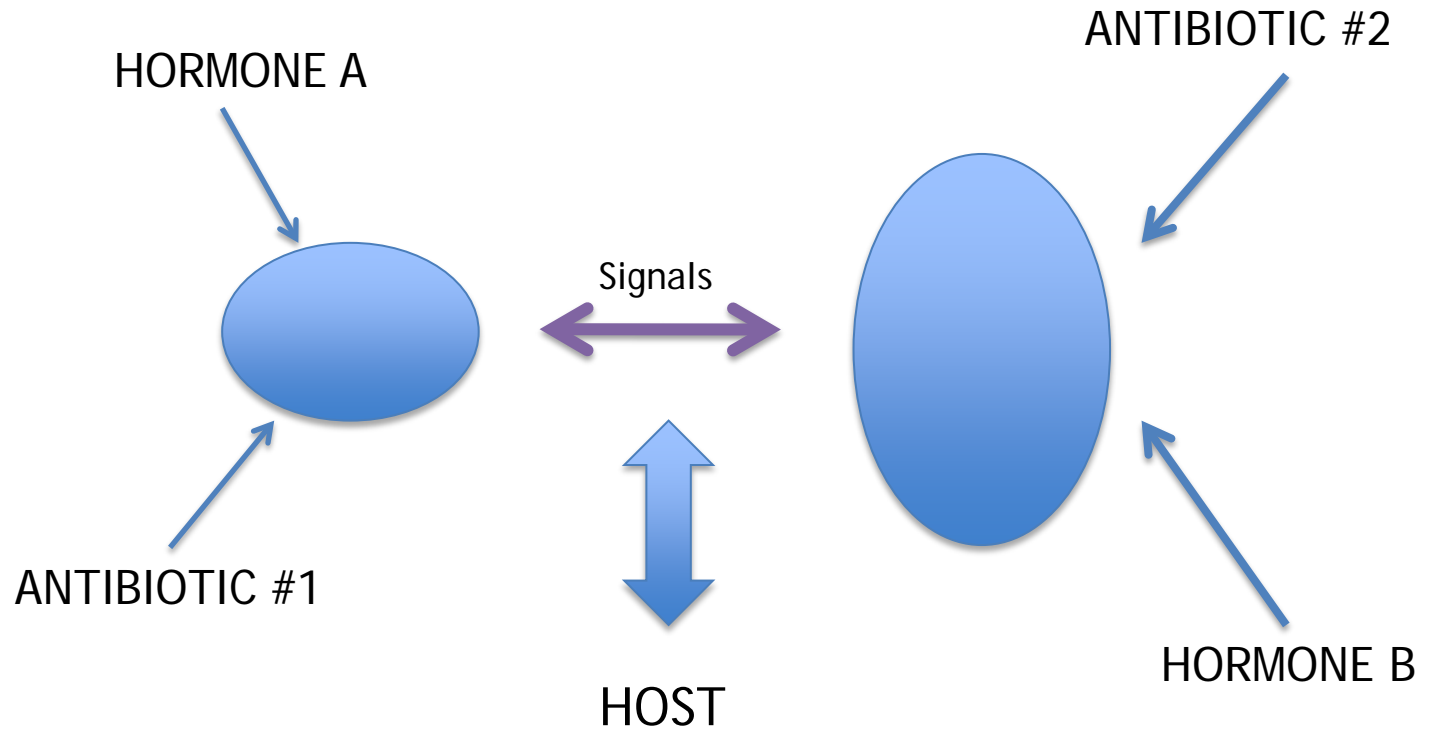
**e** *Active cooperation*

## Microbial Endocrinology

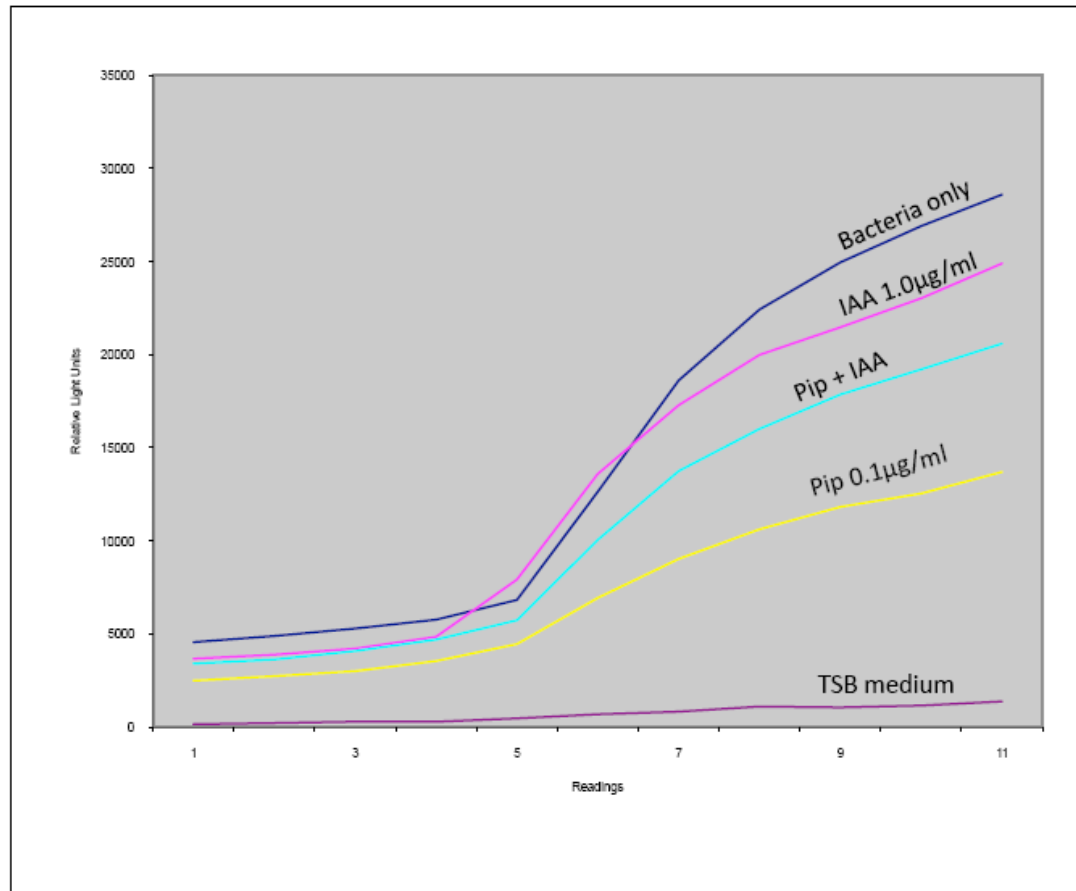
Synergies, antagonisms and interactions between human, animal and plant hormones. These take place at all levels and involve organs, tissues, microbes, etc.

The most extensive studies have been done by Lyte, Freestone, Sperandio, Williams and others. Do hormones influence the activity of antibiotics? Do they modulate cell-cell signaling?

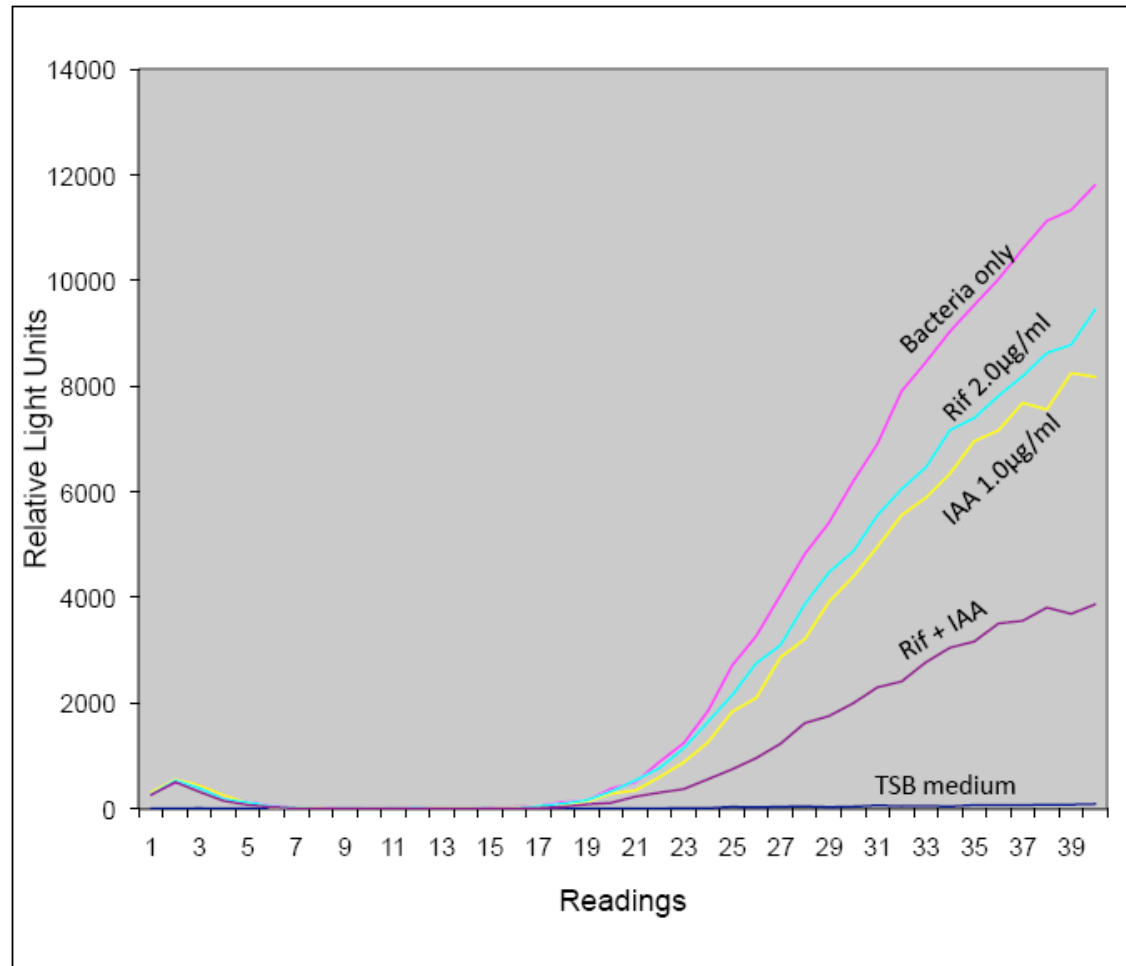
# Bacterial interactions?



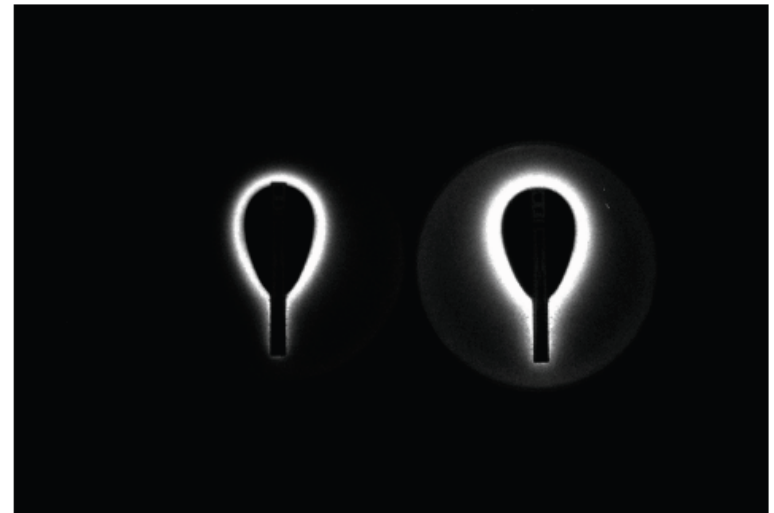
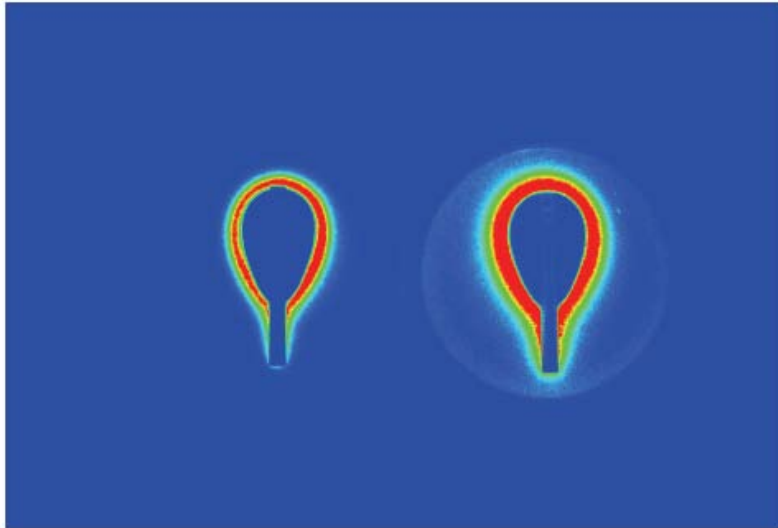
# Indole-3-acetic acid (IAA) partially reverses piperacillin inhibition of *pilv L/G::lux* expression



# Indole-3-acetic acid (IAA) enhances rifampicin inhibition of *pBA2::lux* expression



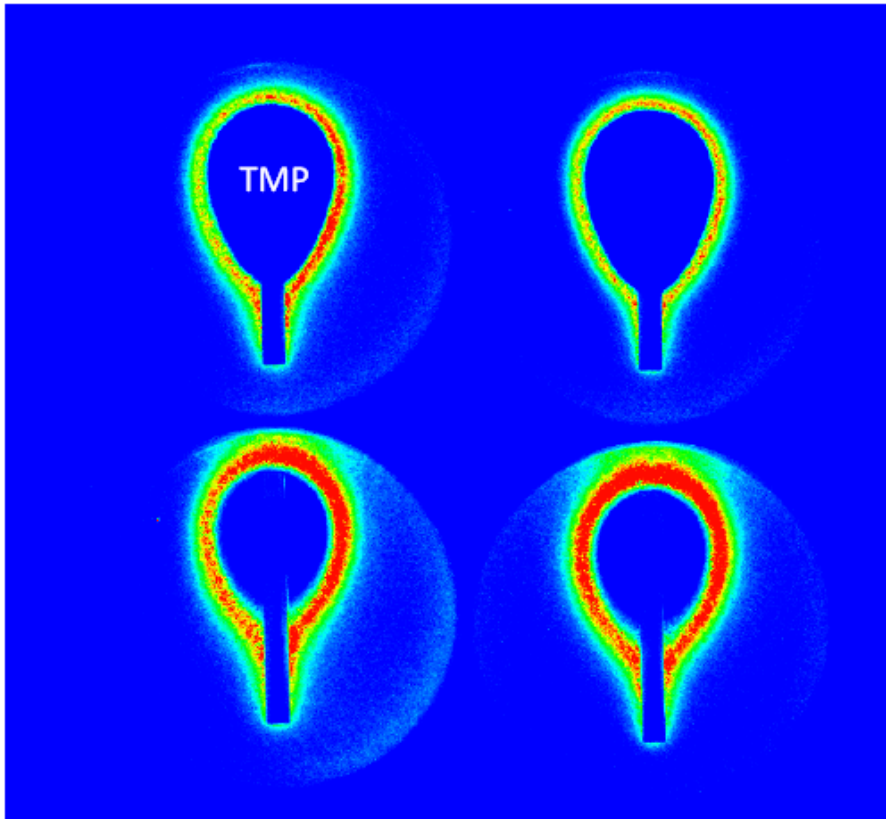
# Effect of Epinephrine on Trimethoprim activity (Etest strips)





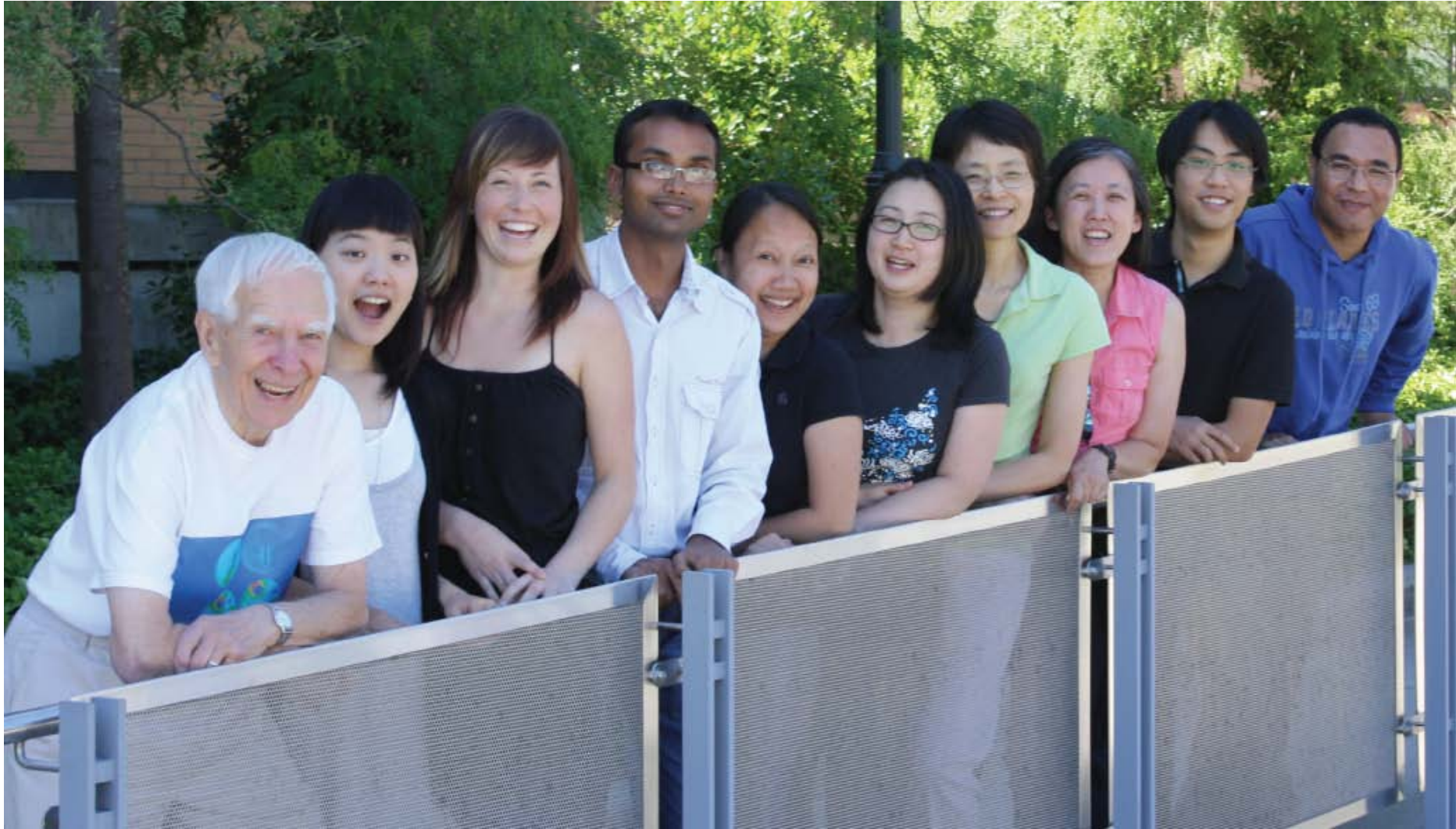
MHA

LBA +  
Epi 10 $\mu$ g/ml



MHA +  
FBS 20%

Effect of epinephrine (Epi)  
and fetal bovine serum (FBS)  
on light induction by  
trimethoprim



The Davies Lab 2010: "Science is Fun"