Host Response

Steven Roberts

Little Background First (my preface)

Main Interest - *Physiology* (how stuff works)

Fish Reproduction

Fish Growth

Shellfish Growth / Metamorphosis

Shellfish Immune Response

Shellfish Response to Environmental Change

Shellfish Epigenetics - Adaptation / Plasticity

Epigenetics

Innate immune memory: towards a better understanding of host defense mechanisms

Jessica Quintin, Shih-Chin Cheng, Jos WM van der Meer, Mihai G Netea

Highlights

- Organisms lacking an adaptive immune system can mount resistance to secondary infections.
- NK cells and monocytes have adaptive (memory) characteristics.
- *Trained immunity* is the term proposed for innate immune memory responses.
- Epigenetic reprogramming is a central mechanism mediating innate immune memory.

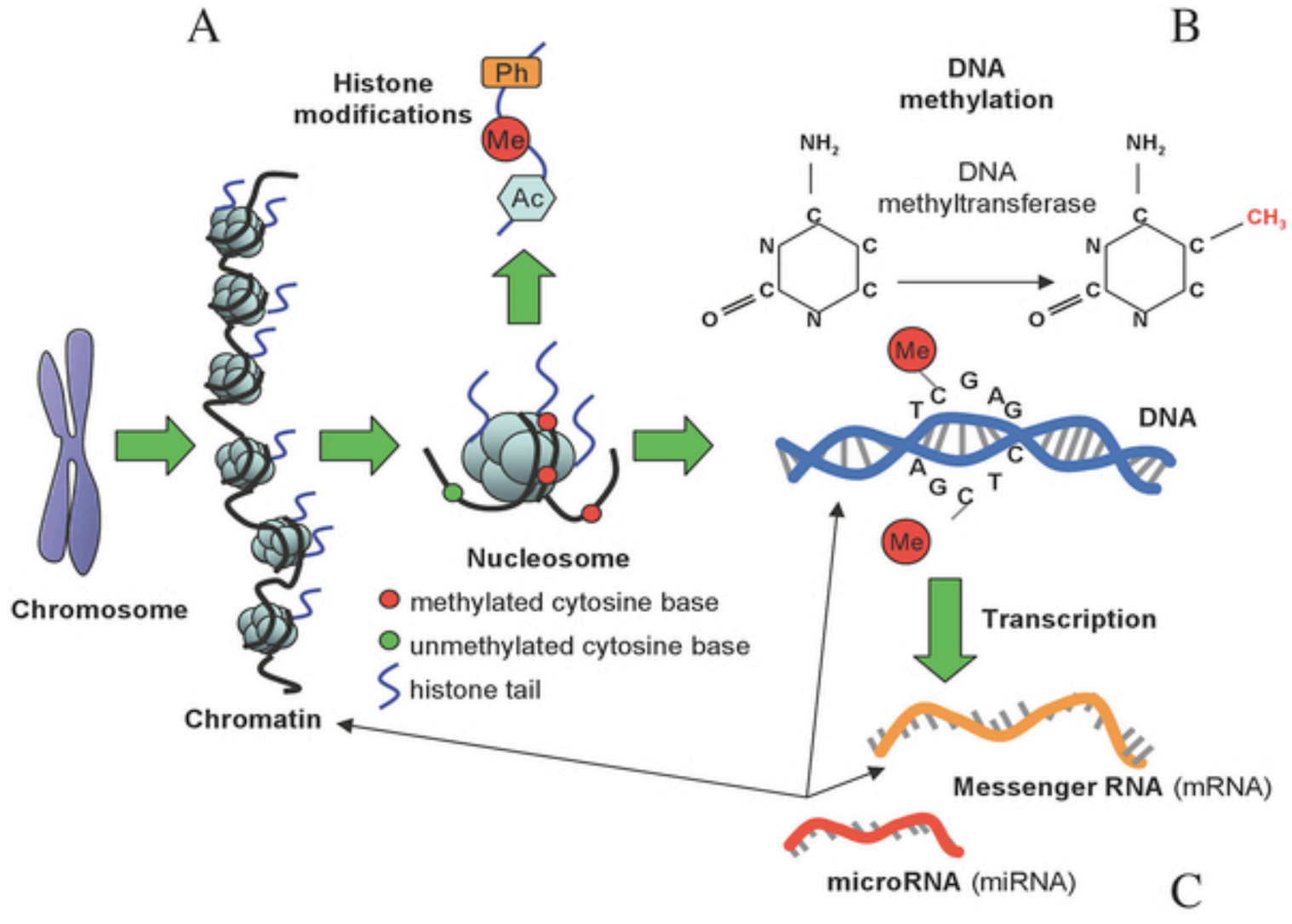
Innate immunity is classically defined as unable to build up immunological memory. Recently however, the assumption of the lack of immunological memory within innate immune responses has been reconsidered. Plants and invertebrates lacking adaptive immune system can be protected against secondary infections. It has been shown that mammals can build cross-protection to secondary infections independently of T-lymphocytes and B-lymphocytes. Moreover, recent studies have demonstrated that innate immune cells such as NK cells and monocytes can display adaptive characteristics, a novel concept for which the term *trained immunity* has been proposed. Several mechanisms are involved in mediating innate immune memory, among which epigenetic histone modifications and modulation of recognition receptors on the surface of innate immune cells are likely to play a central role.

Epigenetics

Epigenetics of Host–Pathogen Interactions: The Road Ahead and the Road Behind

Elena Gómez-Díaz ✉, Mireia Jordà, Miguel Angel Peinado, Ana Rivero

Published: November 29, 2012 • DOI: 10.1371/journal.ppat.1003007



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examples on infection-induced host gene reprogramming [32]. A diverse array of bacterial effectors has been identified that either mimic or inhibit the host cellular machinery, thus facilitating the pathogen's life-cycle. MAPK (mitogen-activated protein kinase), Interferon (IFN), and transcription factor NF-κB signaling pathways are common targets of bacterial-induced post-translational modifications, acetylation, ubiquitylation, and phosphorylation on histones and chromatin-associated proteins [35]. Within the alveolar macrophages, *Mycobacterium tuberculosis*, for example, inhibits interferon-γ-induced expression of several immune genes through histone acetylation [36], which explains the persistence of long-term chronic tuberculosis infections in some patients. This mechanism is not restricted to bacteria but

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Ecology of Infectious Marine Diseases [c... | 0 | + New | 1 Howdy, Steve

Leave a reply

COURSE TWEETS

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#Epigenetics of Host–Pathogen Interactions: The Road Ahead and the Road Behind http://t.co/qGSEZ5L5HU #toread
about 2 hours ago

How do plants achieve immunity? Defence without specialized immune cells http://t.co/QQzHWcNn9g #toread #Epigenetic
about 2 hours ago

Innate immune memory: towards a better understanding of host defense

Host Response

Steven Roberts

Let's Anthropomorphize

What might scare marine invert?

Today: *Physiological Response* to things that are bad

It is important the think about the big picture.

What else is going on with the critter...

resource allocation

Where are these resources coming from?

Today: *Physiological Response* to things that are bad

It is important the think about the big picture.

What else is going on with the critter...

really big picture -

What has the population experienced.

Defense Systems

- Anatomic Features
- **Immunity**

Anatomic Features

Anatomic Features

Key reference: Arnott, S. A., Neil, D. M. and Ansell, A. D. (1999). Escape trajectories of the brown shrimp *Crangon crangon*, and a theoretical consideration of initial escape angles from predators. *J. Exp. Biol*. **202**, 193-209.

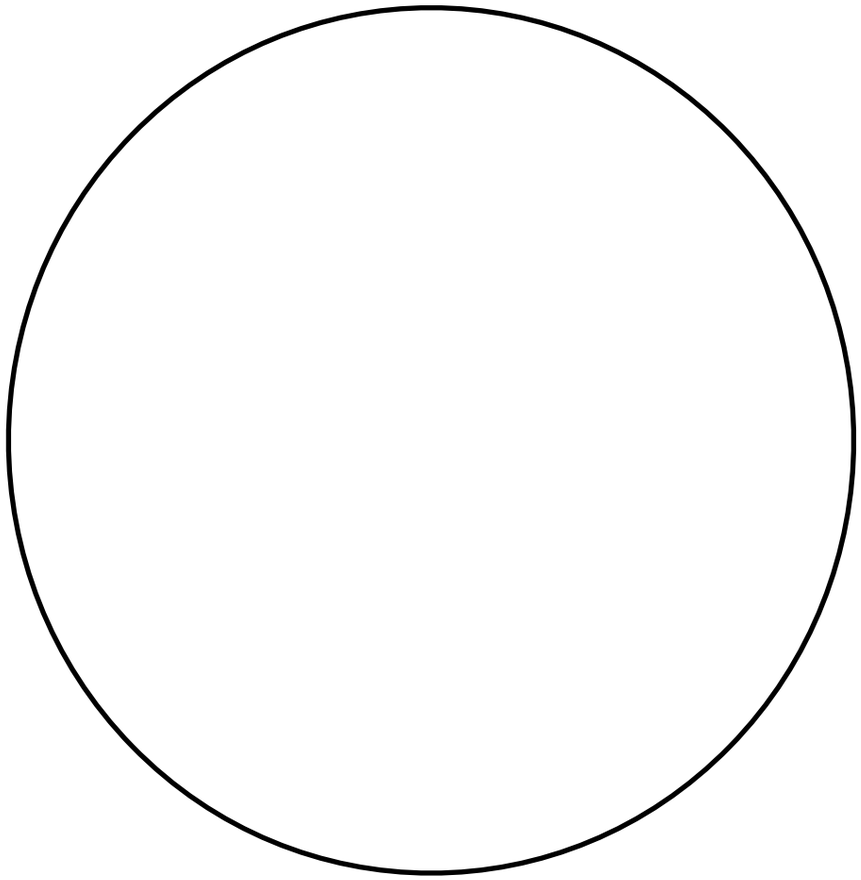
Anatomic Features

FLOWER GARDEN BANKS
NATIONAL MARINE SANCTUARY
NATIONAL MARINE SANCTUARIES

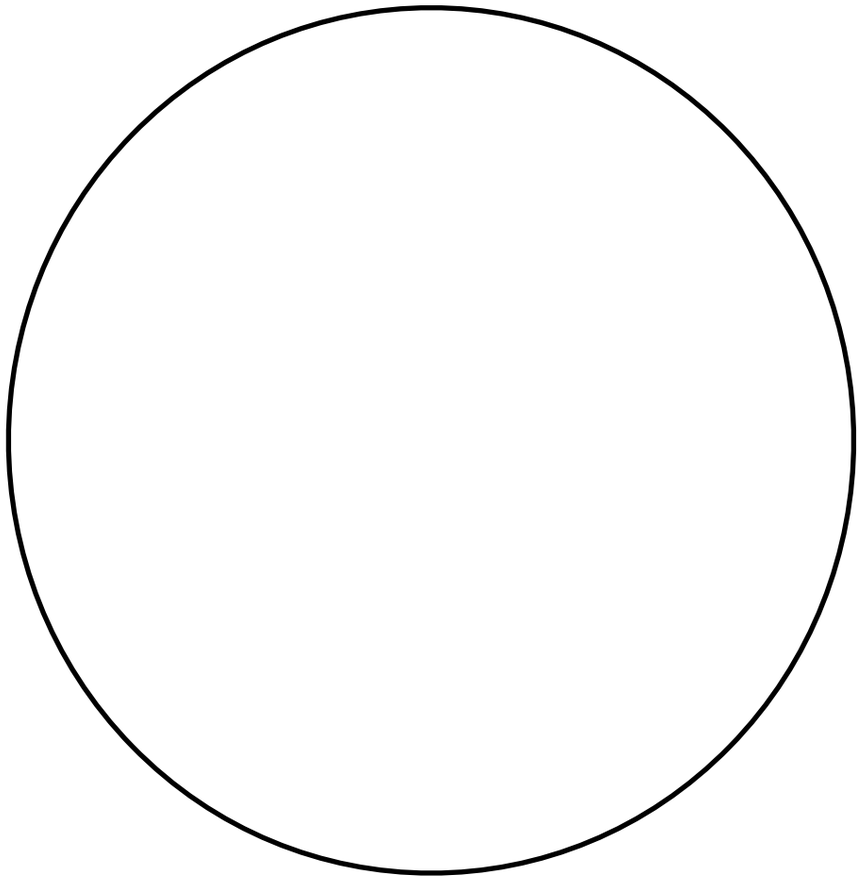
tinyurl.com/cgbso7

What is the overarching fear in those three examples?

What is the overarching fear in those three examples?



What is the overarching fear in those three examples?



Defense Systems

- Anatomic Features
- **Immunity**

Immune System

- Defense against ***pathogens***
- Removal of "worn-out" cells and tissue debris (**wound healing** and tissue repair)
- ID and destruction of **abnormal cells** that originate in the body.

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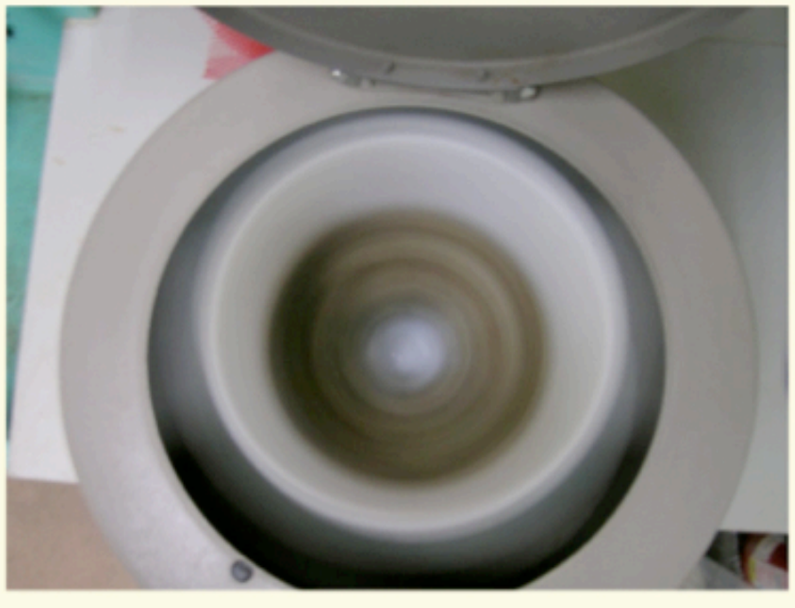
Immune response and mechanical stress susceptibility in diseased oysters, *Crassostrea virginica*

Steven B. Roberts · Inke Sunila · Gary H. Wikfors

Immune response and mechanical stress susceptibility in diseased oysters, *Crassostrea virginica*

Steven B. Roberts · Inke Sunila · Gary H. Wikfors

- Experimental Design
  - 1. Compare *C. virginica* exposed to *P. marinus* with ones without the parasite
  - 2. Evaluate effects of physical stress



Immune response and mechanical stress susceptibility in diseased oysters, *Crassostrea virginica*

Steven B. Roberts · Inke Sunila · Gary H. Wikfors

Table 2 Hematology of oysters, *C. virginica*, from two cohorts, infected with *P. marinus* ($n = 17$) and uninfected ($n = 19$), determined by flow cytometry (mean ± SE)

	P. marinus infected	Uninfected
Granular cells × 10^6 ml^{-1}	0.214 ± 0.0556	0.0614 ± 0.014
Agranular cells × 10^6 ml^{-1}	2.27 ± 0.458	0.586 ± 0.065
Granular cell diameter in μm	8.52 ± 0.30	11.4 ± 0.20
Agranular cell diameter in μm	5.31 ± 0.10	6.29 ± 0.31

No effect of mechanical stress was observed; therefore, data from stressed and unstressed were combined

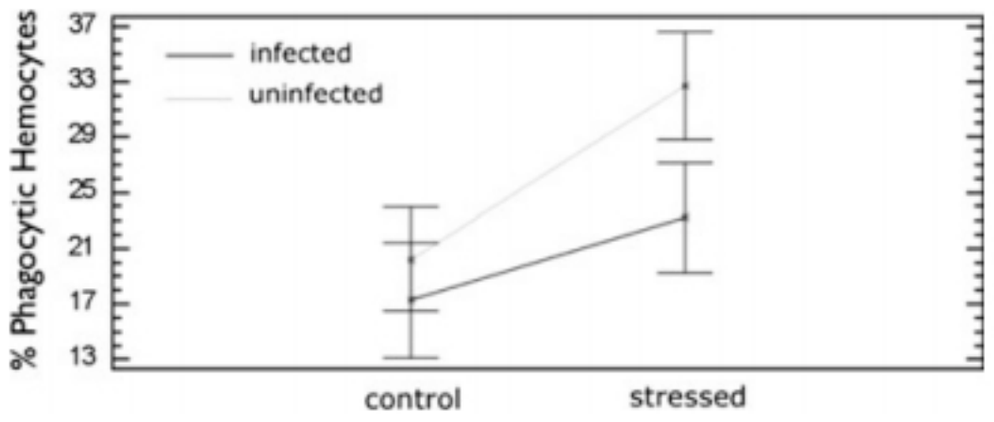
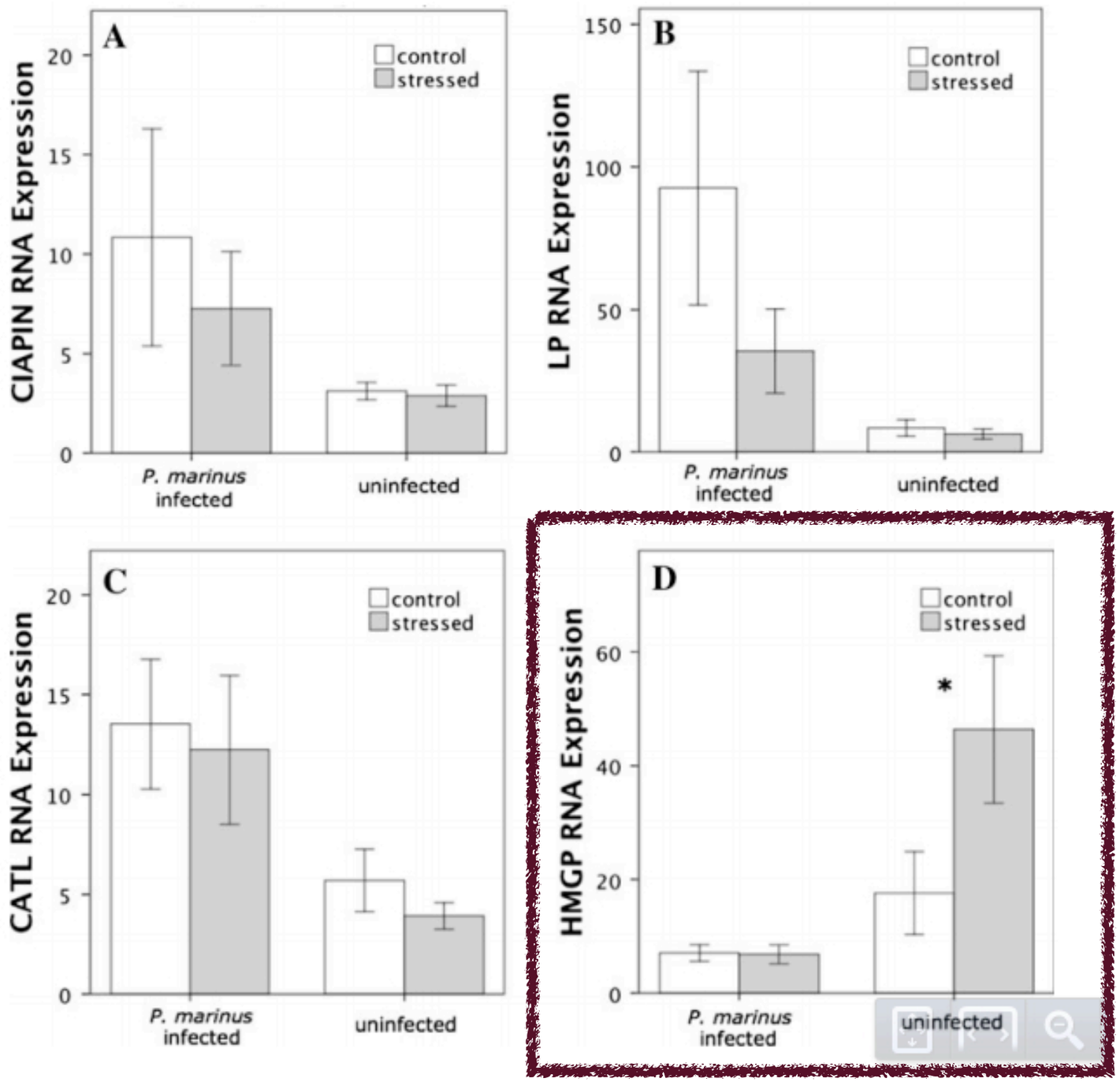


Fig. 2 Percentage of phagocytic hemocytes in *P. marinus*-infected ($n = 17$) and uninfected oysters ($n = 19$). A significant difference was observed after mechanical stress only in uninfected oysters (ANOVA $p < 0.05$)

Immune response and mechanical stress susceptibility in diseased oysters, *Crassostrea virginica*

Steven B. Roberts · Inke Sunila · Gary H. Wikfors



resource allocation

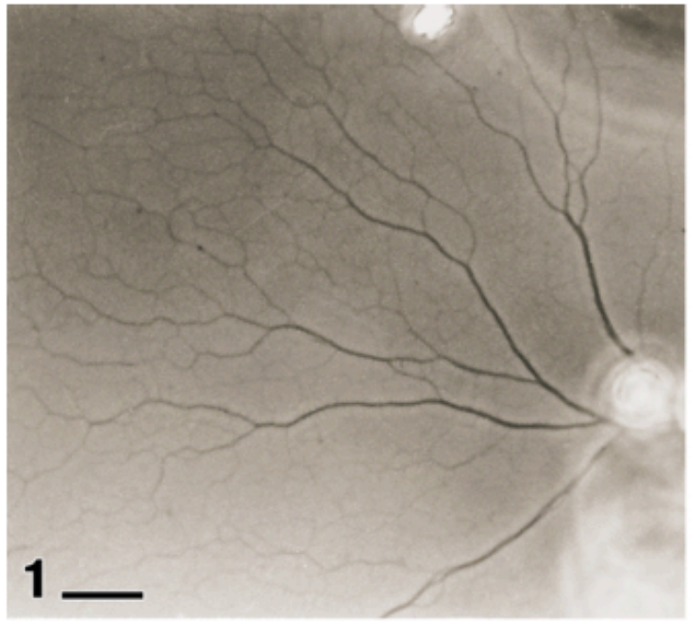
Pathogens

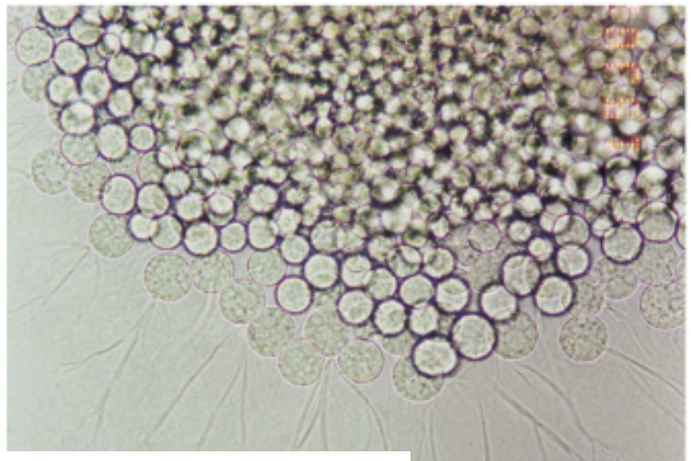
Pathogens

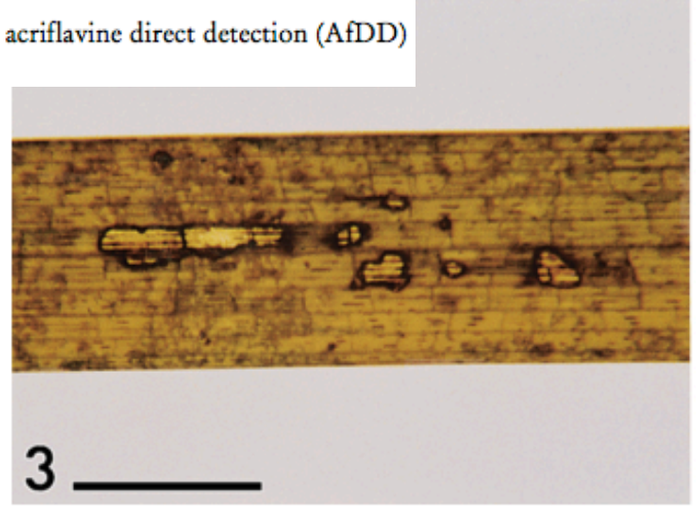
- Disease producing power known as _____
- Bacteria - release enzymes or toxins
- Internal parasites (larger; protozoa, fungi) - use resources, damage tissue
- Virus - not self sustaining; lack ability to for *energy production* and *protein synthesis*

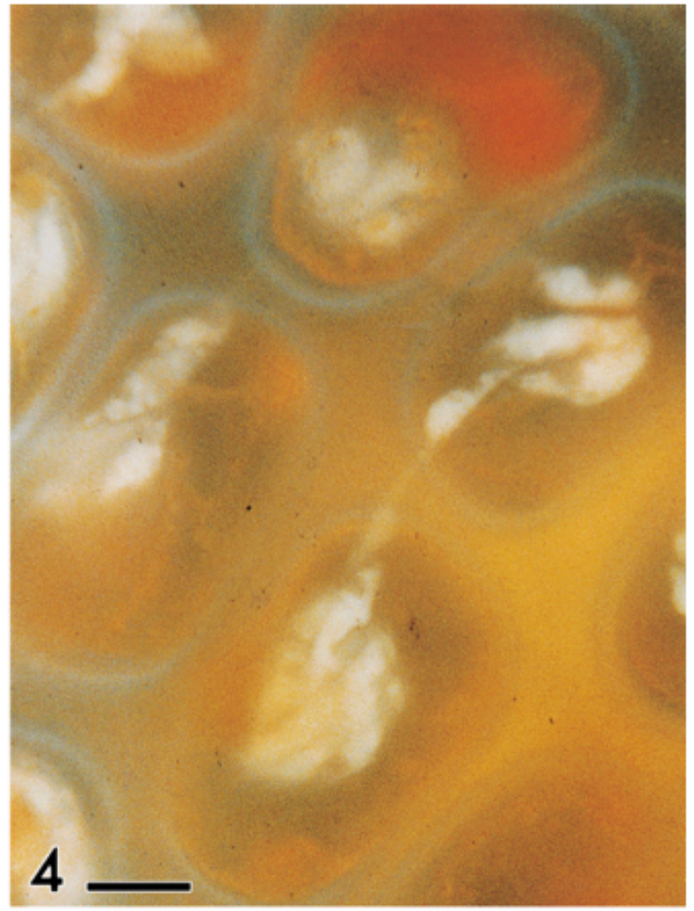
Bacteria - Vibrio

Protists
Fungi-like
Thraustochytrids









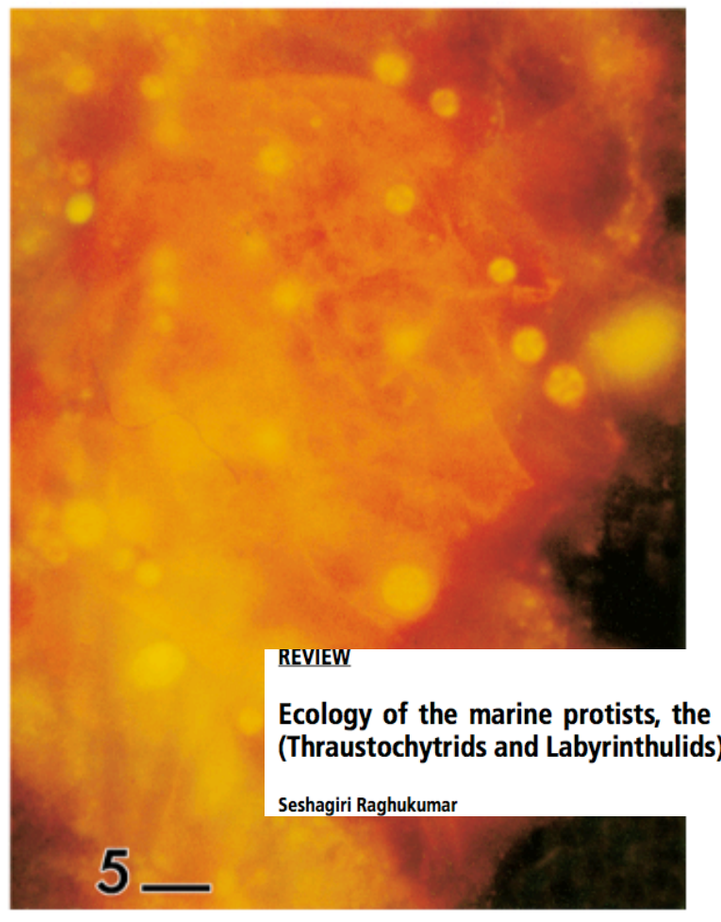


Fig. 1. Cells of a thraustochytrid growing on a nutrient agar medium. Bar represents 50 µm.

Fig. 2. Ectoplasmic net elements of a thraustochytrid cell. Scale bar = 20 µm.

Fig. 3. Leaves of the seagrass *Thalassia hemprichii* Escherson showing necrosis, presumably caused by *Labyrinthula* sp. Scale bar = 1 cm.

Fig. 4. Epifluorescence micrograph of cells of *Labyrinthula* within the tissue of the seagrass *Thalassia hemprichii* Escherson, labelled with Calcofluor. Scale bar = 20 µm.

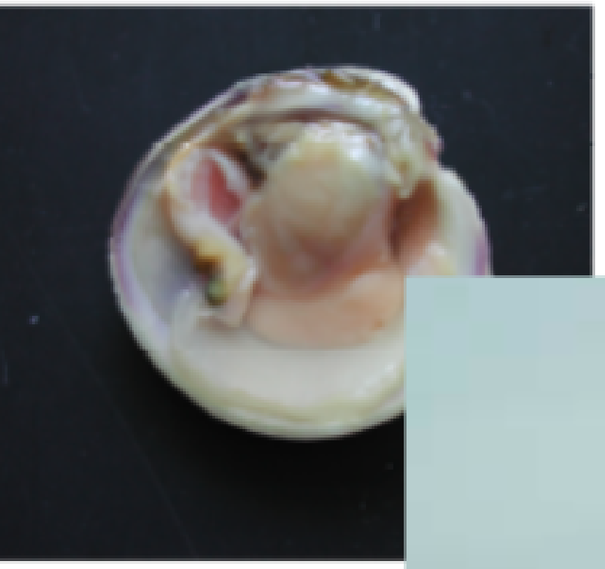
Fig. 5. Cells of thraustochytrids in phytoplankton detritus, stained using the acriflavine direct detection (AfDD) technique. Scale bar = 10 µm.

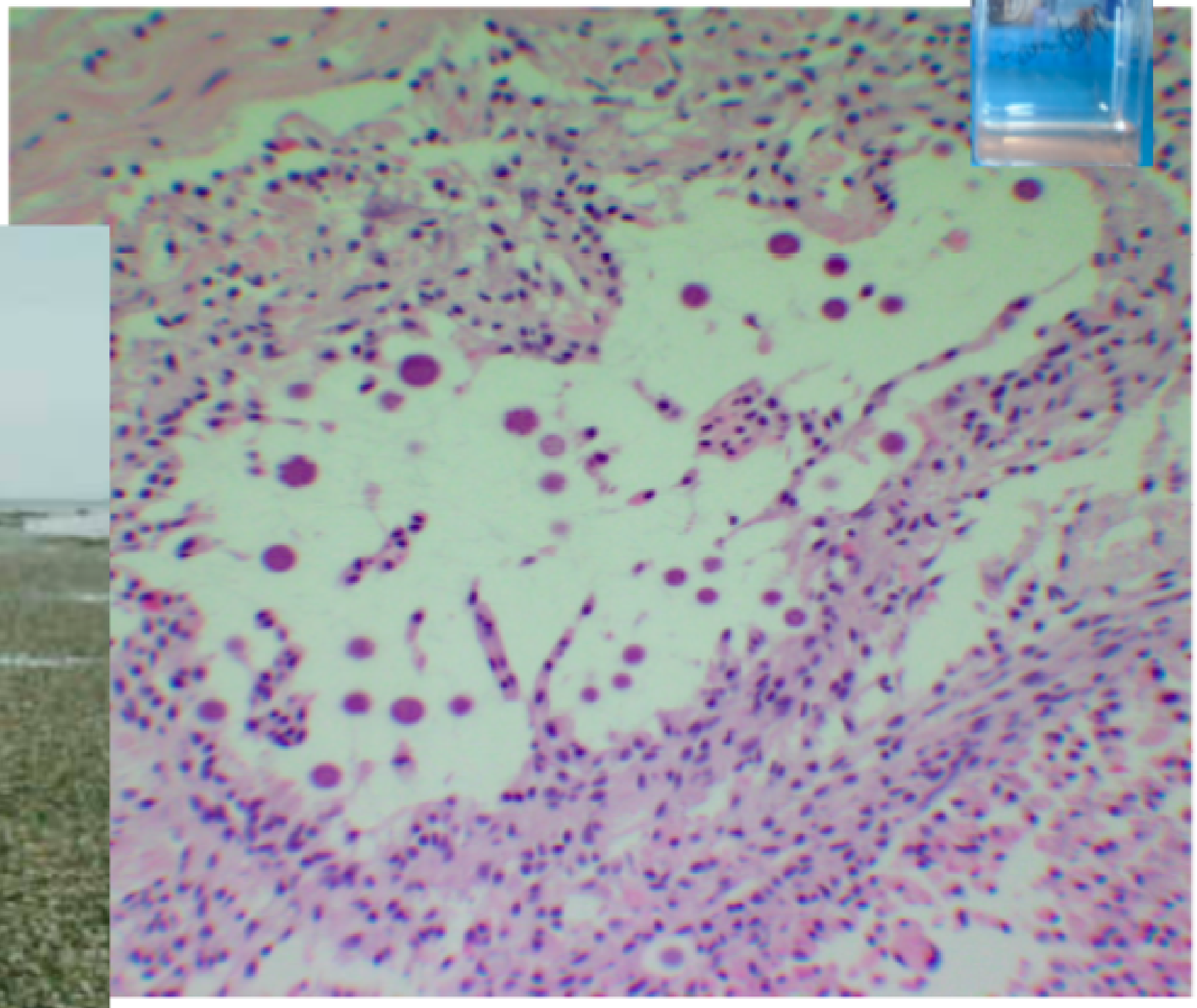
REVIEW

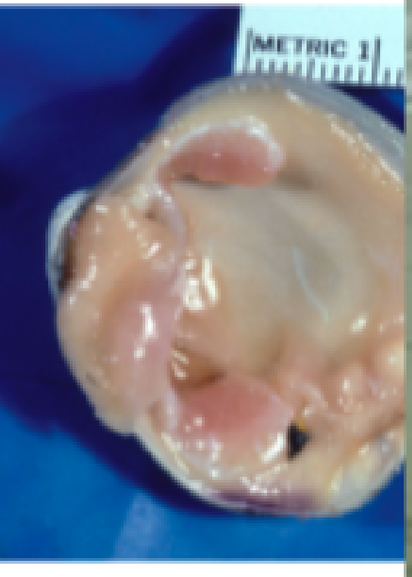
Ecology of the marine protists, the Labyrinthulomycetes (Thraustochytrids and Labyrinthulids)

Seshagiri Raghukumar

Fungi - QPX



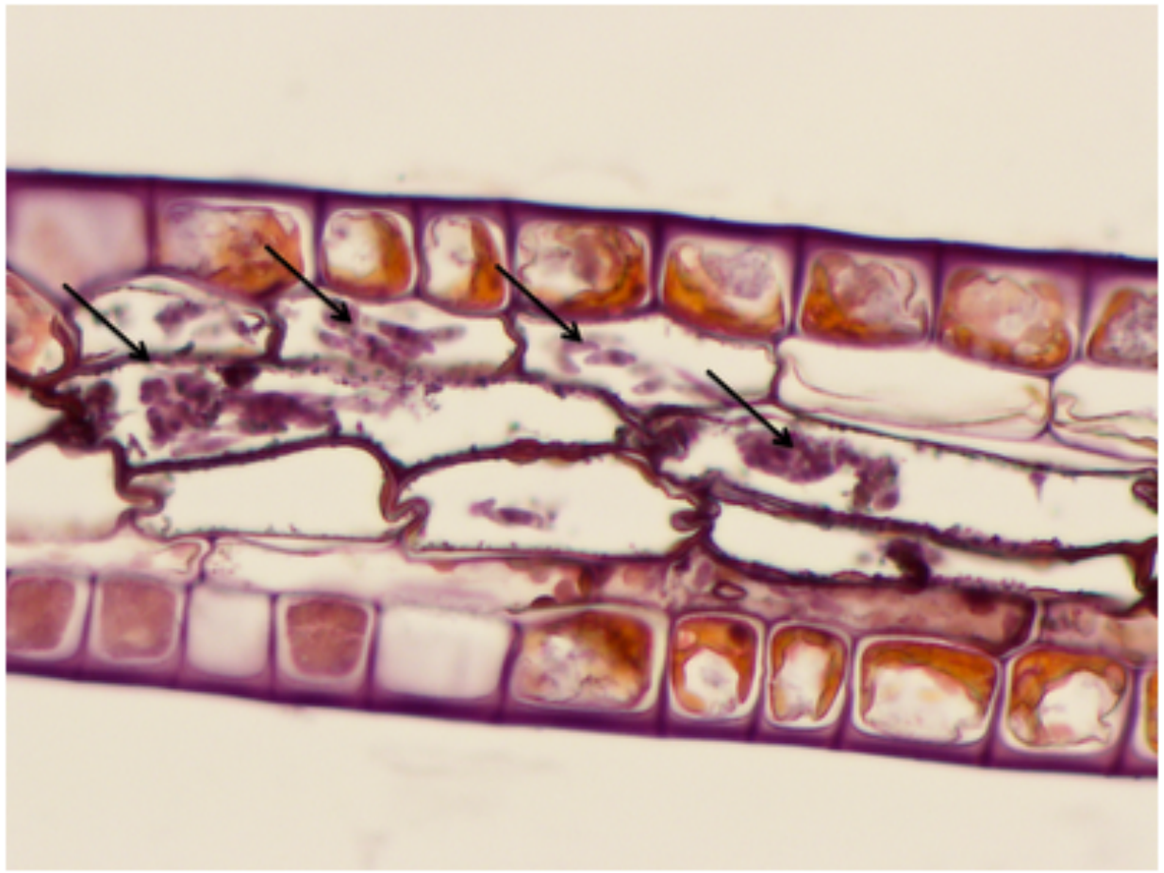




Roxanna Smolowitz

Colleen Burge - Oct 14, 2011 - Limited

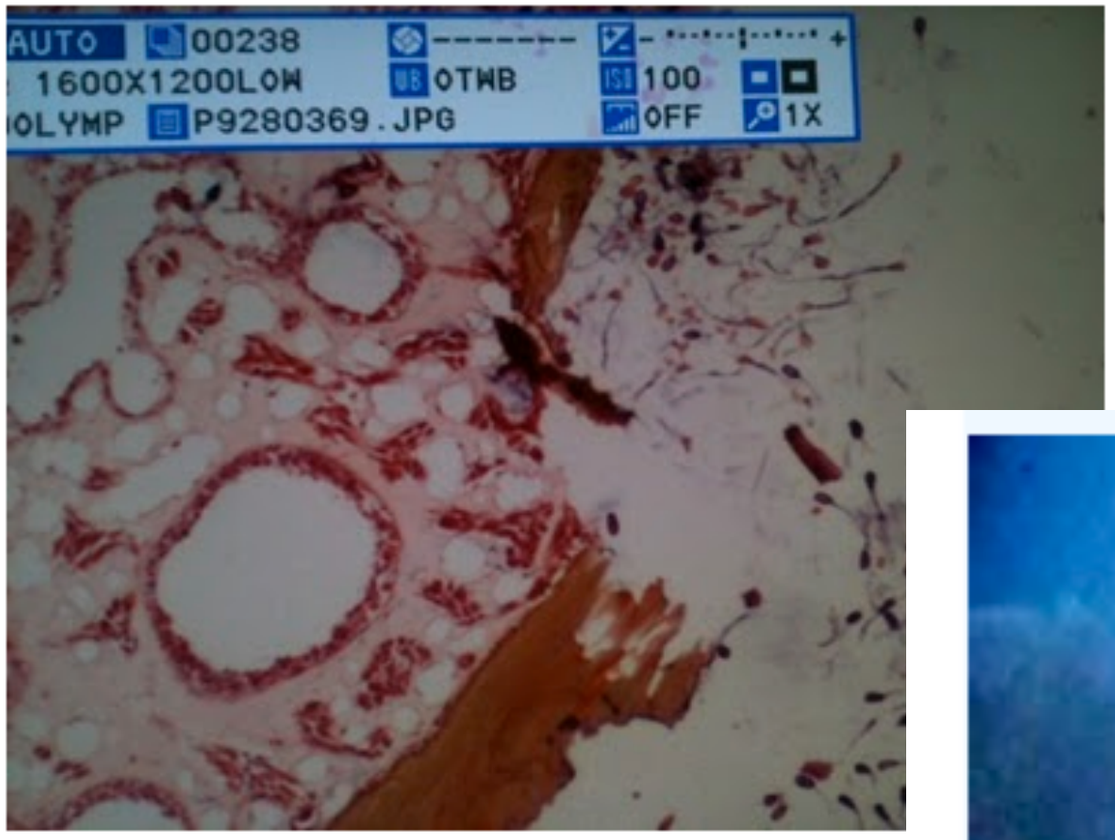
arrows point to sea grass Labyrinthula, I think (40X), don't ask me about th



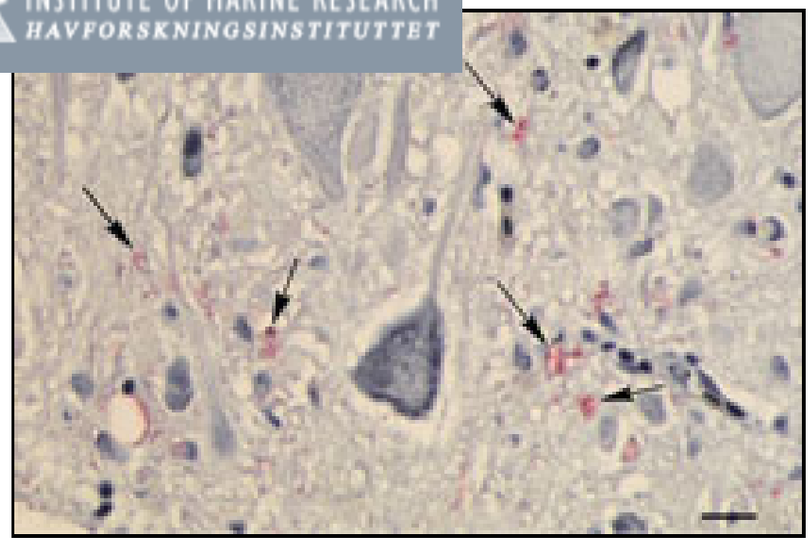
More photos from Colleen Burge

Colleen Burge - Sep 28, 2011 - Mobile - Limited

Really sad sea fan, really happy Laby



Virus - Nodavirus



Brain of salmon contaminated by nodavirus.

Development of diagnostic and management techniques to select cod broodstocks and hatchery stocks free from nodavirus

Northeastern Regional AQUACULTURE Center

Phage

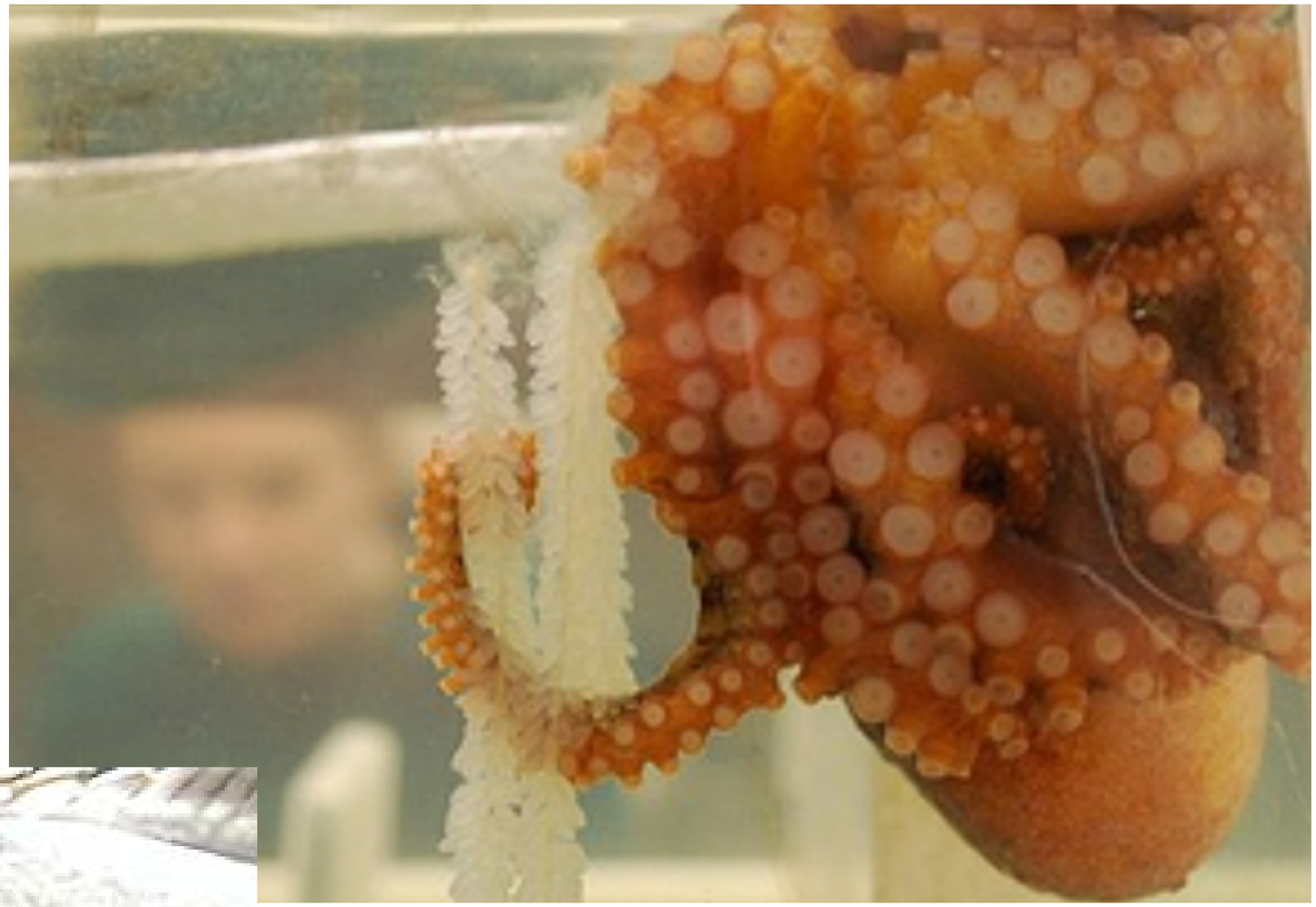
Abalone

Caused by a bacteria..

Immune Response

- **Innate Immunity - non-specific**
- Acquired Immunity- adaptive; selectively targets

Chemico-physical Barrier

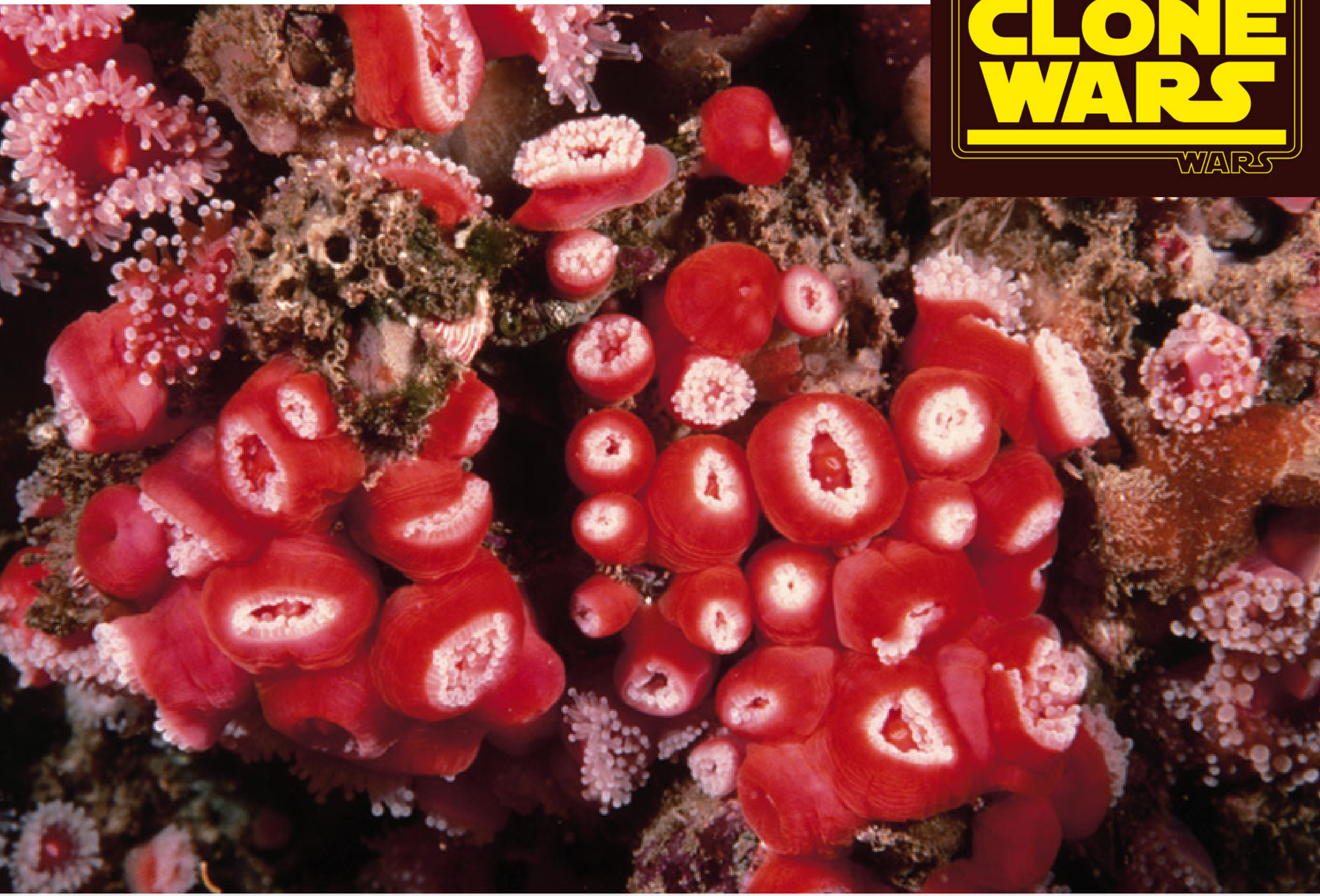


anti-microbial peptides

beneficial microbial communities

from the beginning...

How do organisms distinguish self from non-self?

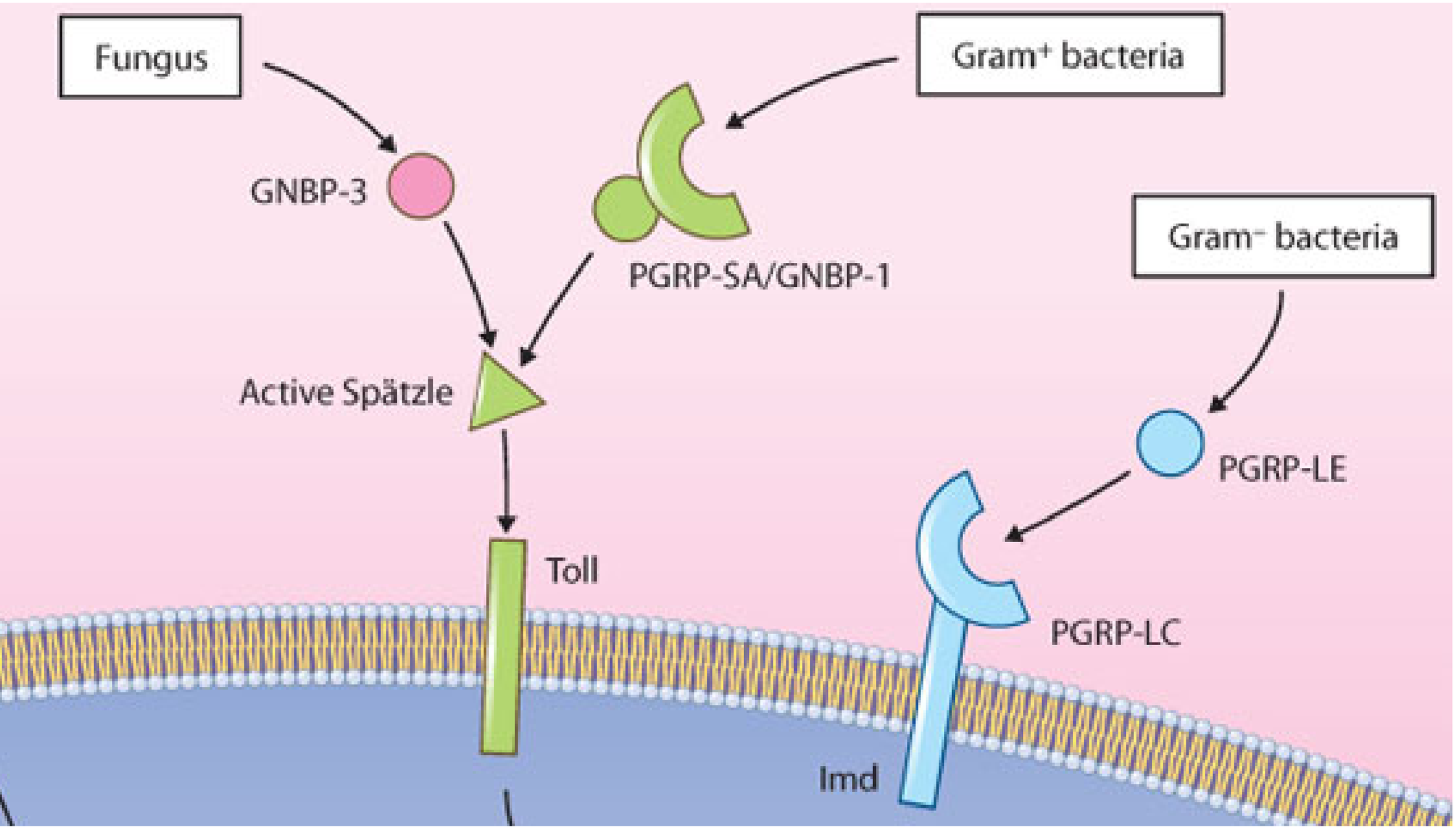


This is a picture of two *A elegantissima* or *A. sola* fighting with acrorhagia. Taken at San Simeon, CA by Dave Cowles i

How do organisms distinguish self from non-self?

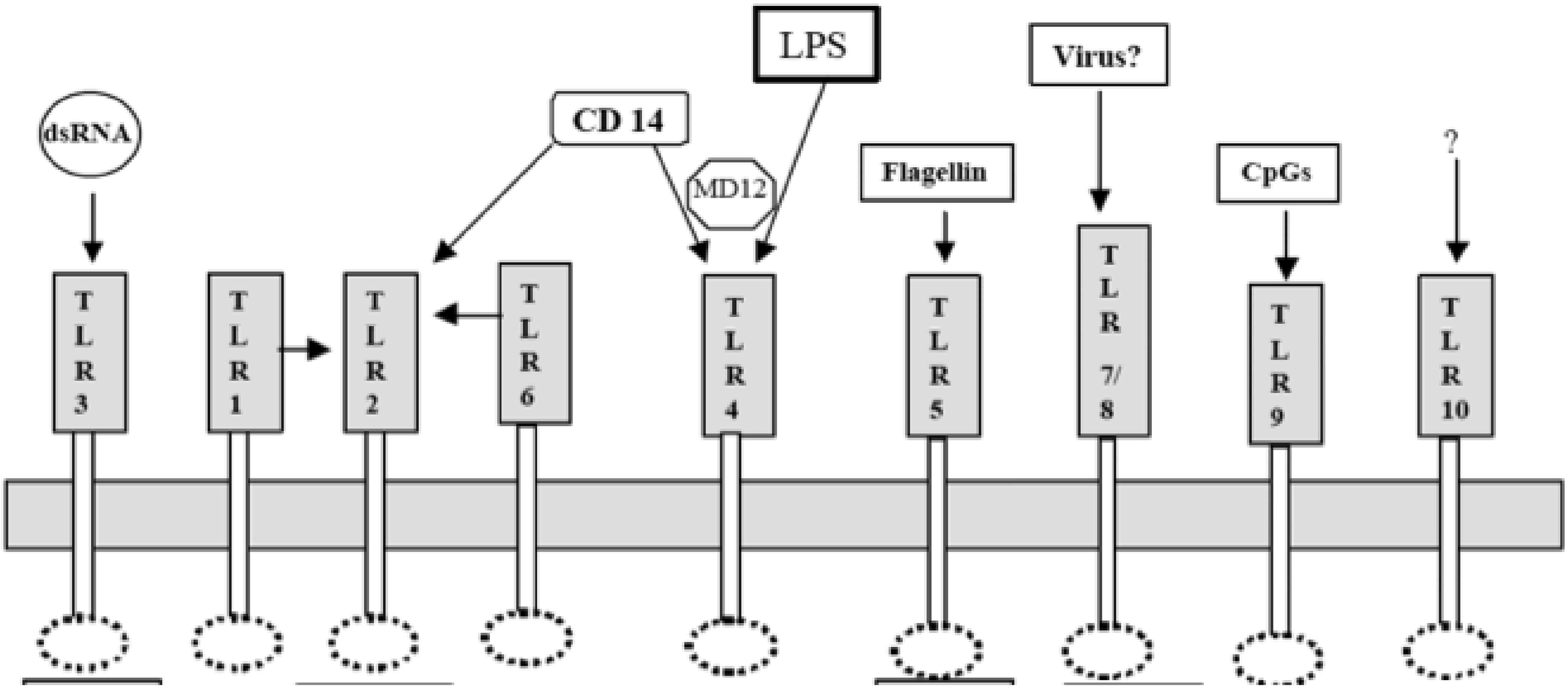
pattern recognitions proteins (PRPs)

PRPs



Toll-like Receptors
Peptidoglycan recognition proteins

PRPs - Toll-like Receptors



Soluble?

Soluble?

Week 3 we can look for them.

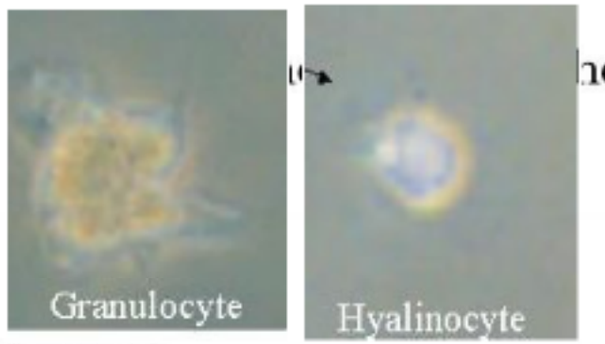
That's how the immune system knows bad things are there...

Innate Immunity

Chemico-physical barrier (shell, mucus)

Hemolymph

CELLS:



hemocytes

SERUM:
soluble lectins
hydrolytic enzymes
antimicrobial peptides

chemokinesis
chemotaxis
binding and internalization
oxidative burst activation
lysosomal enzymes
antimicrobial peptides

Laura Canesi, Gabriella Gallo, Miriam Gavioli, and Carla Pruzzo
Bacteria–hemocyte Interactions and Phagocytosis in Marine
Bivalves. 2002. Microscopy Research And Technique 57:469–476

Innate Immunity

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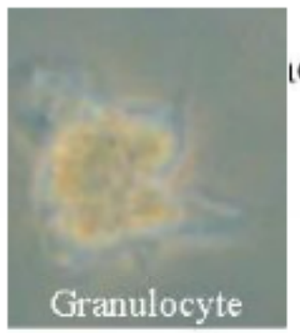

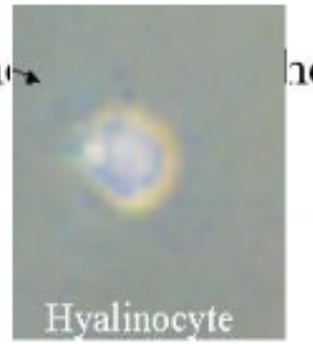

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What else?

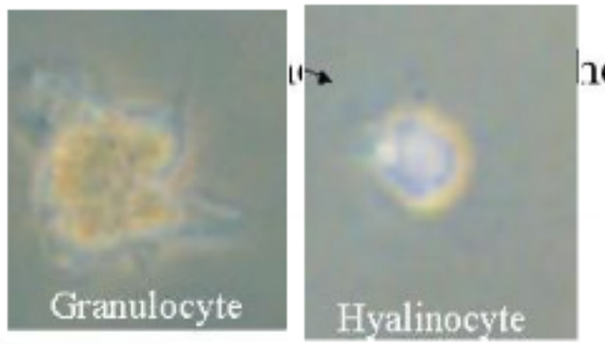
BUT WAIT - How do these immune cells know where to go?

Innate Immunity

Chemico-physical barrier (shell, mucus)

Hemolymph

CELLS:



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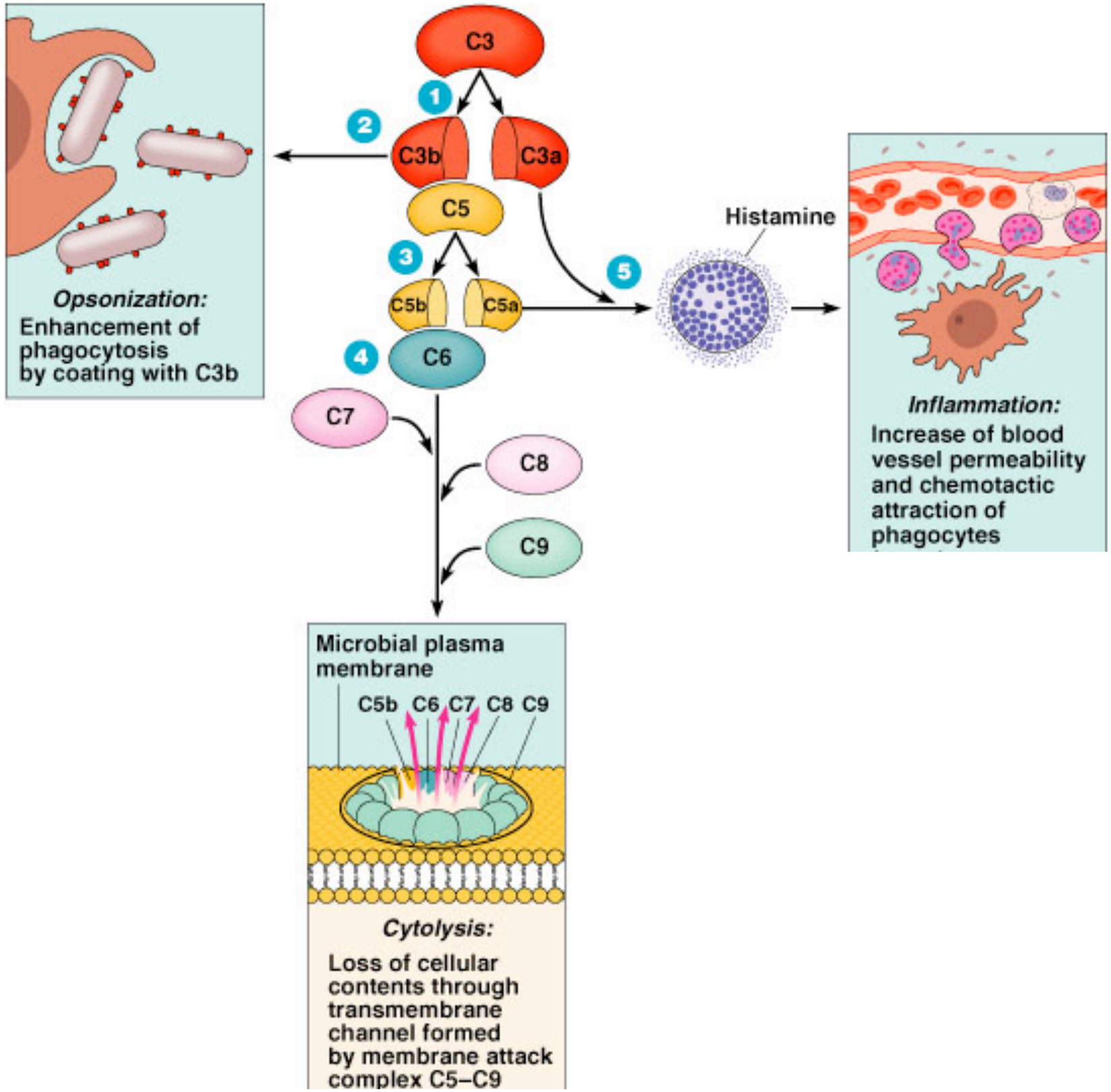
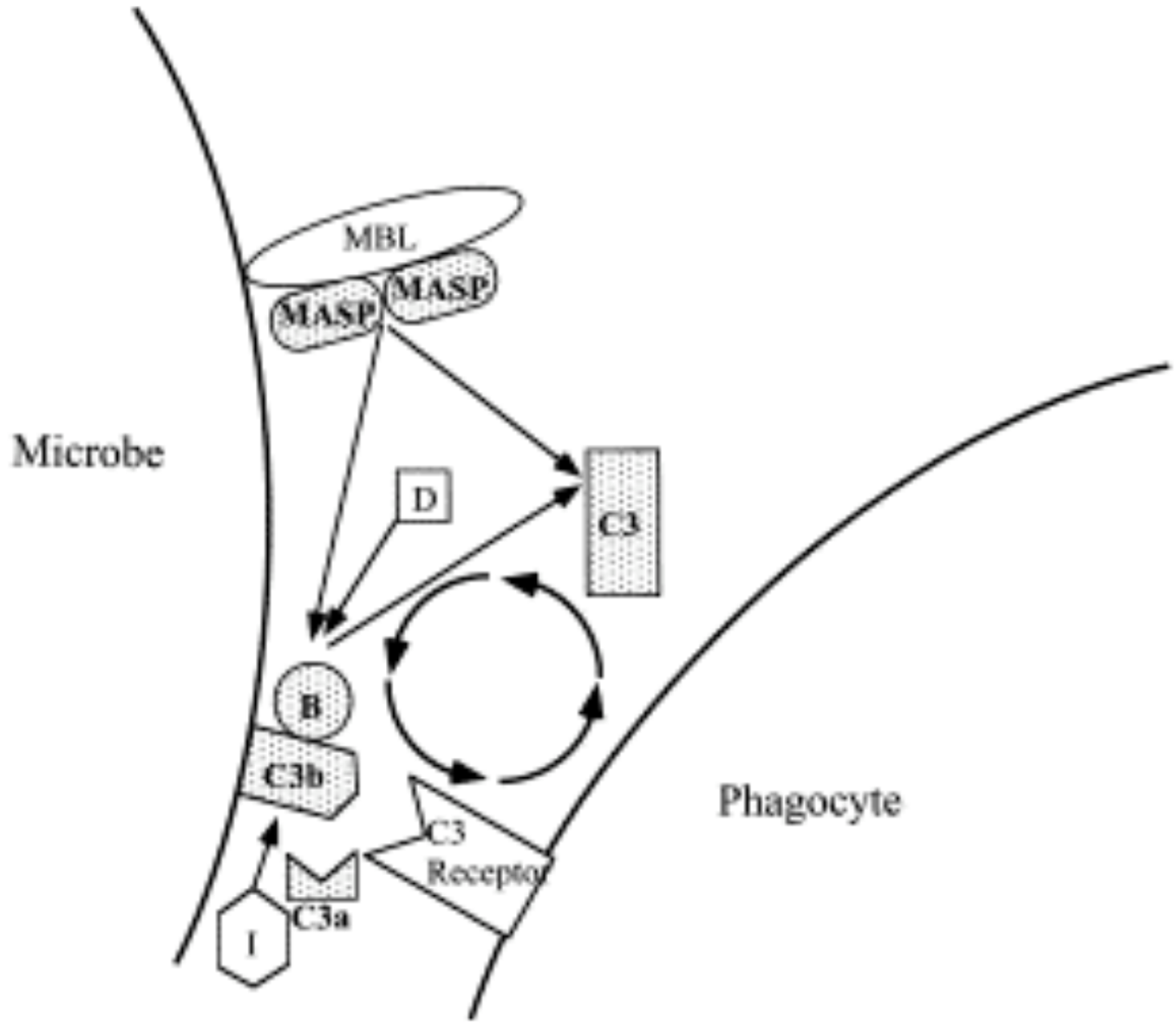
Complement System



Complement System - Invertebrates



Complement systems in invertebrates. The ancient alternative and lectin pathways

L. Courtney Smith[a,*], Kaoru Azumi[b] and Masaru Nonaka[c]

Immune Response

- **Innate Immunity** - non-specific
- Acquired Immunity

Today: *Physiological Response* to things that are bad

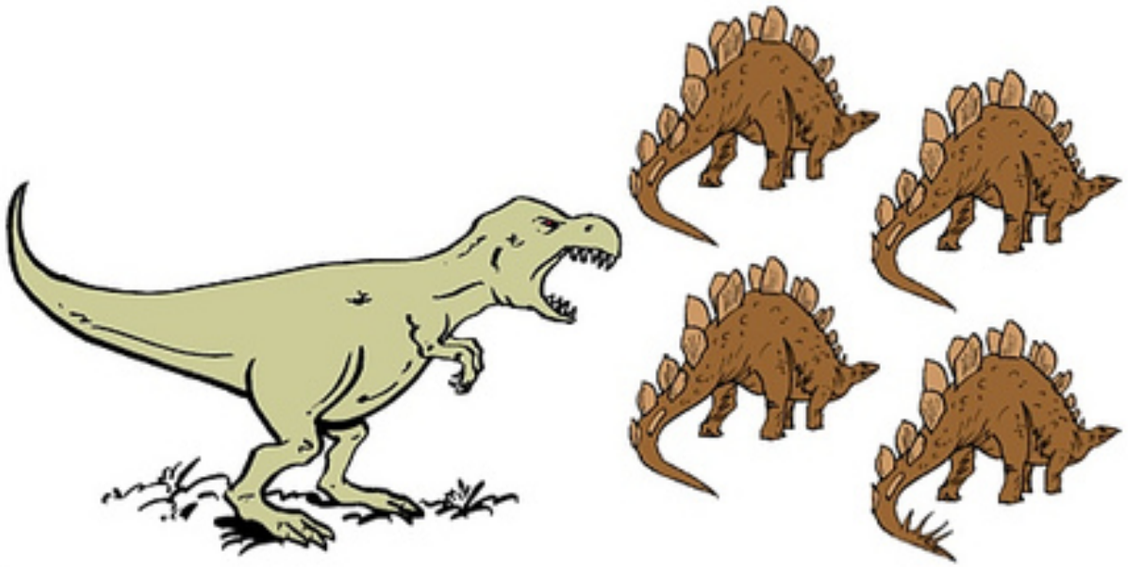
It is important the think about the big picture.

What else is going on with the critter...

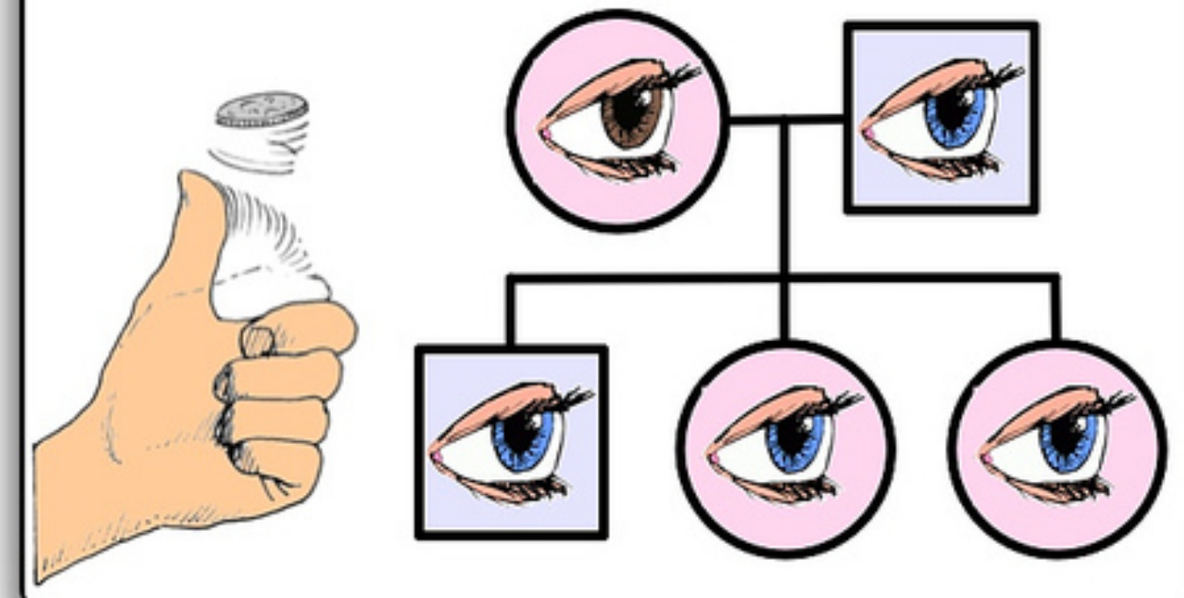
really big picture -

What has the population experienced.

NATURAL SELECTION

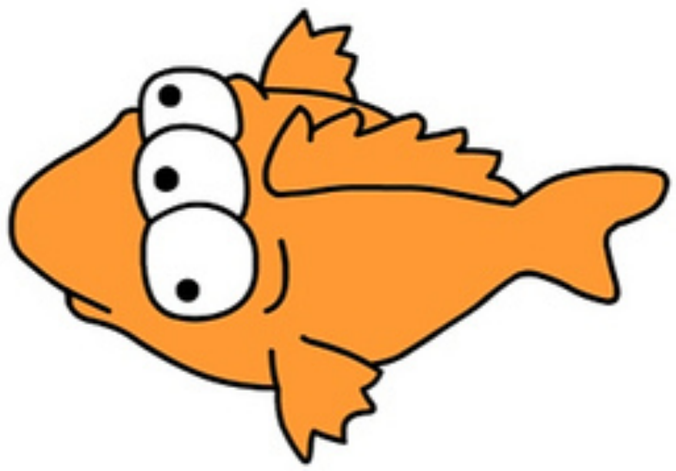


GENETIC DRIFT

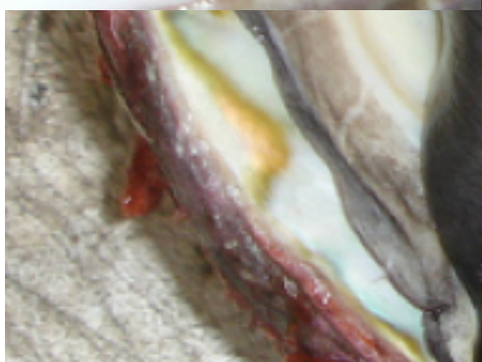


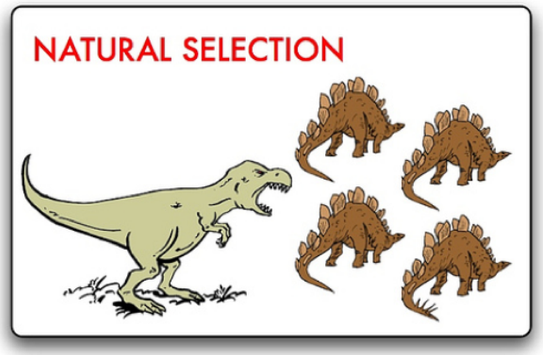
MIGRATION

MUTATION



Two part story





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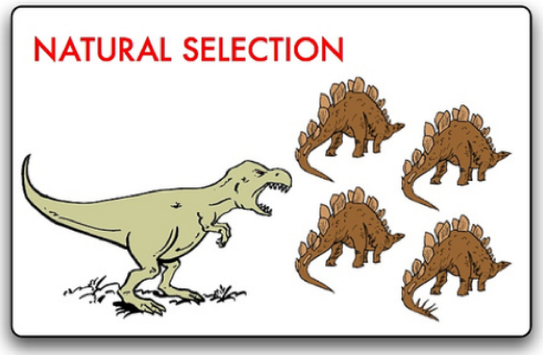
Roxannna Smolowitz
Rick Karney

Disease Resistance ?



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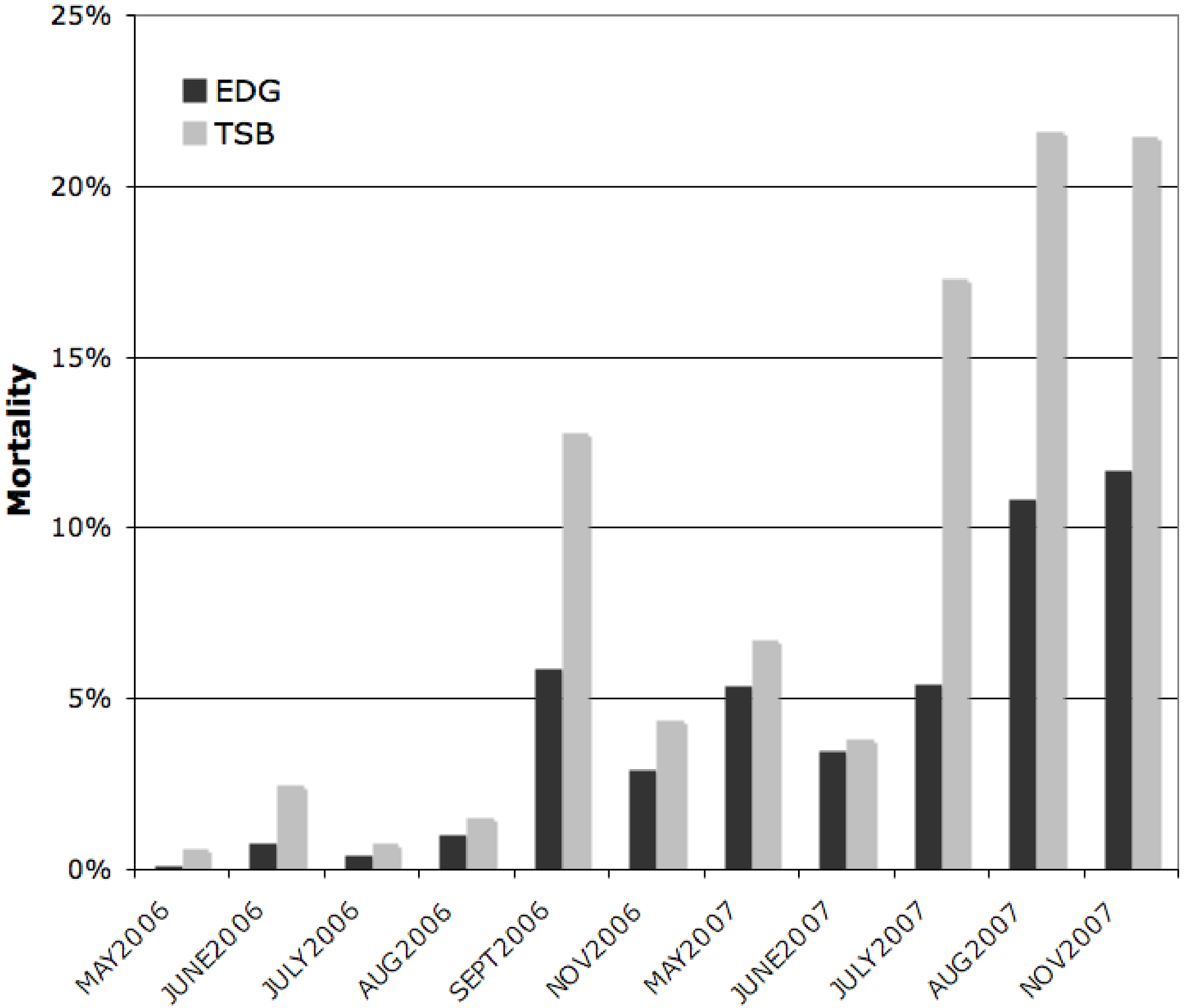
Roxannna Smolowitz
Rick Karney


Water Rd
Bold Water Rd
Kanonika Rd
Kanonika Rd
Brown
Meeting House Way
Hotchkiss Ln
Wilson's Landing
Rd to the Plains
Court St
Zoll Rd
Wilson's Landing
Wilson's Landing
Meeti
Jacob's Neck Rd
Bold Water Rd
Turkeyland Cove Rd
Turkeyland Cove Rd
Kingspoint Way
Loon Cove Rd
Slough Cove Rd
Motick Trail
Jacob's Neck Rd
Jacob's Neck Rd
Swan Lake Farm
Eastern Point
Jobes Neck Cove Rd
Eastern Point
Swan Lake Farm
Edgartown
Great Pond
Slough Cove Rd
Herring Creekfarm Rd
Herring Creekfarm Rd
Fuller's Cove Rd
Crackatuxet Cove Rd
Great Pai
Garden Cove Rd
Crackatuxet
Cove


25%
20%
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Mortality
EDG
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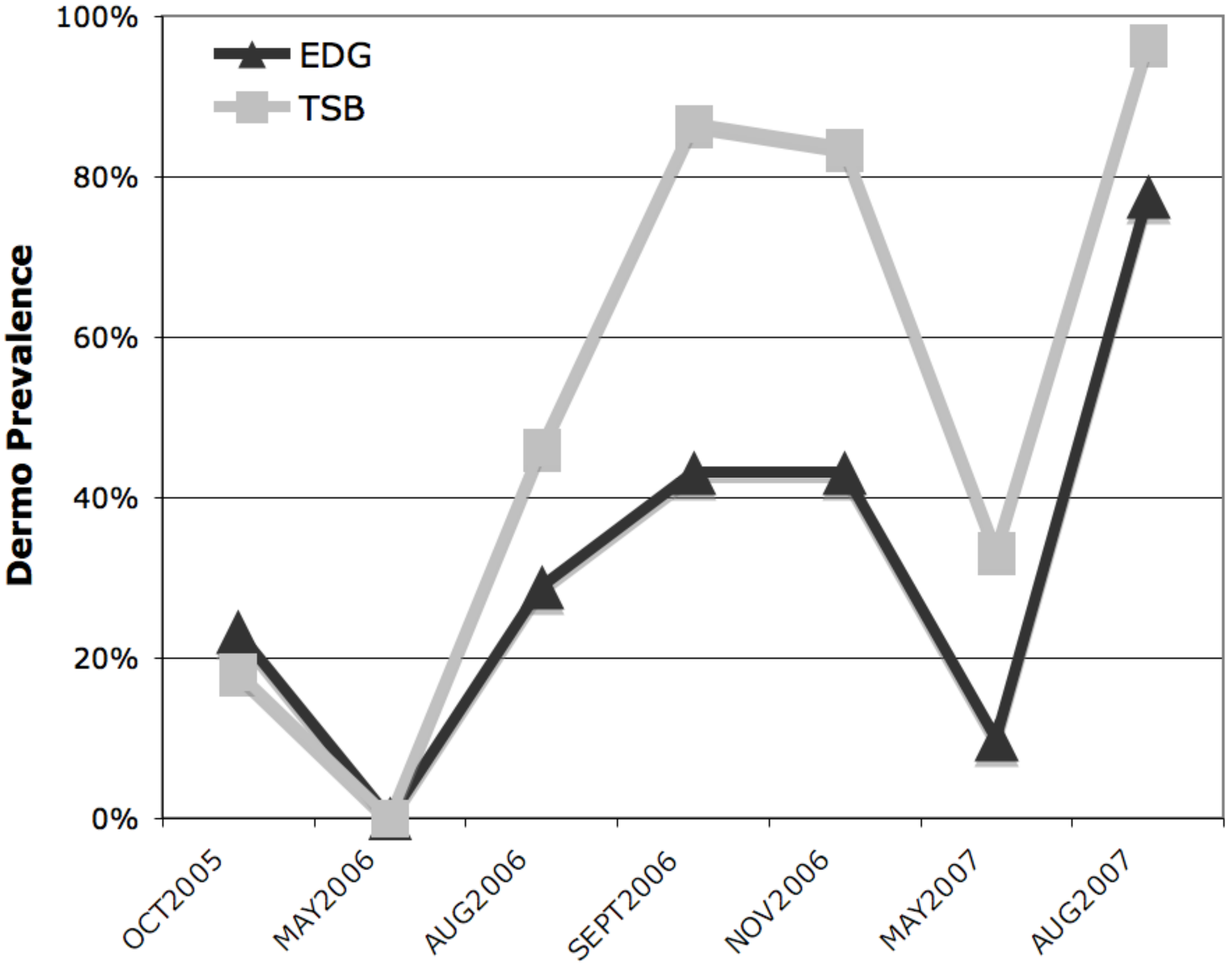
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80%
60%
40%
20%
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Dermo Prevalence
EDG
TSB
OCT2005
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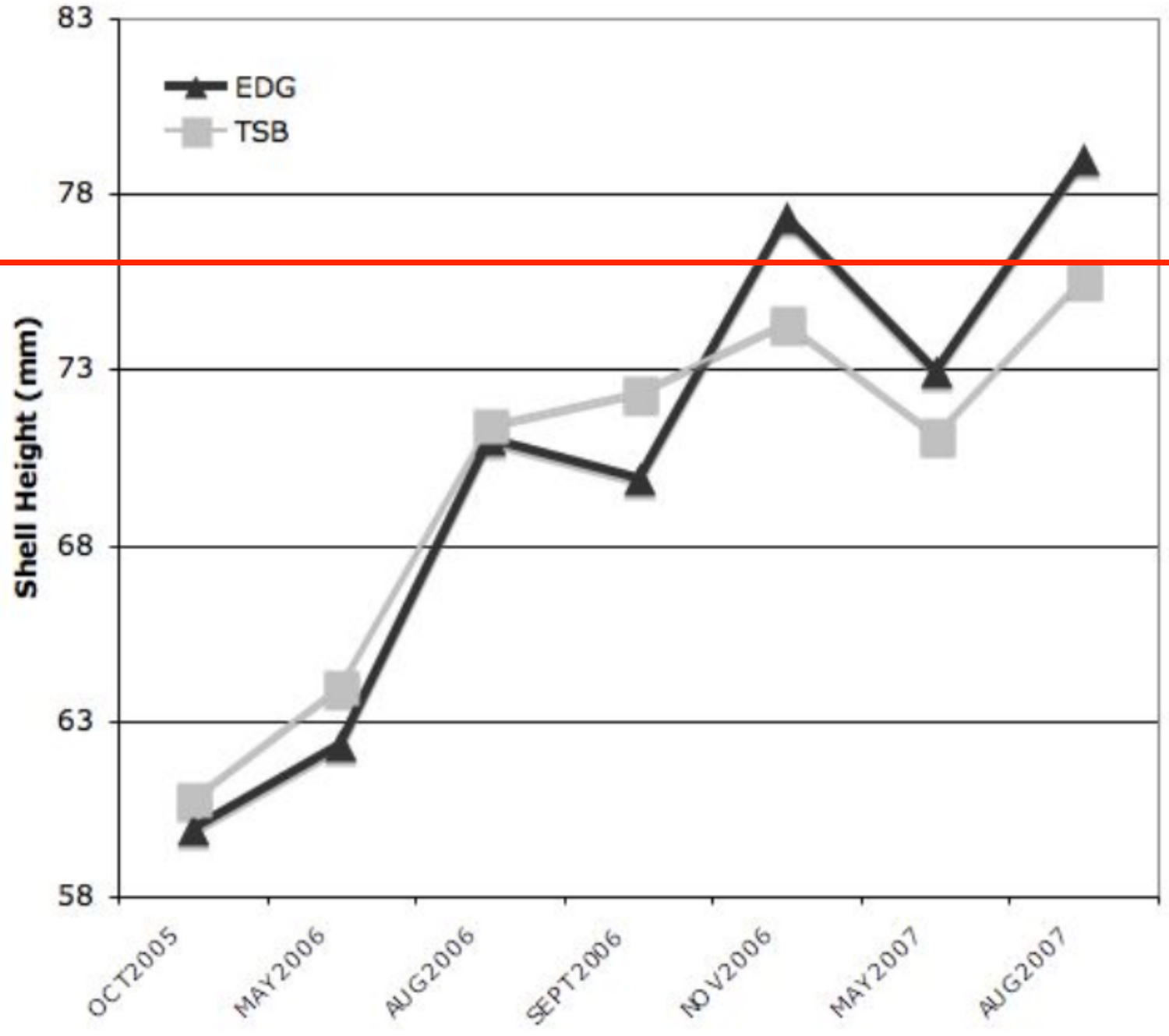
SEPT2006
NOV2006
MAY2007
AUG2007

Market size


83
78
73
68
63
58
EDG
TSB
Shell Height (mm)
OCT2005
MAY2006
AUG2006
SEPT2006
NOV2006
MAY2007
AUG2007

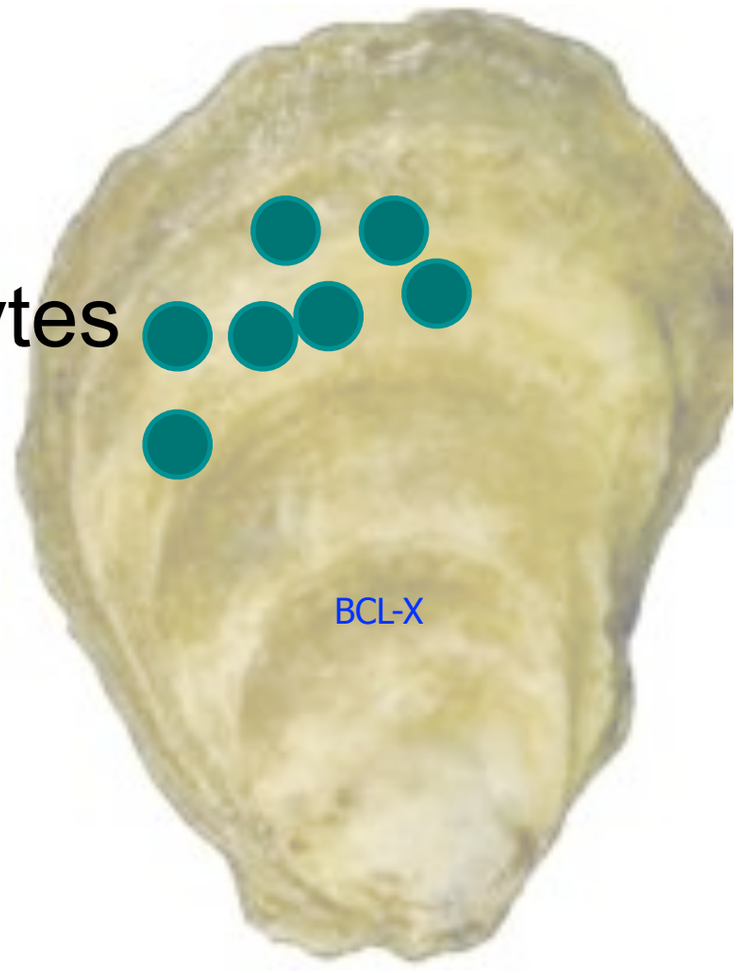
Mechanisms

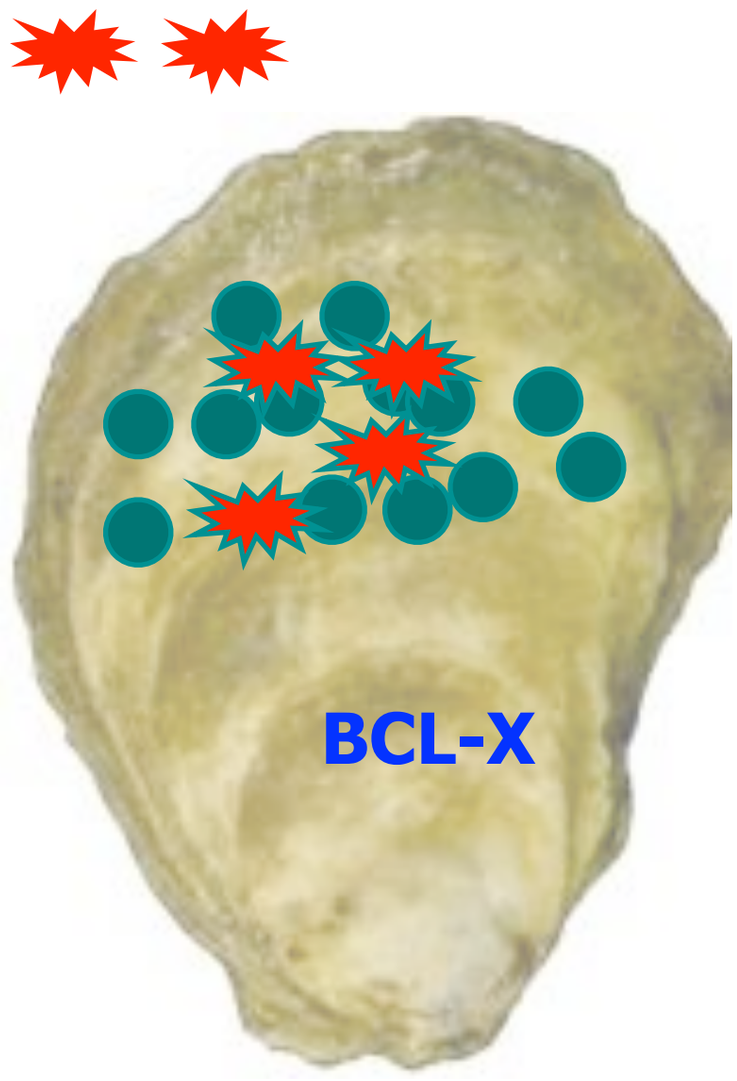
They are different,
but how / why?

Schematic

Parasite

Hemocytes





Resistant

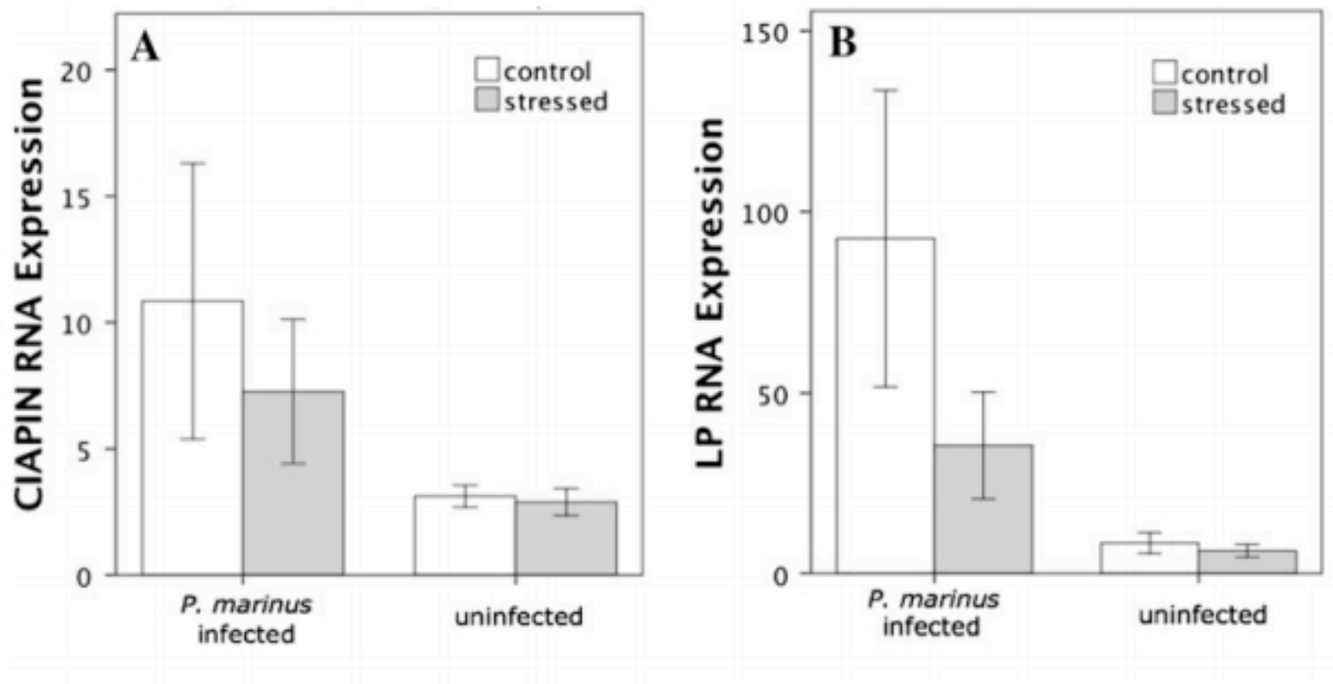
Wild-type

Apoptosis – BCL-X

- Resistant oyster strains could downregulate apoptosis suppression
- Allowing for increased apoptosis
- Decreasing number of cells available for *Perkinsus* proliferation

Immune response and mechanical stress susceptibility in diseased oysters, *Crassostrea virginica*

Steven B. Roberts · Inke Sunila · Gary H. Wikfors



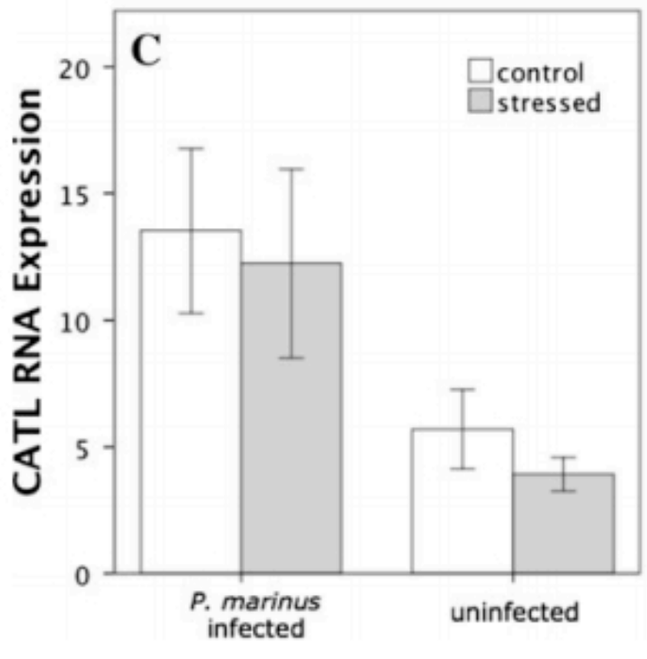


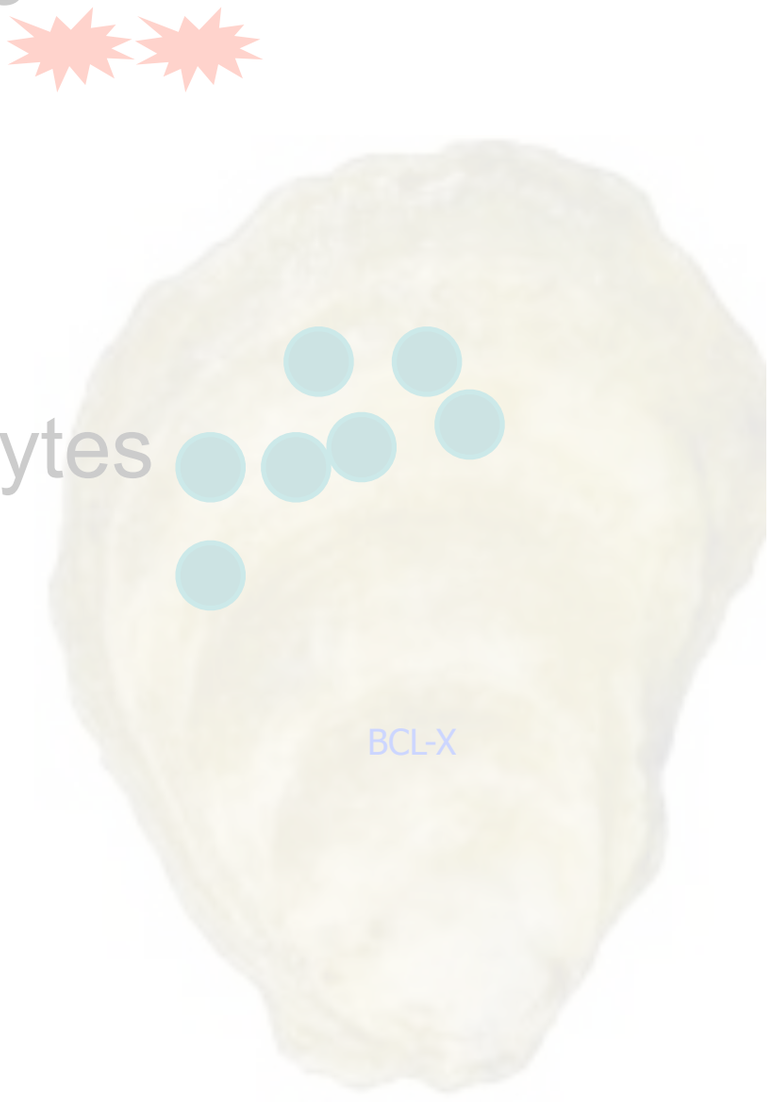
Table 2 Hematology of oysters, *C. virginica*, from two cohorts, infected with *P. marinus* ($n = 17$) and uninfected ($n = 19$), determined by flow cytometry (mean ± SE)

	P. marinus infected	Uninfected
Granular cells × 10^6 ml^{-1}	0.214 ± 0.0556	0.0614 ± 0.014
Agranular cells × 10^6 ml^{-1}	2.27 ± 0.458	0.586 ± 0.065
Granular cell diameter in µm	8.52 ± 0.30	11.4 ± 0.20
Agranular cell diameter in µm	5.31 ± 0.10	6.29 ± 0.31

No effect of mechanical stress was observed; therefore, data from stressed and unstressed were combined

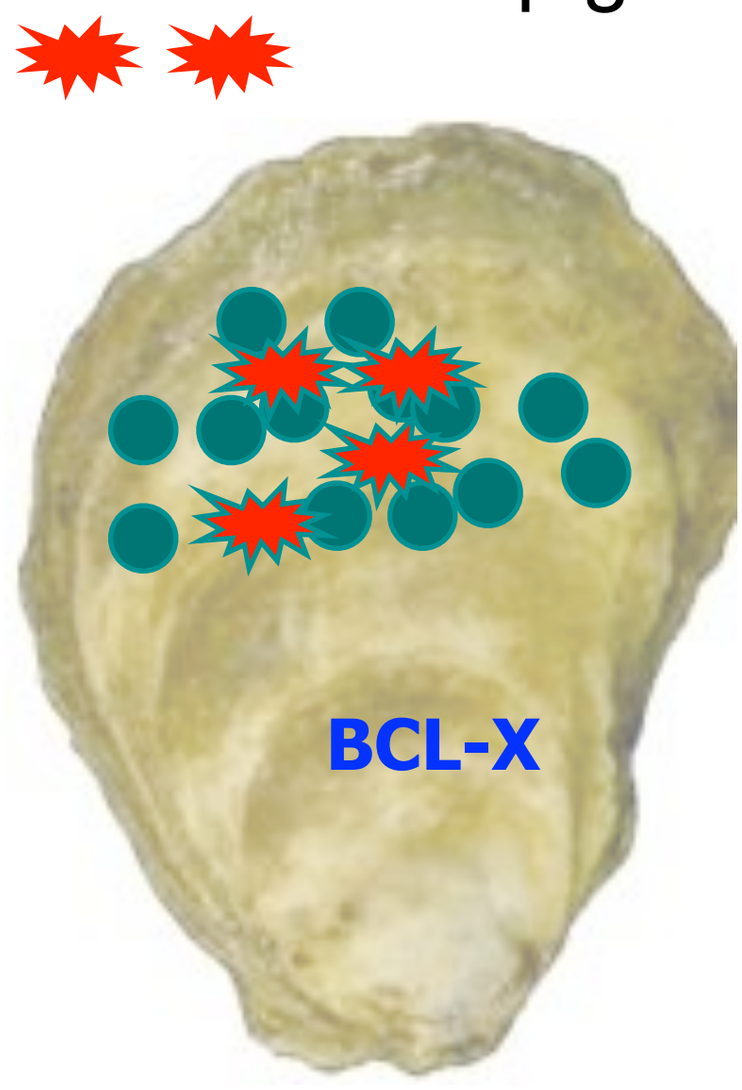
Schematic

Parasite



Resistant

Epigenetic?



Wild-type

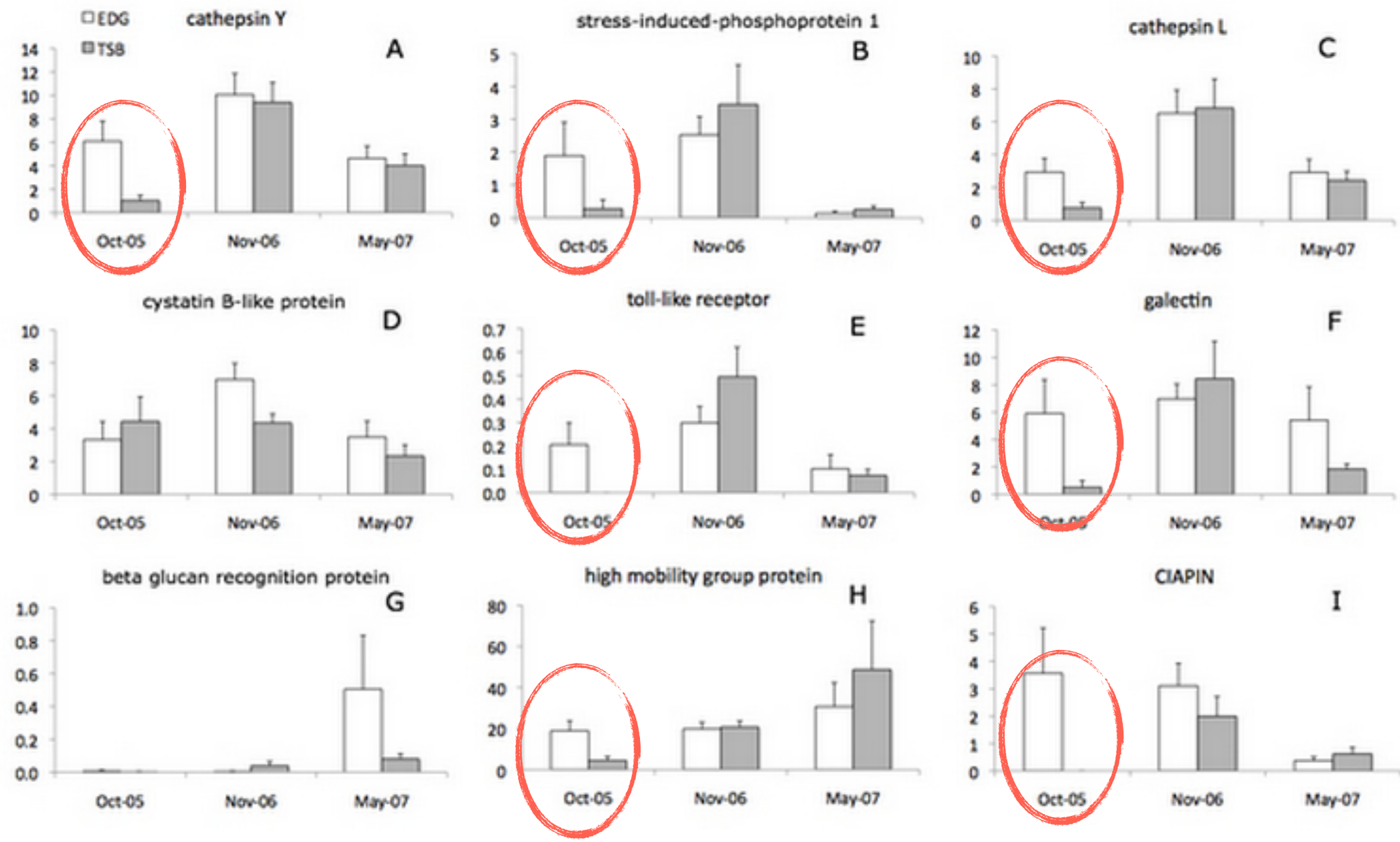
Summary - Oyster

- Offspring of survivors of heavy disease pressure are more tolerant to disease
- Mechanisms involved in host responses to *P. marinus* include proteases and apoptosis

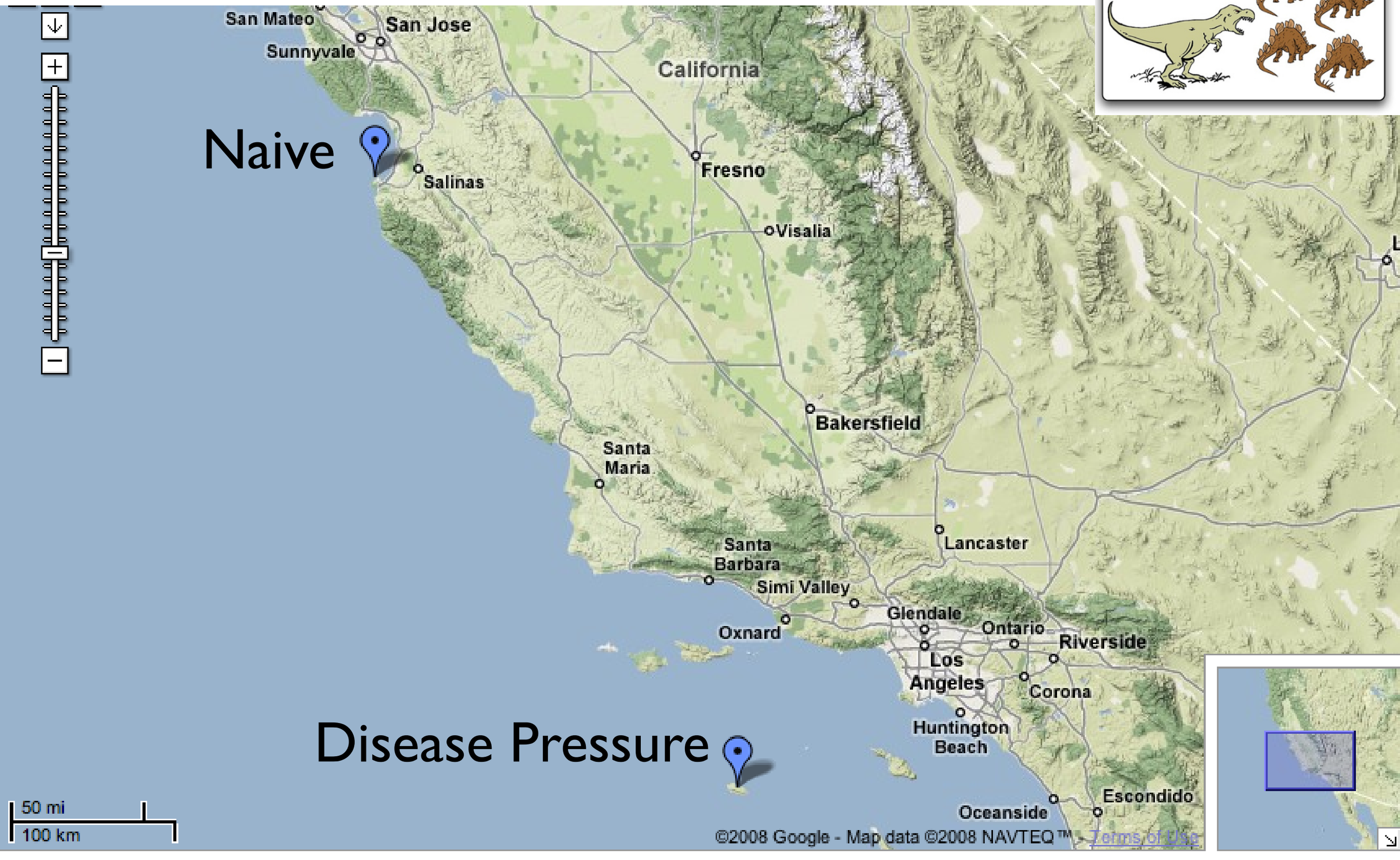
General Observation

on selection

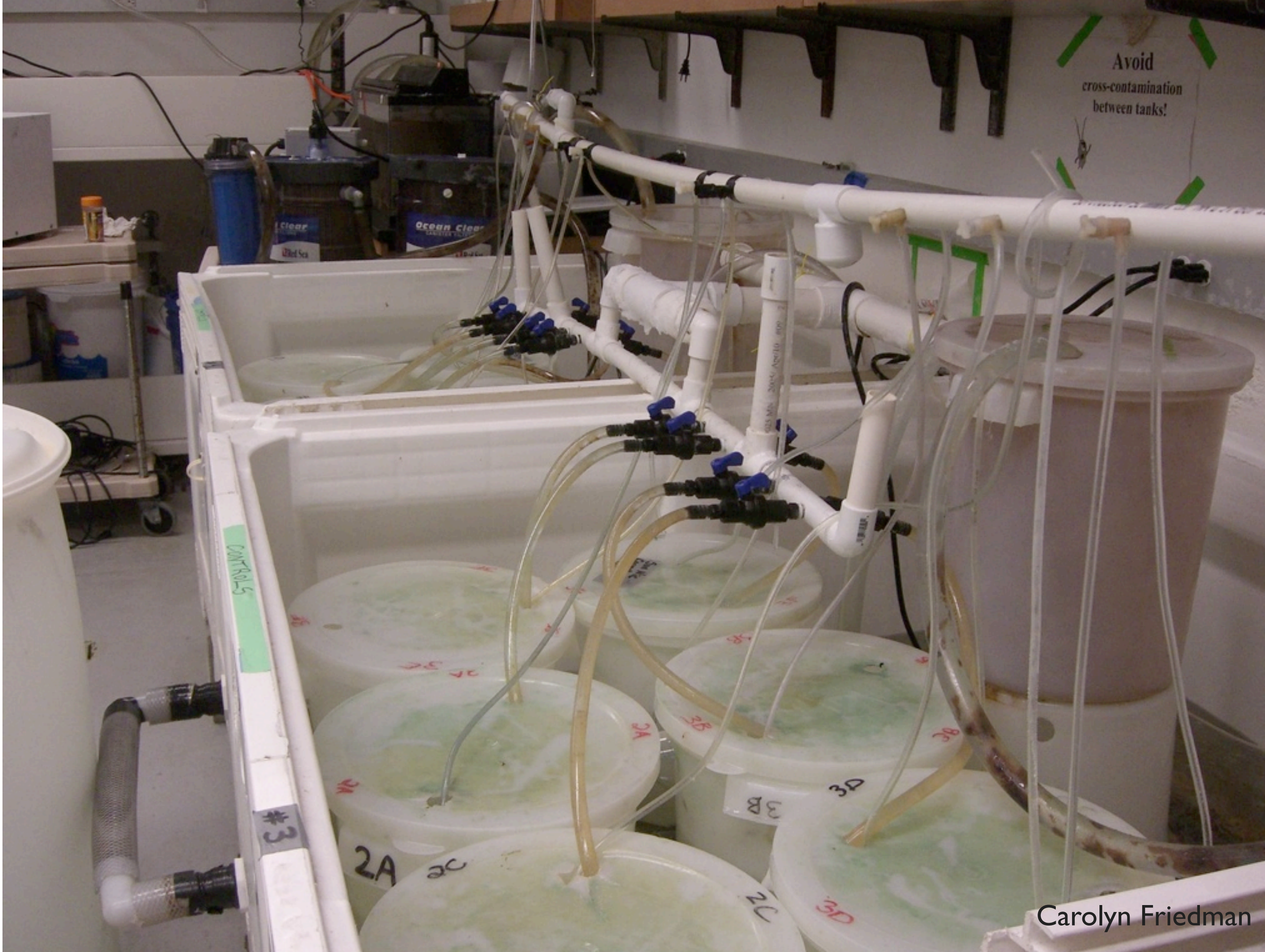
General Observation



Abalone

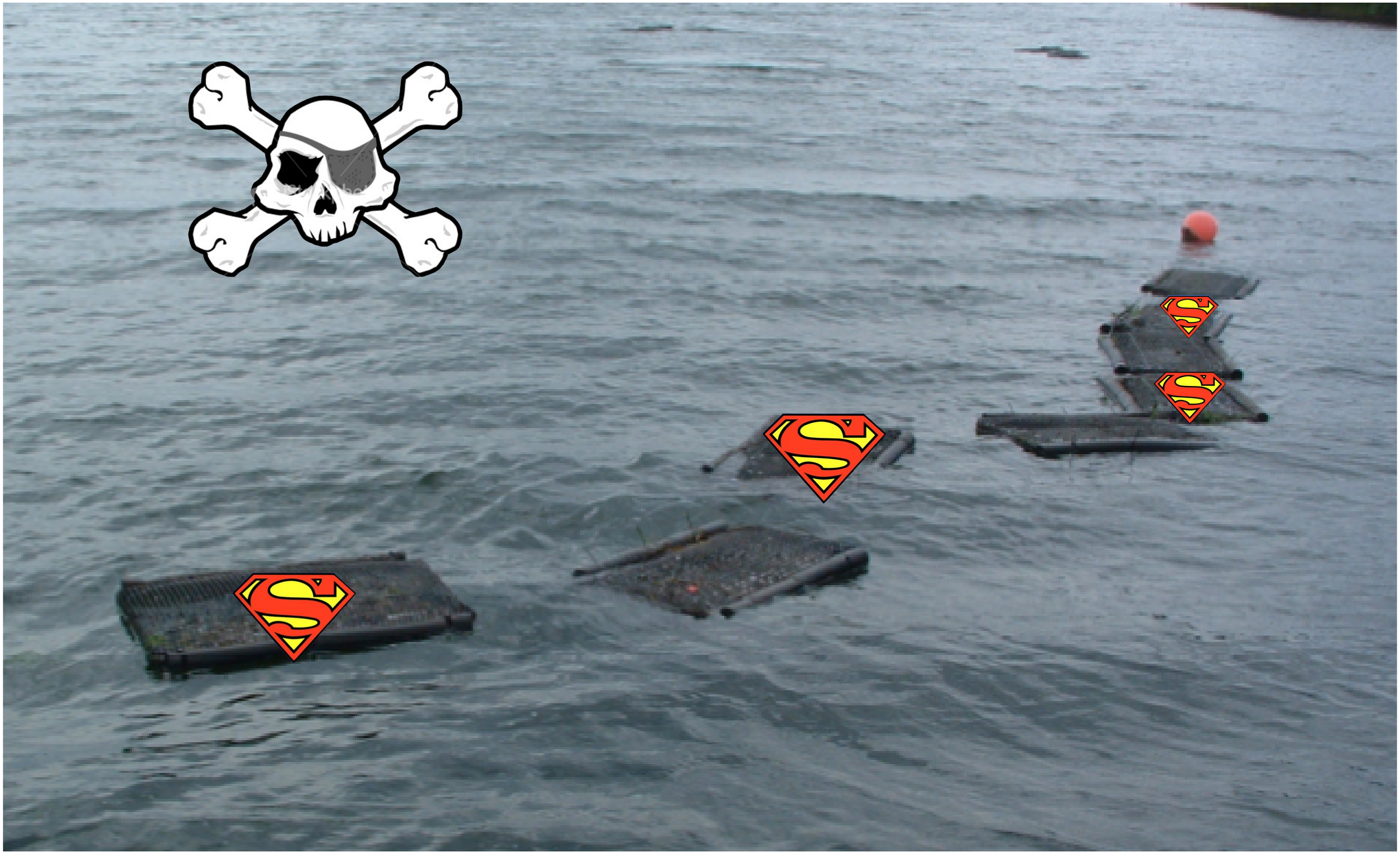


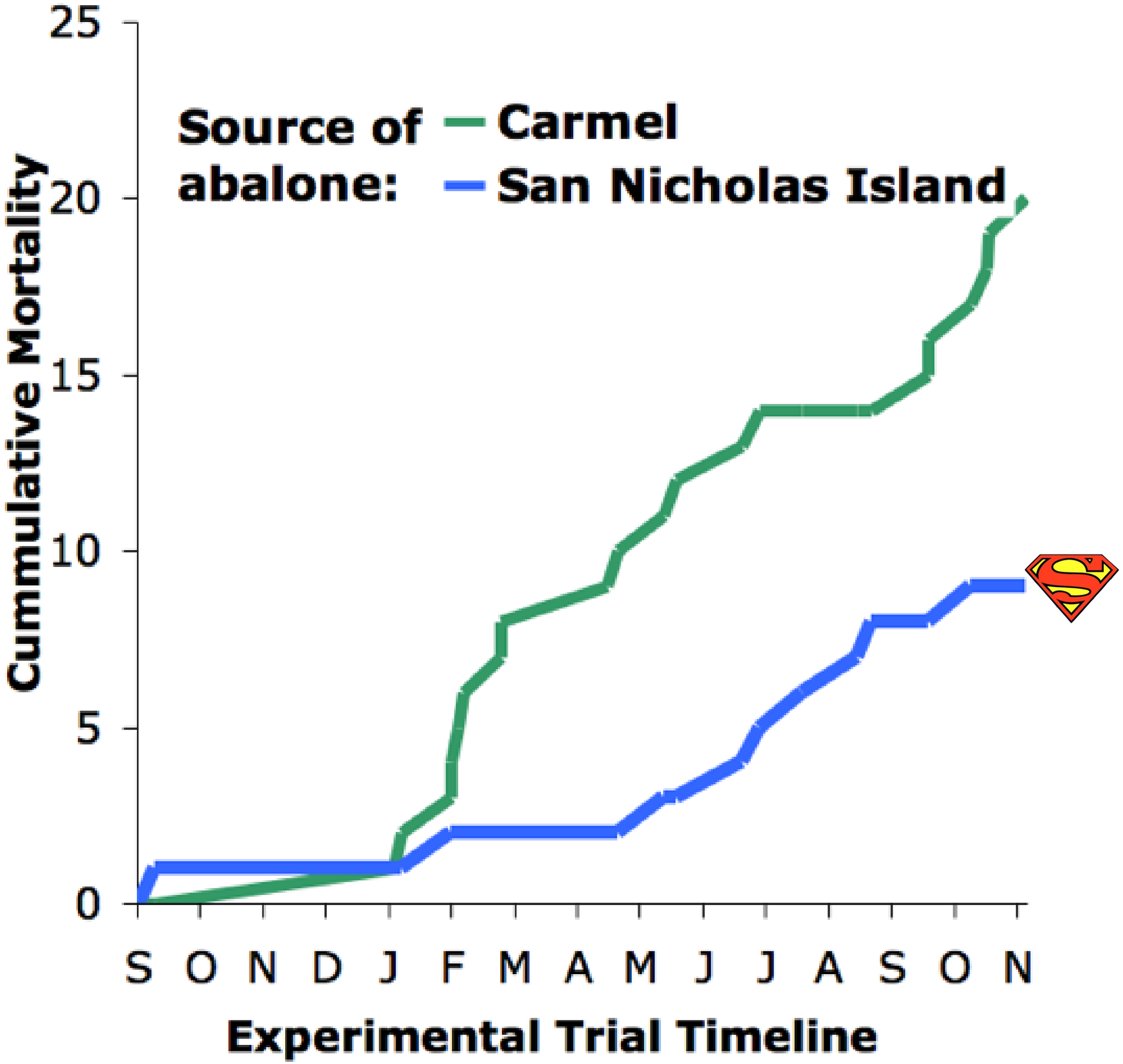
Glenn VanBlaricom, Carolyn Friedman

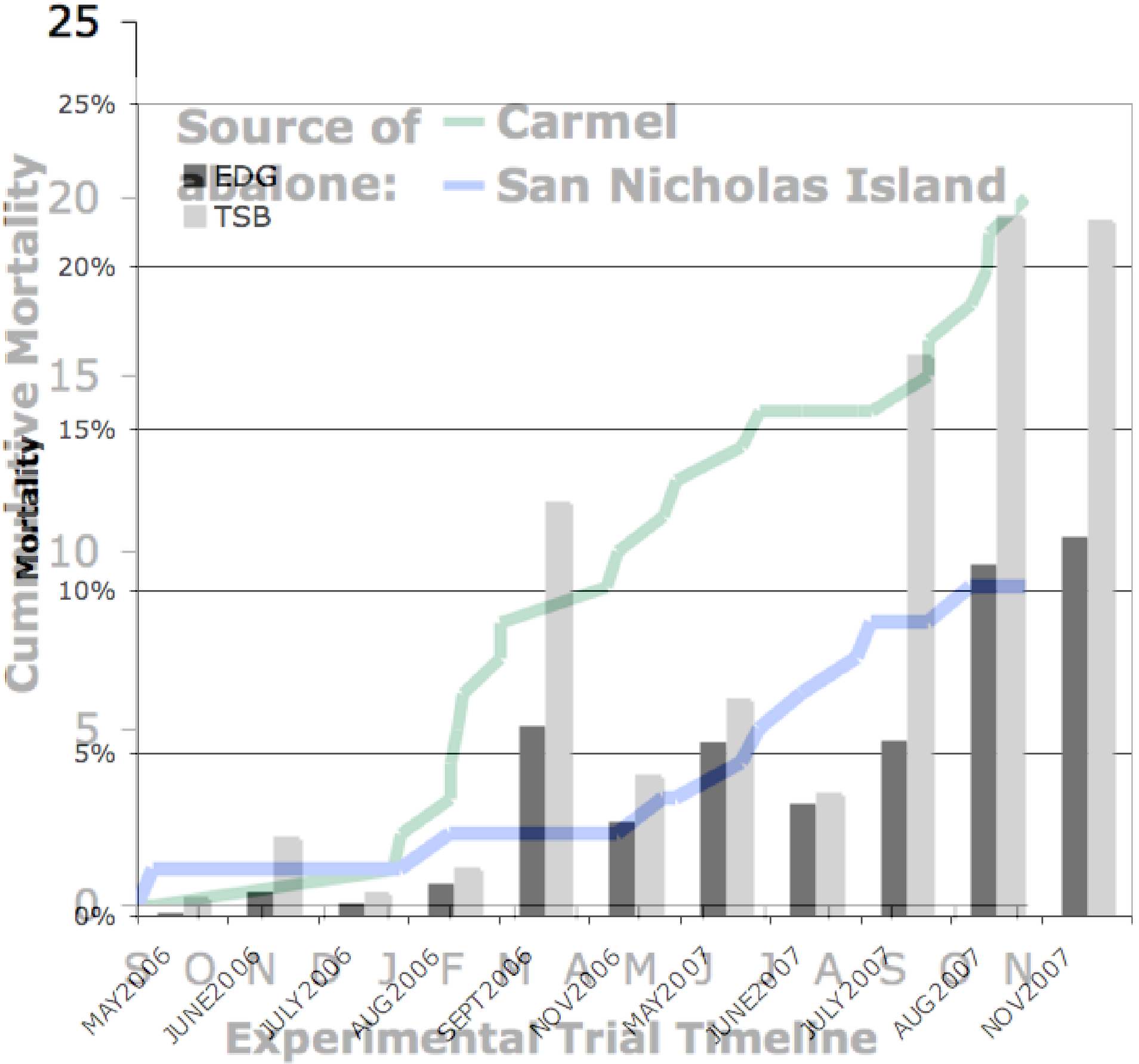

Avoid
cross-contamination
between tanks!
Ocean Clear
Red Sea
CONTROLS
#3
2A
2C
3B
3D
Carolyn Friedman

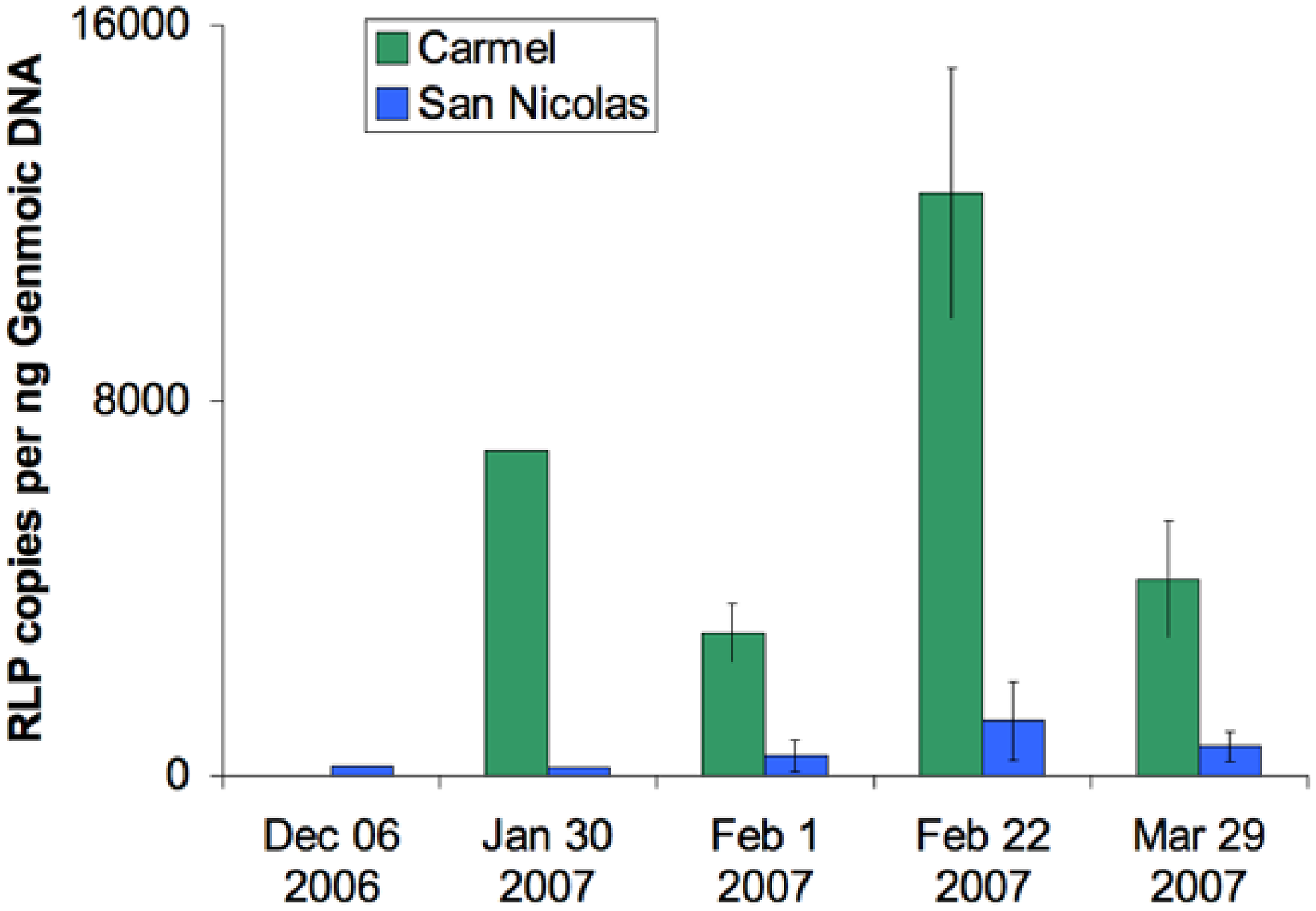
Carolyn Friedman

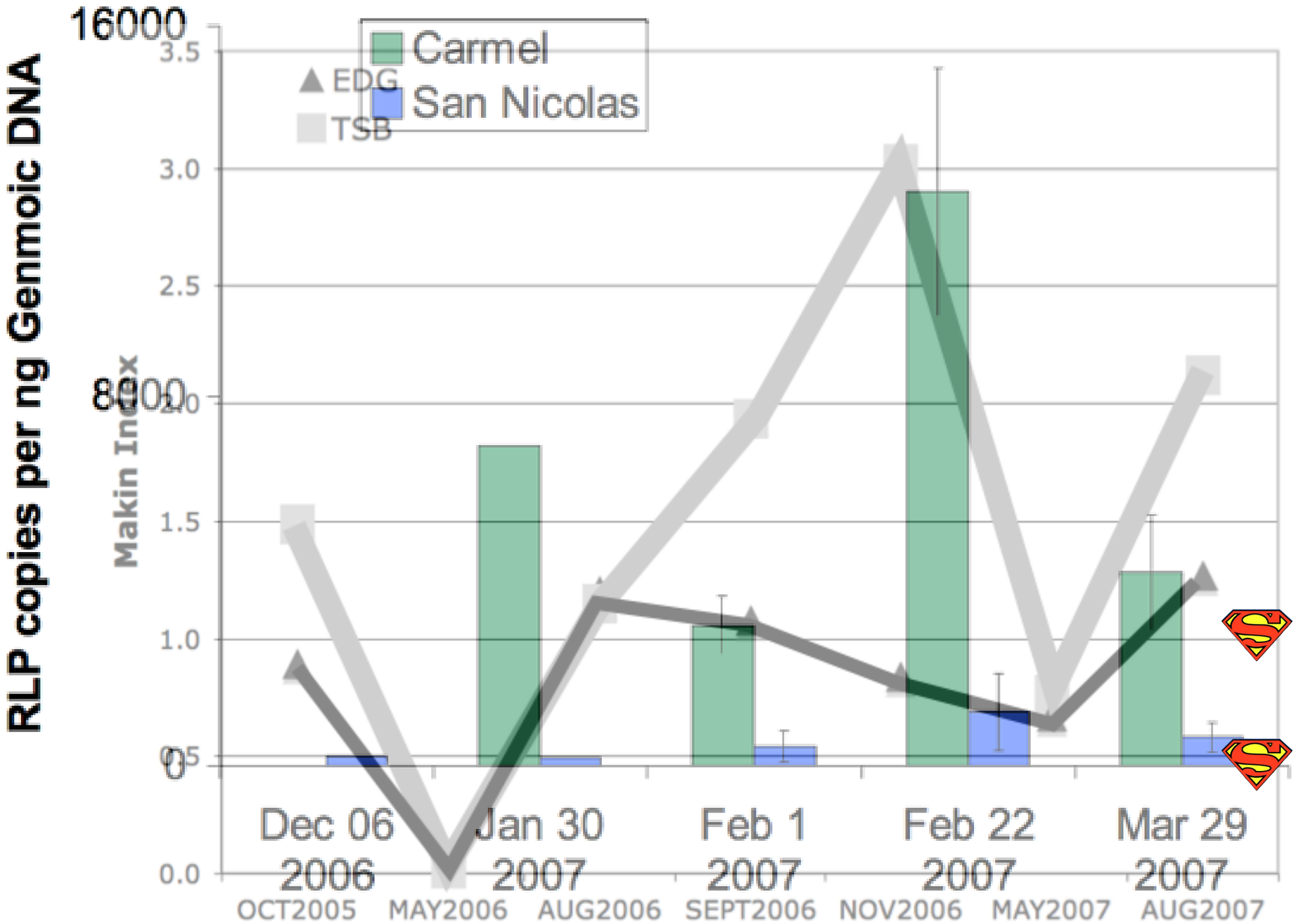
analagous to ...




Source of abalone:
Carmel
San Nicholas Island
Cumulative Mortality
25
20
15
10
5
0
S O N D J F M A M J J A S O N
Experimental Trial Timeline


25
25%
20
20%
15
15%
10
10%
5
5%
0
0%
Cumulative Mortality
Source of abalone:
EDG
TSB
Carmel
San Nicholas Island
S O N D J F M A M J J A S O N
MAY2006
JUNE2006
JULY2006
AUG2006
SEPT2006
NOV2006
MAY2007
JUNE2007
JULY2007
AUG2007
NOV2007
Experimental Trial Timeline


RLP copies per ng Genmoic DNA
16000
8000
0
Carmel
San Nicolas
Dec 06
2006
Jan 30
2007
Feb 1
2007
Feb 22
2007
Mar 29
2007


RLP copies per ng Genmoic DNA
16000
8000
0
Makin Index
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Carmel
San Nicolas
EDG
TSB
Dec 06 2006
Jan 30 2007
Feb 1 2007
Feb 22 2007
Mar 29 2007
OCT2005
MAY2006
AUG2006
SEPT2006
NOV2006
MAY2007
AUG2007

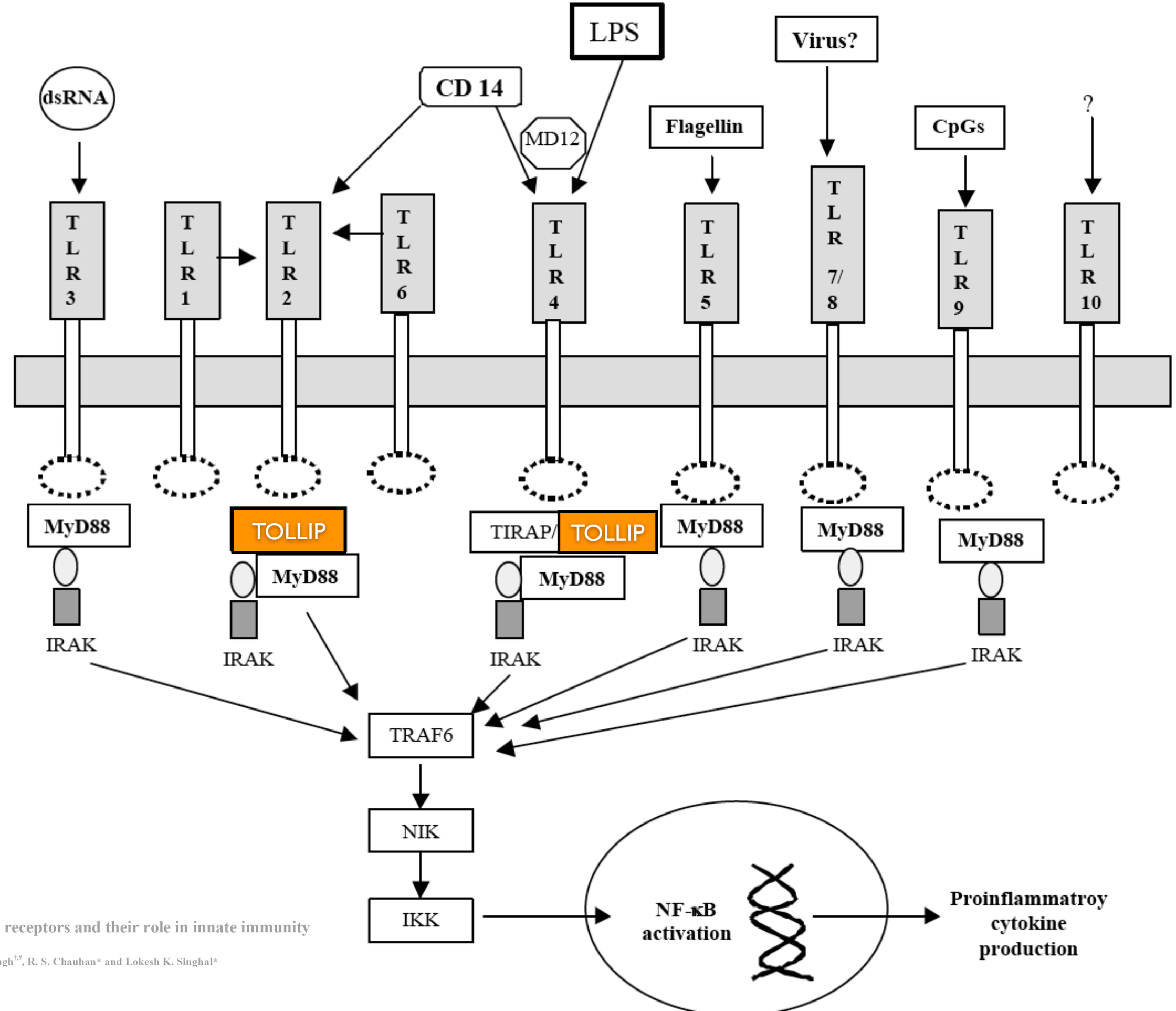
Increased Resistance

Better survival AND less pathogen load

How?

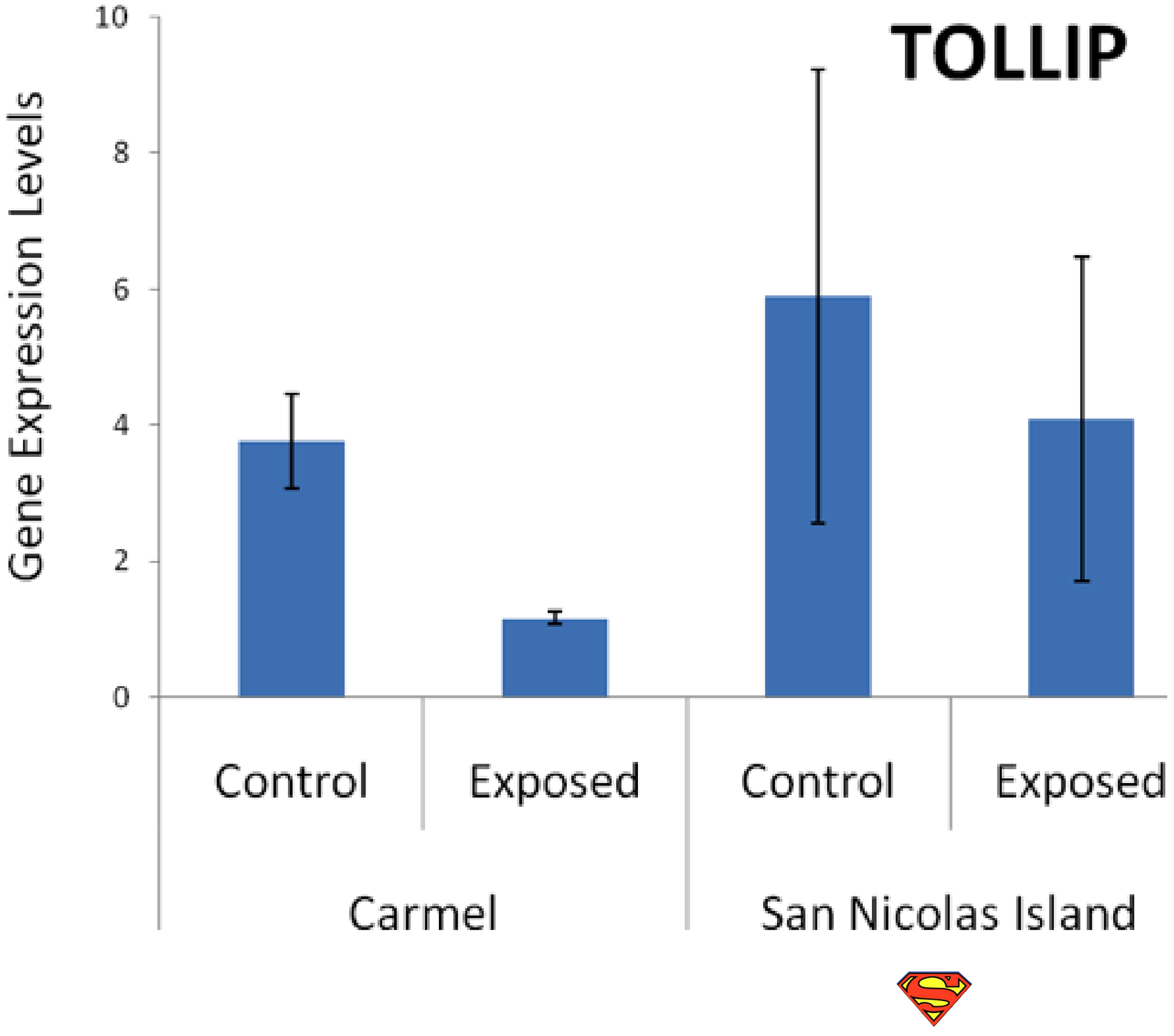
Differences?

Only Lisa Knows



Toll-like receptors and their role in innate immunity

Bhanu P. Singh[+,#], R. S. Chauhan* and Lokesh K. Singhal*


TOLLIP
Gene Expression Levels
10
8
6
4
2
0
Control
Exposed
Control
Exposed
Carmel
San Nicolas Island

bacteria recognition protein