

Host Response

FISH441 Lecture 15

Steven Roberts

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.

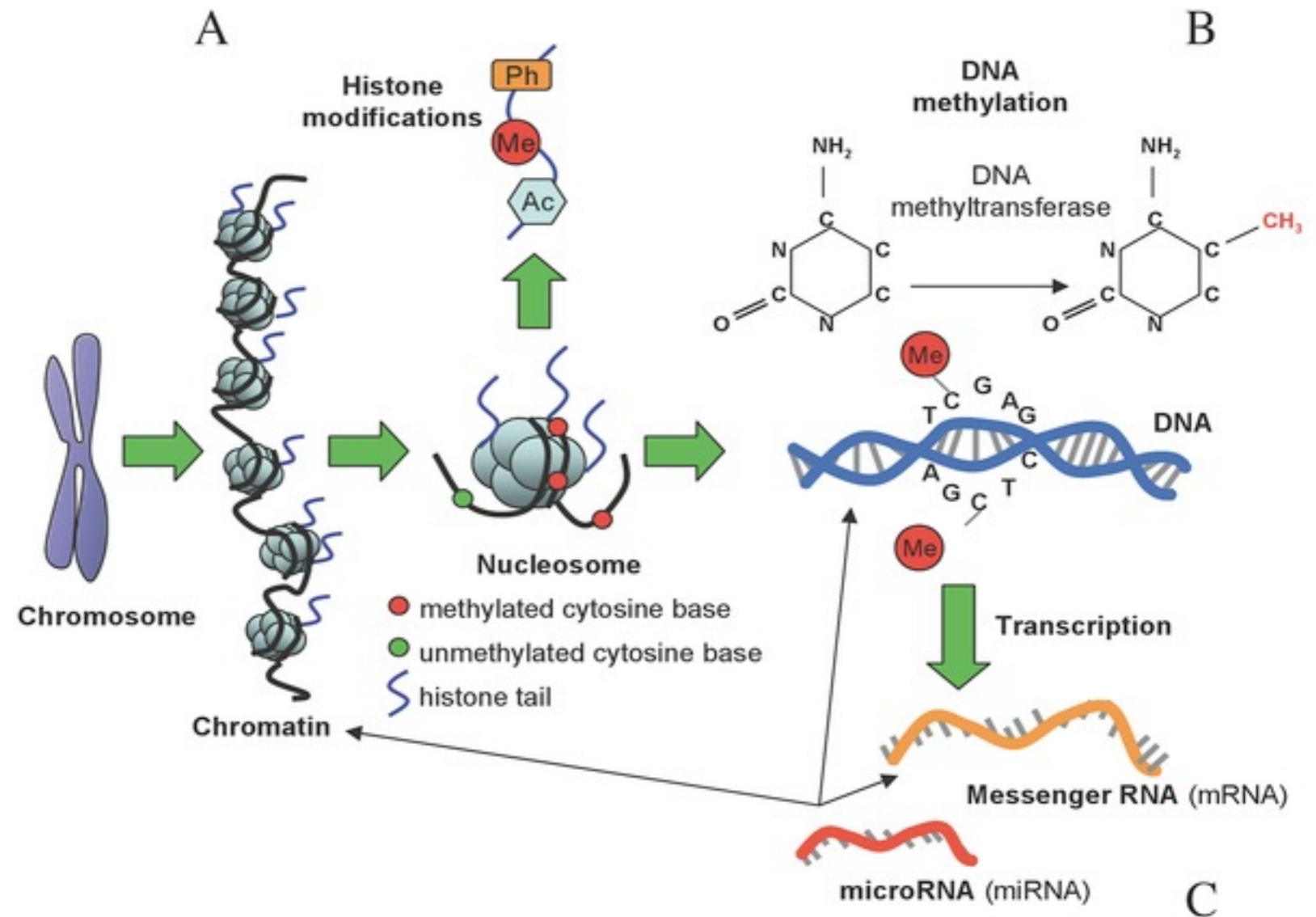
Innate immunity is classically defined as unable to build up immunological memory. Recently however, the assumption of the lack of immunological memory within innate immune responses has been reconsidered. Plants and invertebrates lacking adaptive immune system can be protected against secondary infections. 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- κ B 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

Host Response

Let's Anthropomorphize

What might scare marine invert?



Today: *Physiological Response* to things that are bad

It is important to 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 to 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

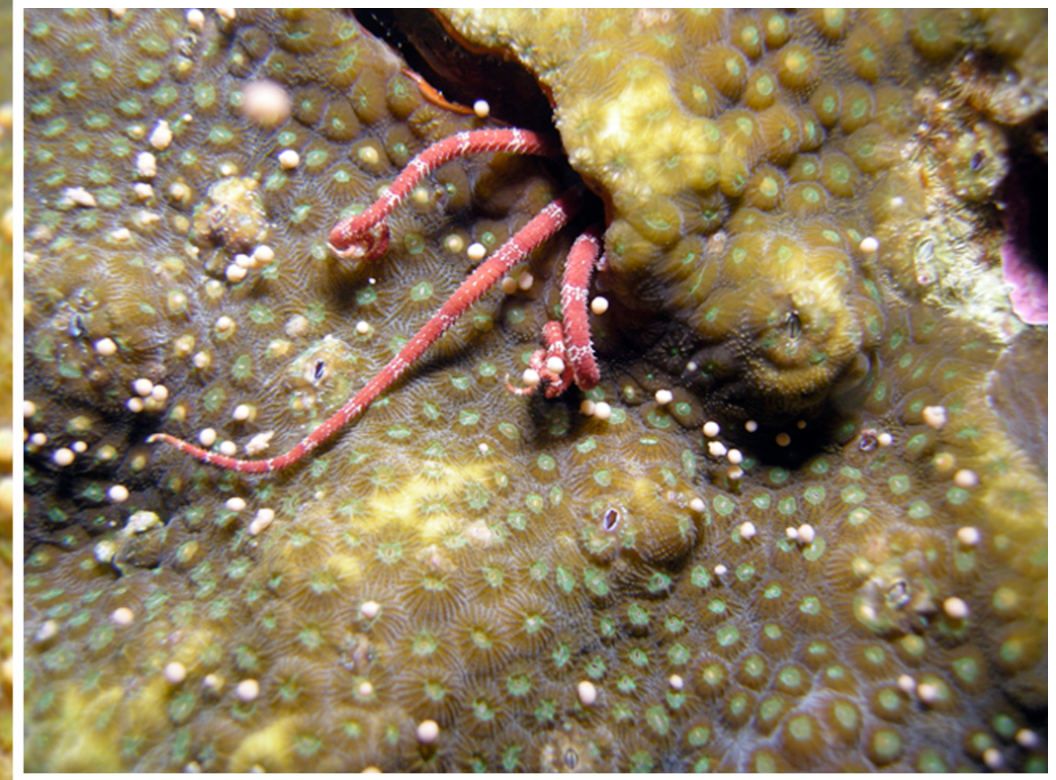


Anatomic Features



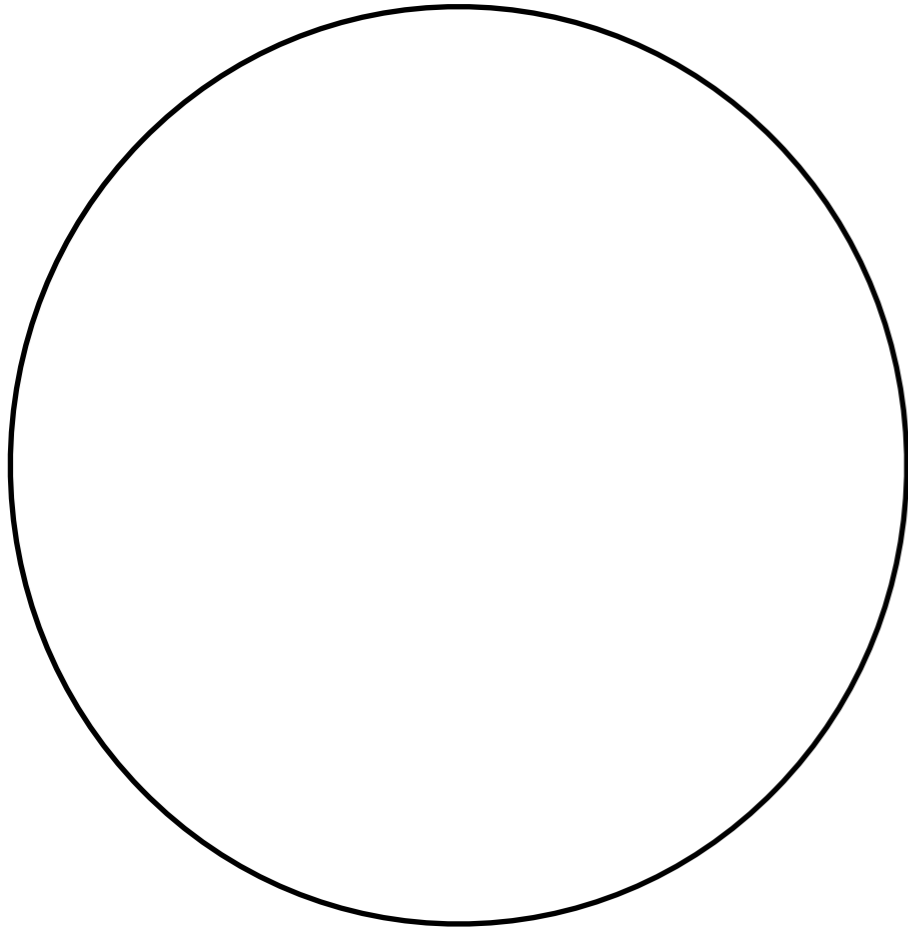
Key reference: Arnott, S. A., Neil, D. M. and Ansell, A. D. (1999). Escape trajectories of the brown shrimp *Crangon crangon*, and a theoretical consideration of initial escape angles from predators. *J. Exp. Biol.* **202**, 193-209.

Anatomic Features

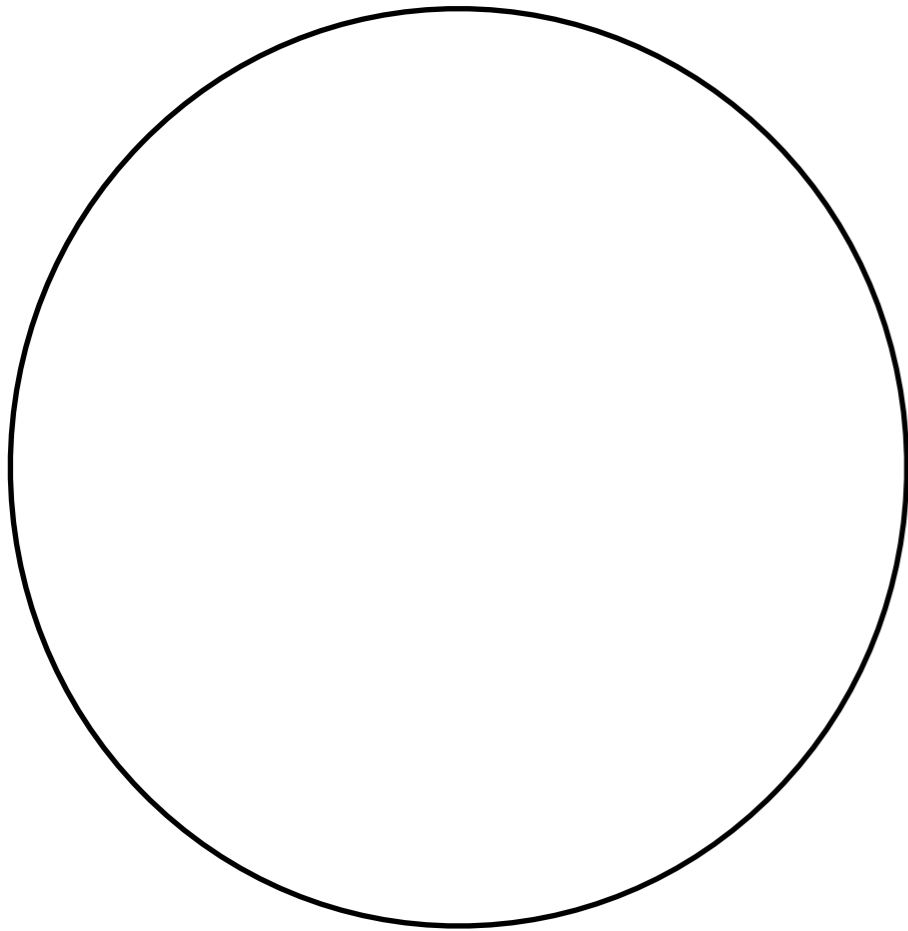


What is the overarching fear in those three examples?

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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

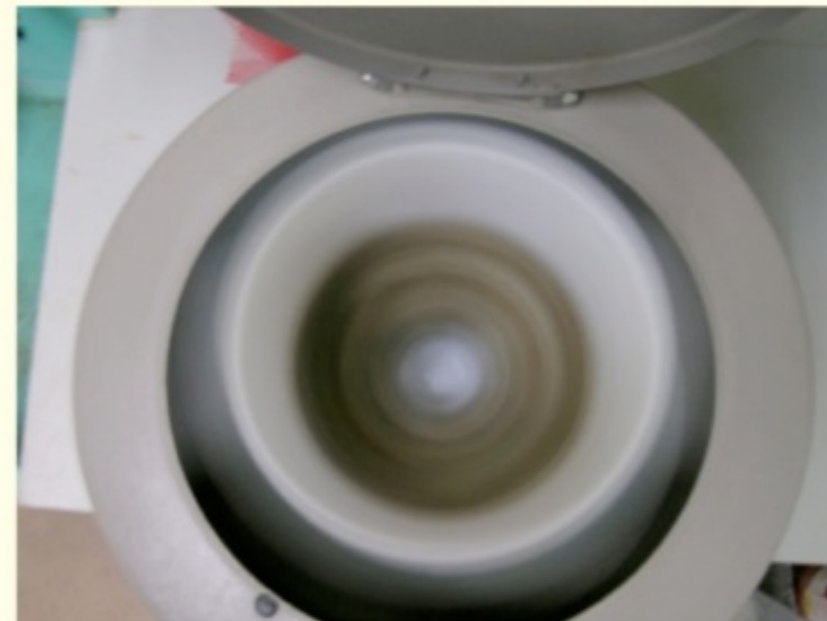
Immune response and mechanical stress susceptibility in diseased oysters, *Crassostrea virginica*

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• 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*

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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 \pm SE)

	<i>P. marinus</i> infected	Uninfected
Granular cells $\times 10^6 \text{ ml}^{-1}$	0.214 \pm 0.0556	0.0614 \pm 0.014
Agranular cells $\times 10^6 \text{ ml}^{-1}$	2.27 \pm 0.458	0.586 \pm 0.065
Granular cell diameter in μm	8.52 \pm 0.30	11.4 \pm 0.20
Agranular cell diameter in μm	5.31 \pm 0.10	6.29 \pm 0.31

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

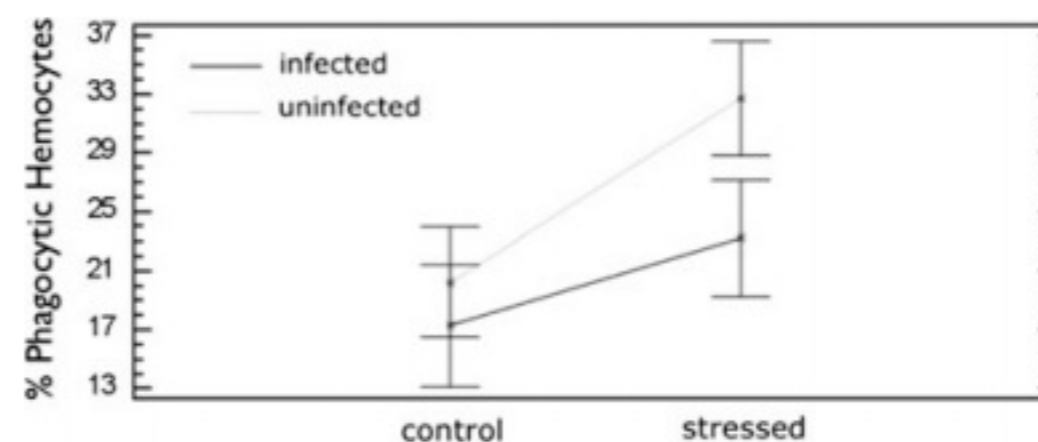
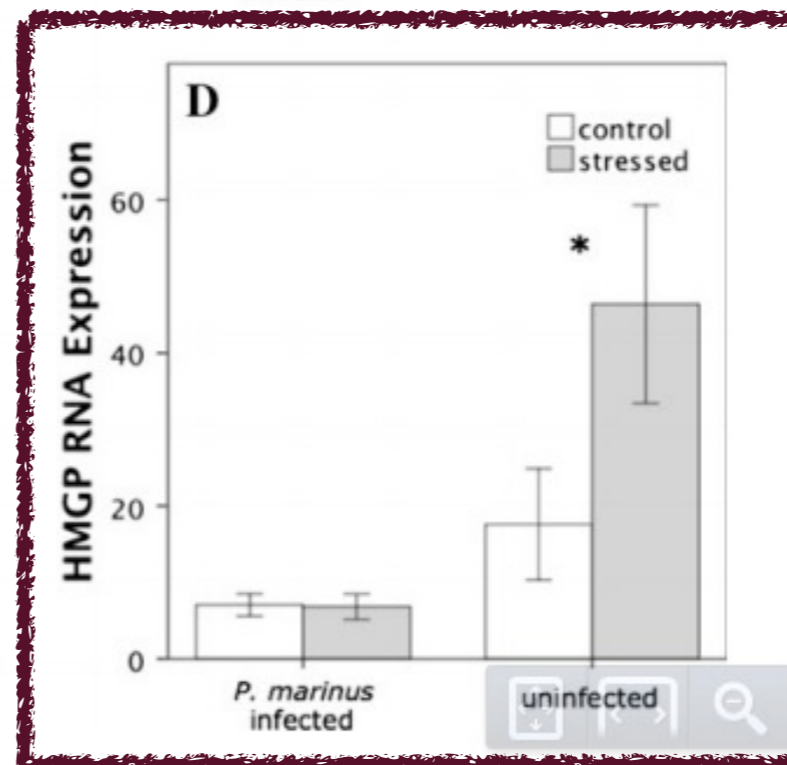
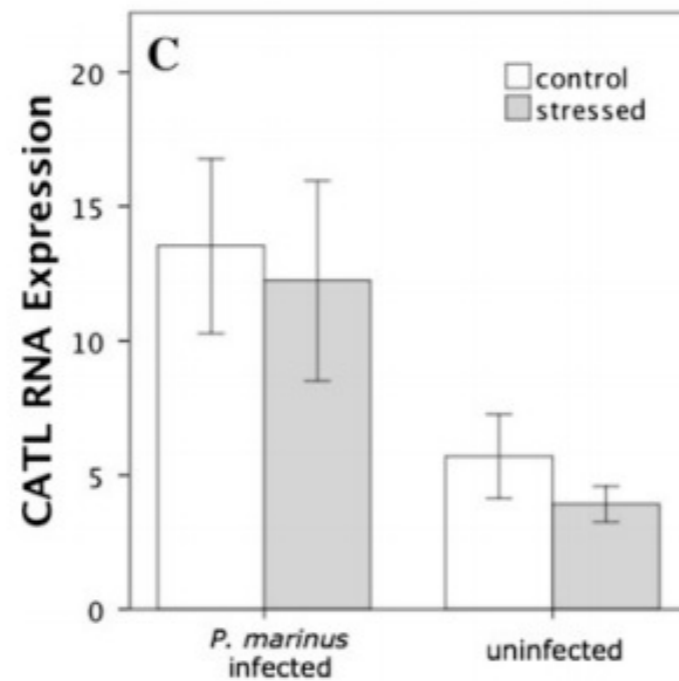
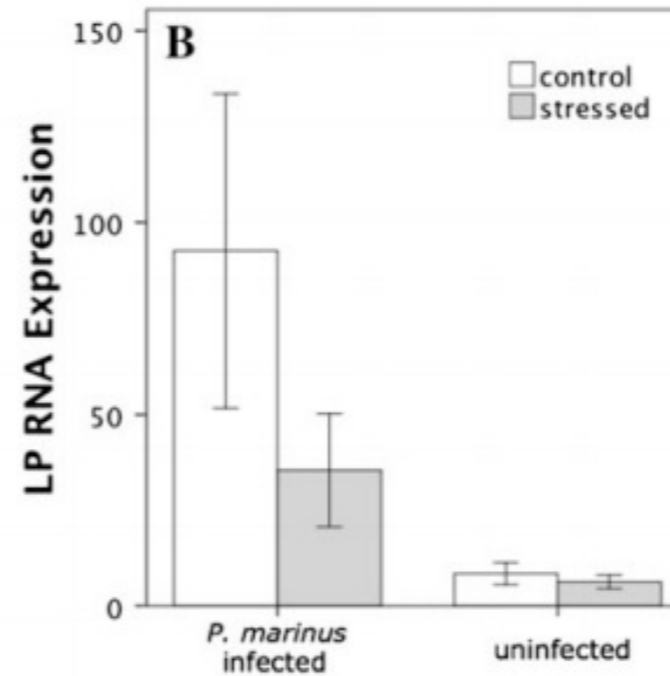
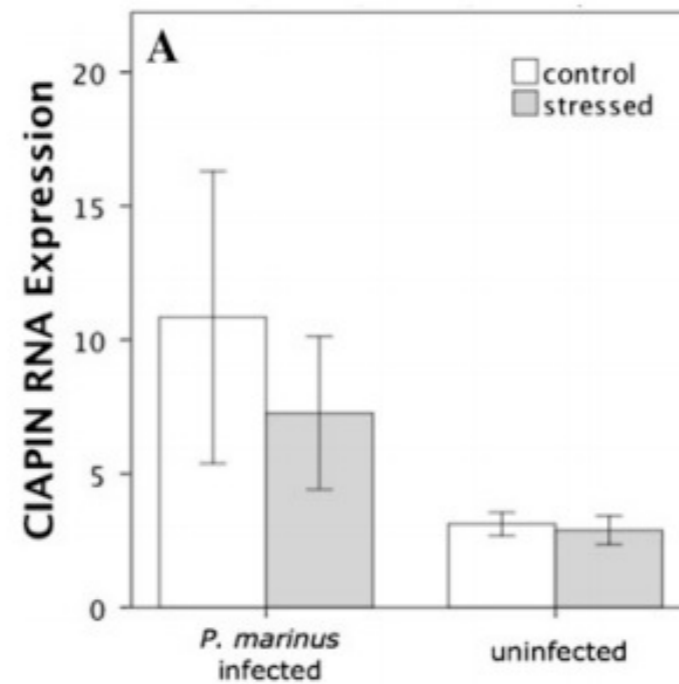


Fig. 2 Percentage of phagocytic hemocytes in *P. marinus*-infected ($n = 17$) and uninfected oysters ($n = 19$). A significant difference was observed after mechanical stress only in uninfected oysters (ANOVA $p < 0.05$)

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

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



resource allocation

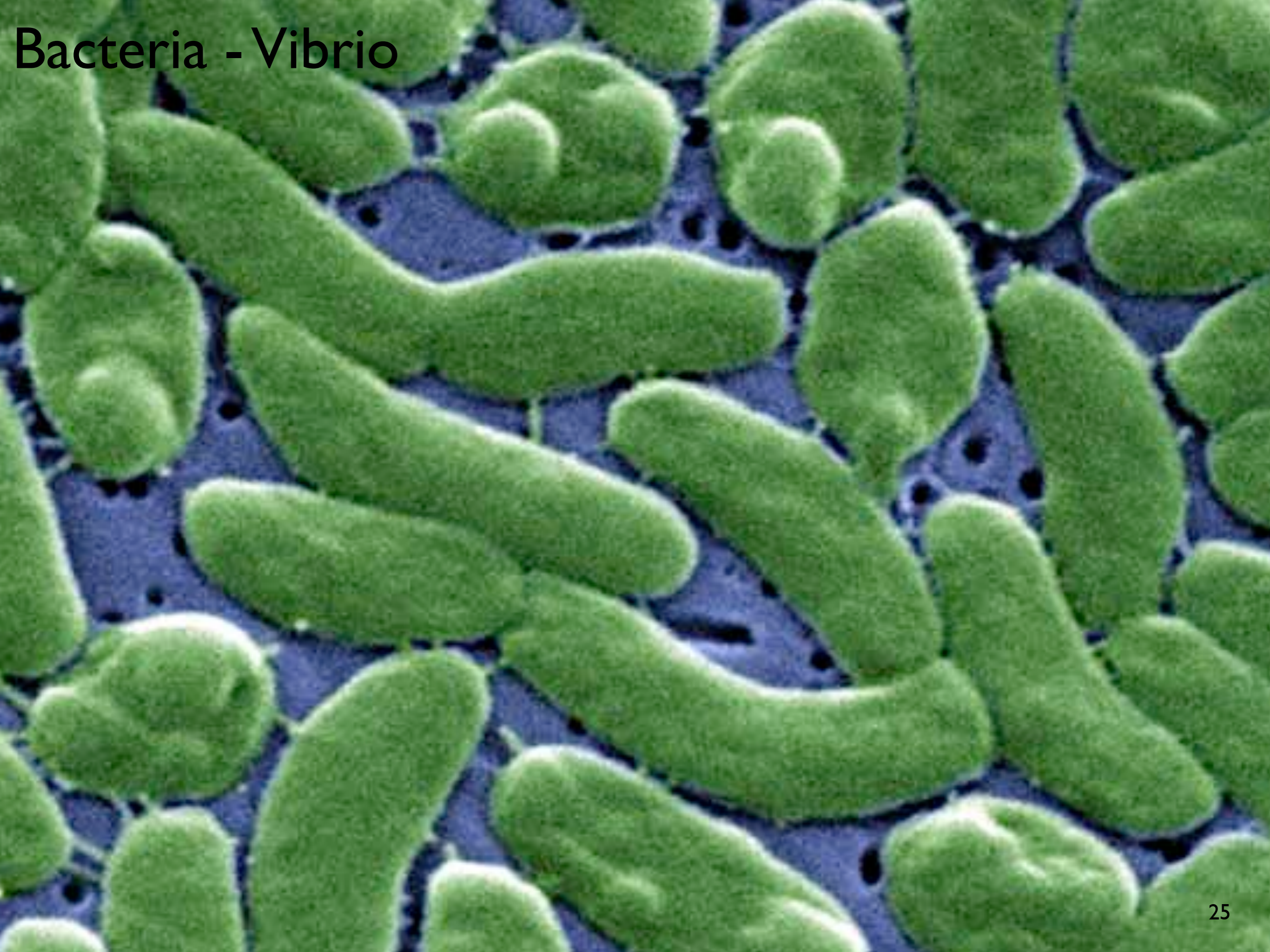
Pathogens

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

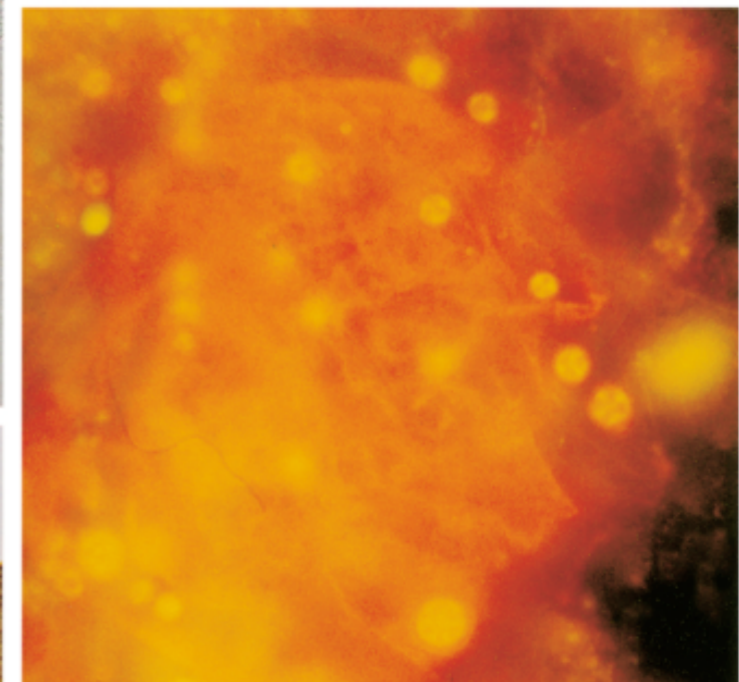
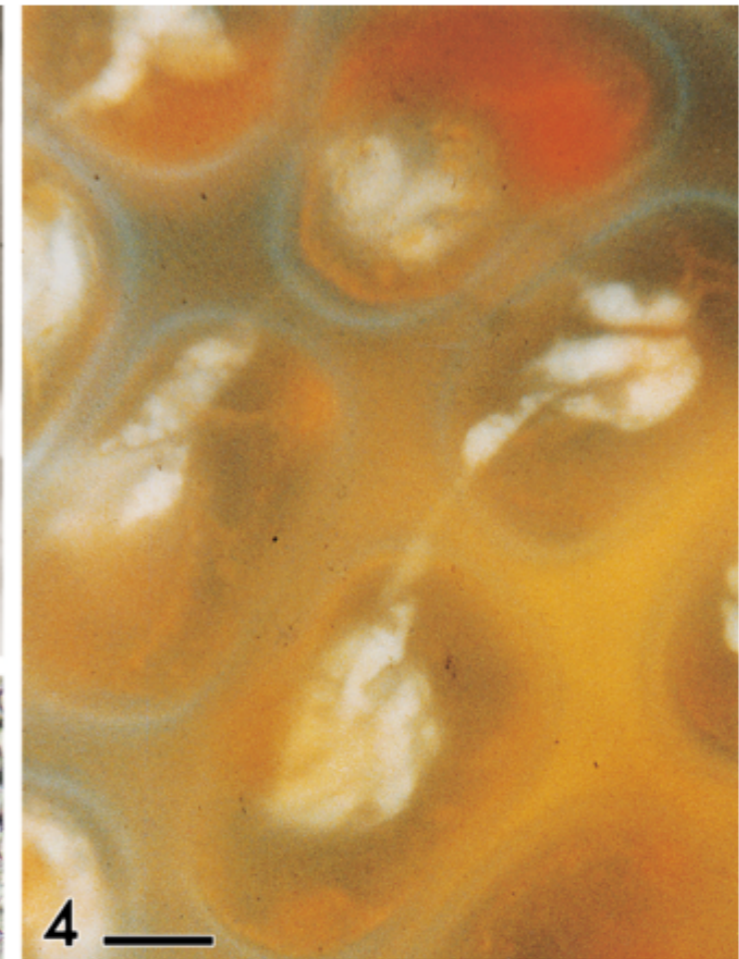
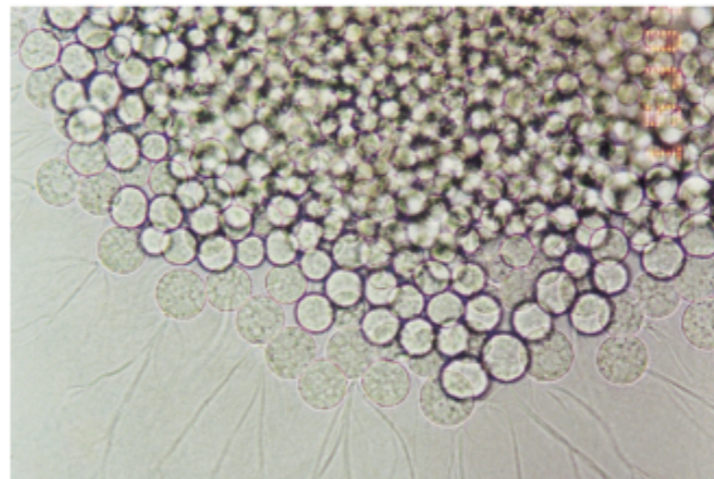
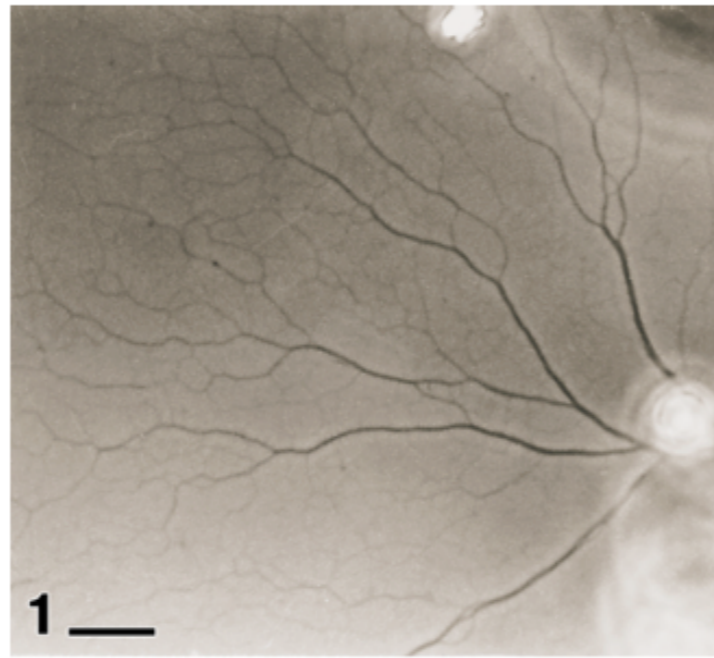


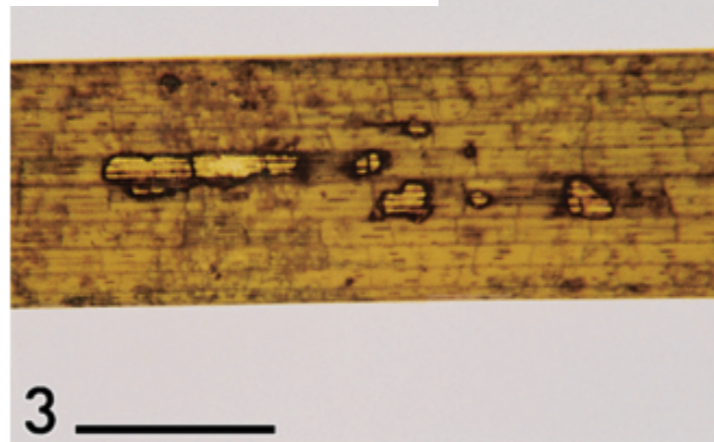
Fig. 1. Cells of a thraustochytrid growing on a nutrient agar medium. Bar represents 50 μm .

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 .

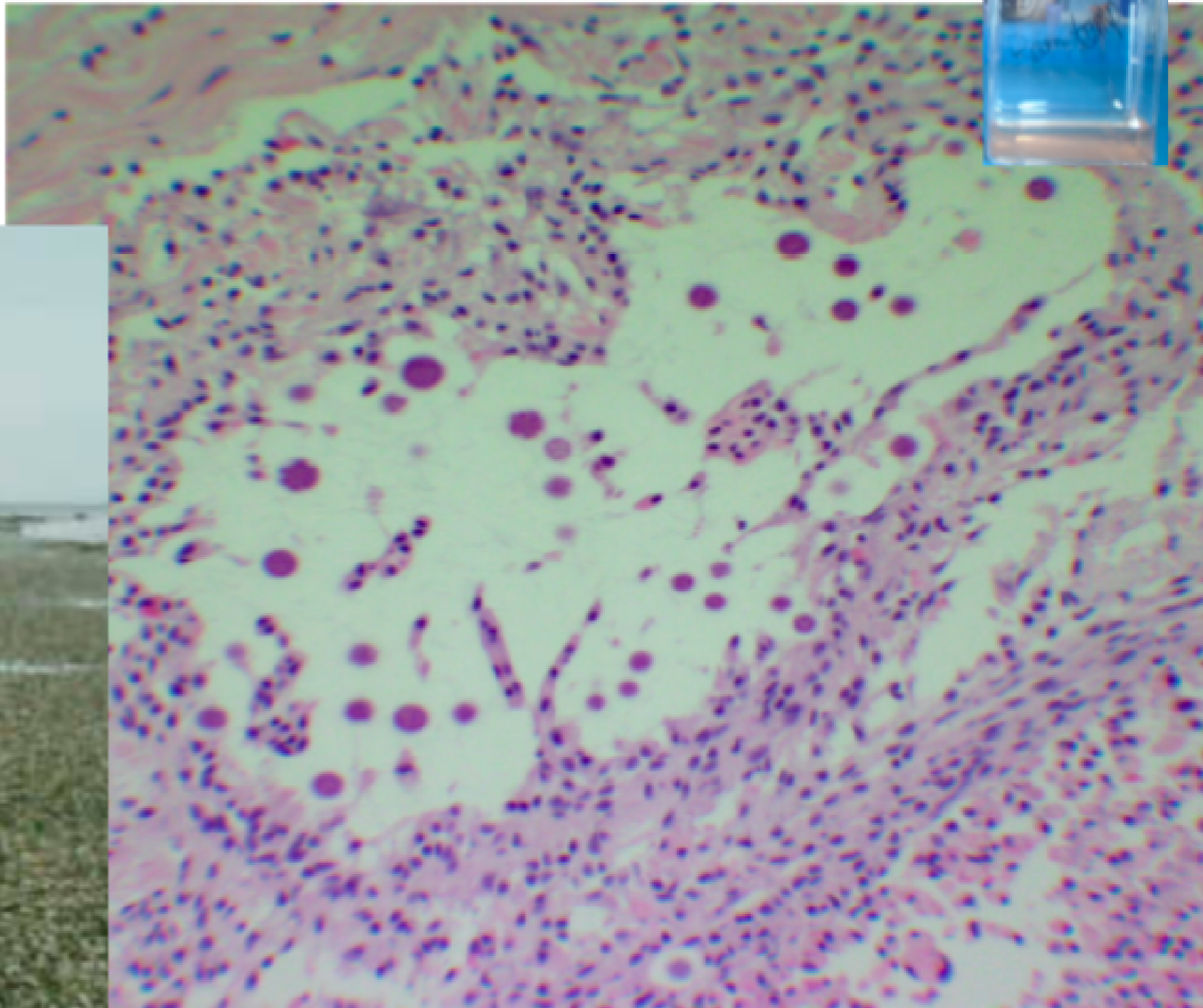
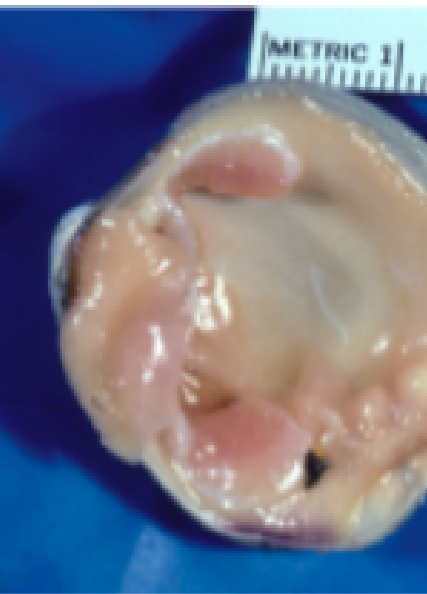
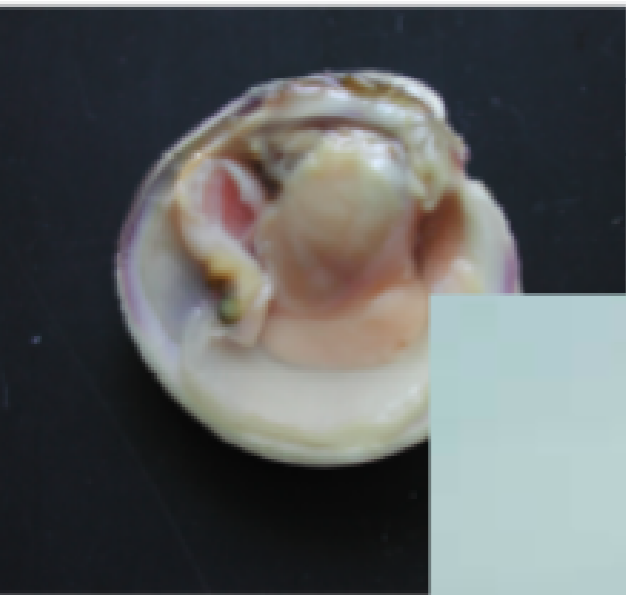


REVIEW

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

Seshagiri Raghukumar

Fungi - QPX

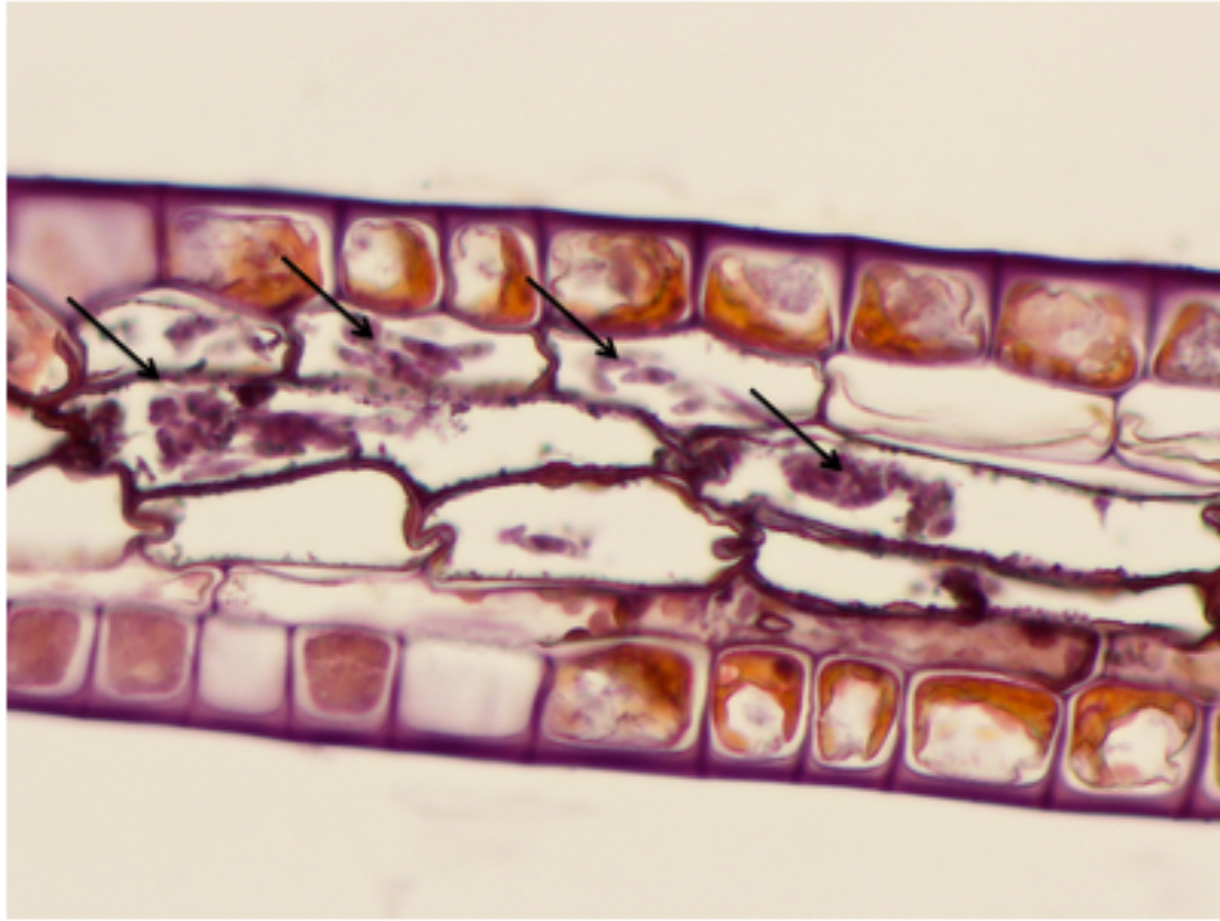


Roxanna Smolowitz



Colleen Burge - Oct 14, 2011 - Limited

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

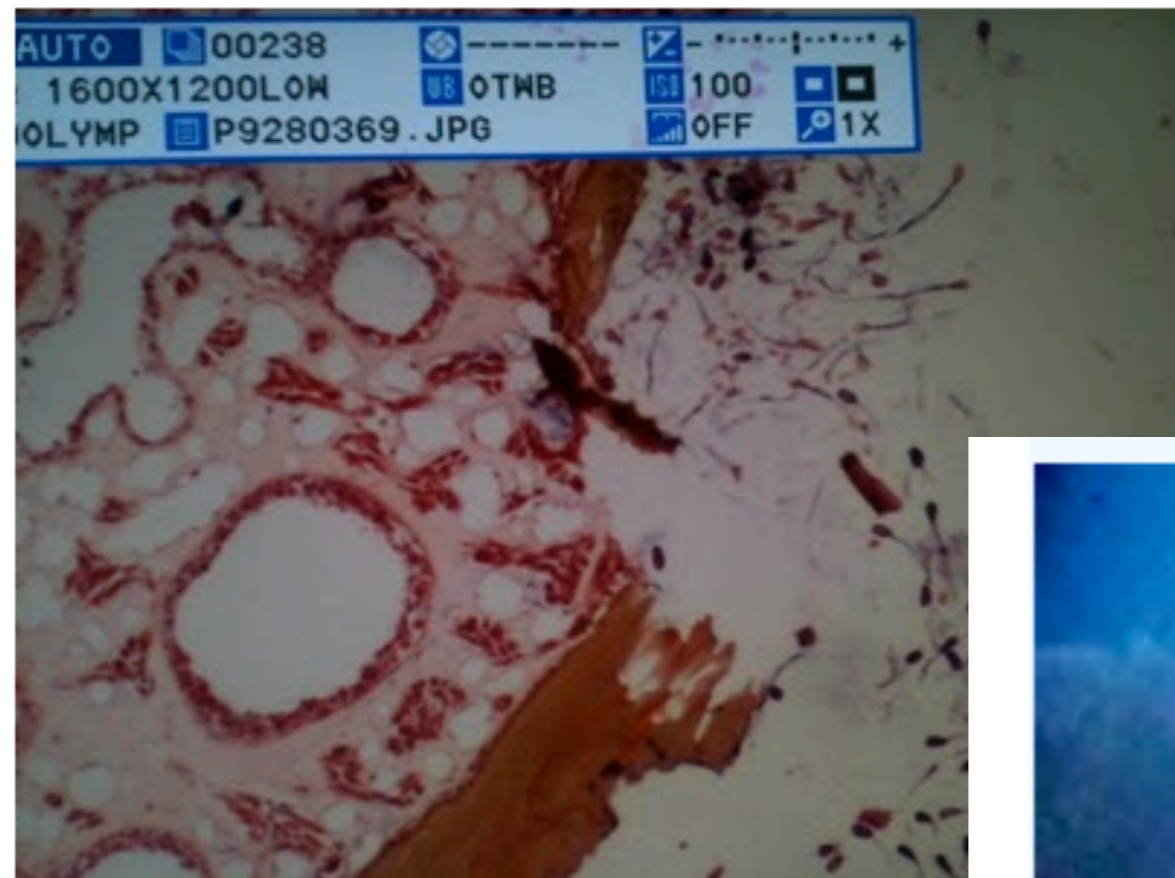


[More photos from Colleen Burge](#)



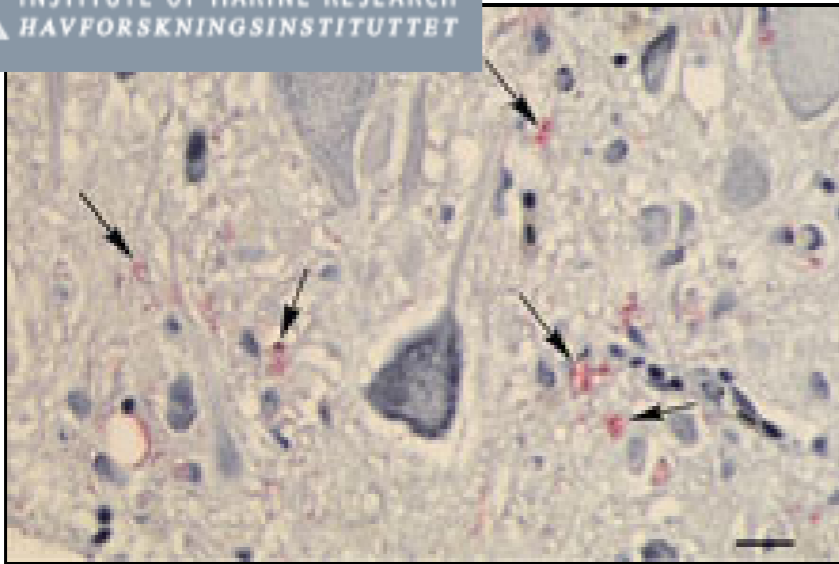
Colleen Burge - Sep 28, 2011 - Mobile - Limited

Really sad sea fan, really happy Laby



Virus - Nodavirus

INSTITUTE OF MARINE RESEARCH
HAVFORSKNINGSINSTITUTTET



Brain of salmon contaminated by nodavirus.



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



Phage



Abalone



Caused by a bacteria..

Immune Response

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

Chemico-physical Barrier



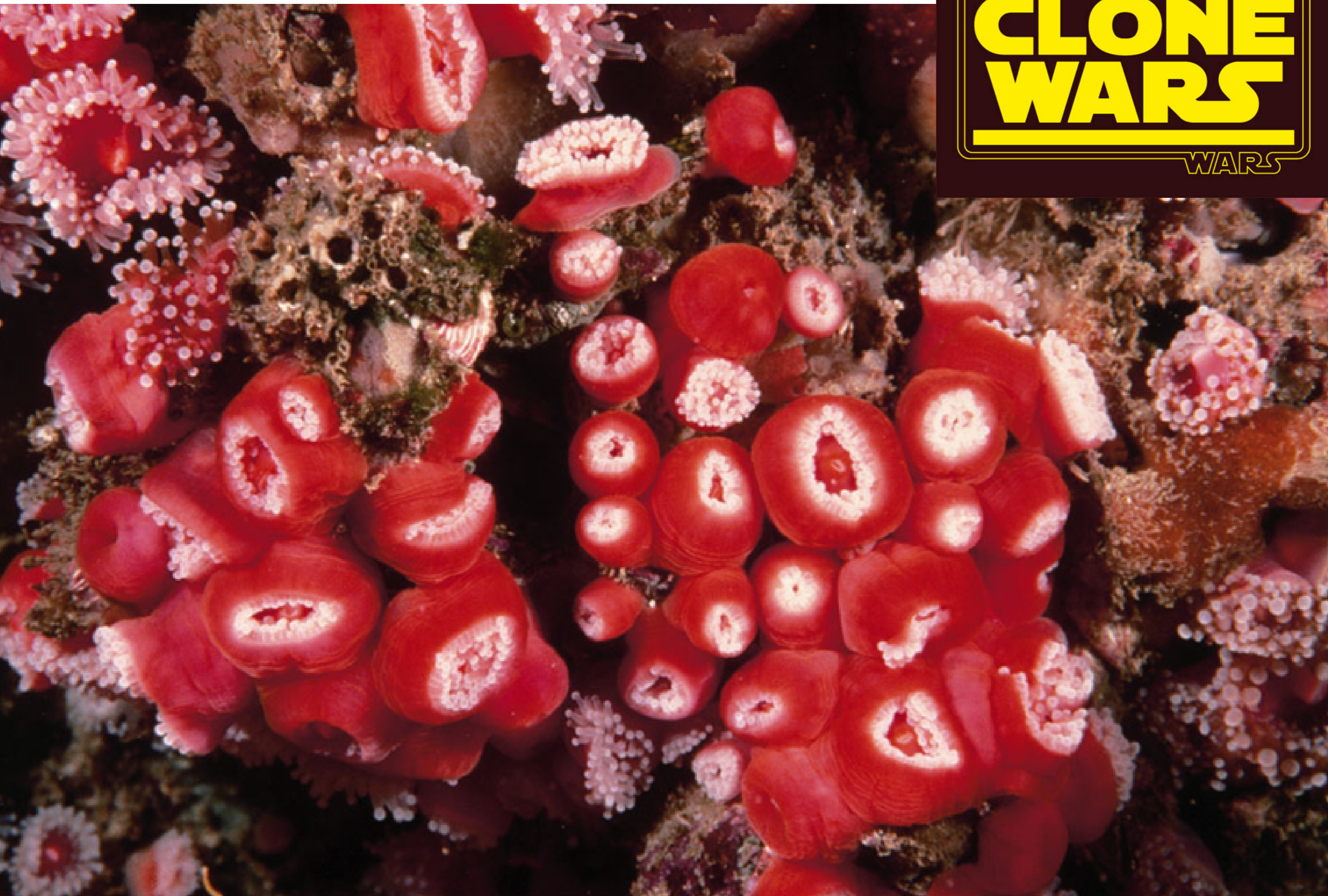
anti-microbial peptides

*beneficial microbial
communities*

from the beginning...

**How do organisms distinguish self from
non-self?**

STAR
THE
**CLONE
WARS**
WARS



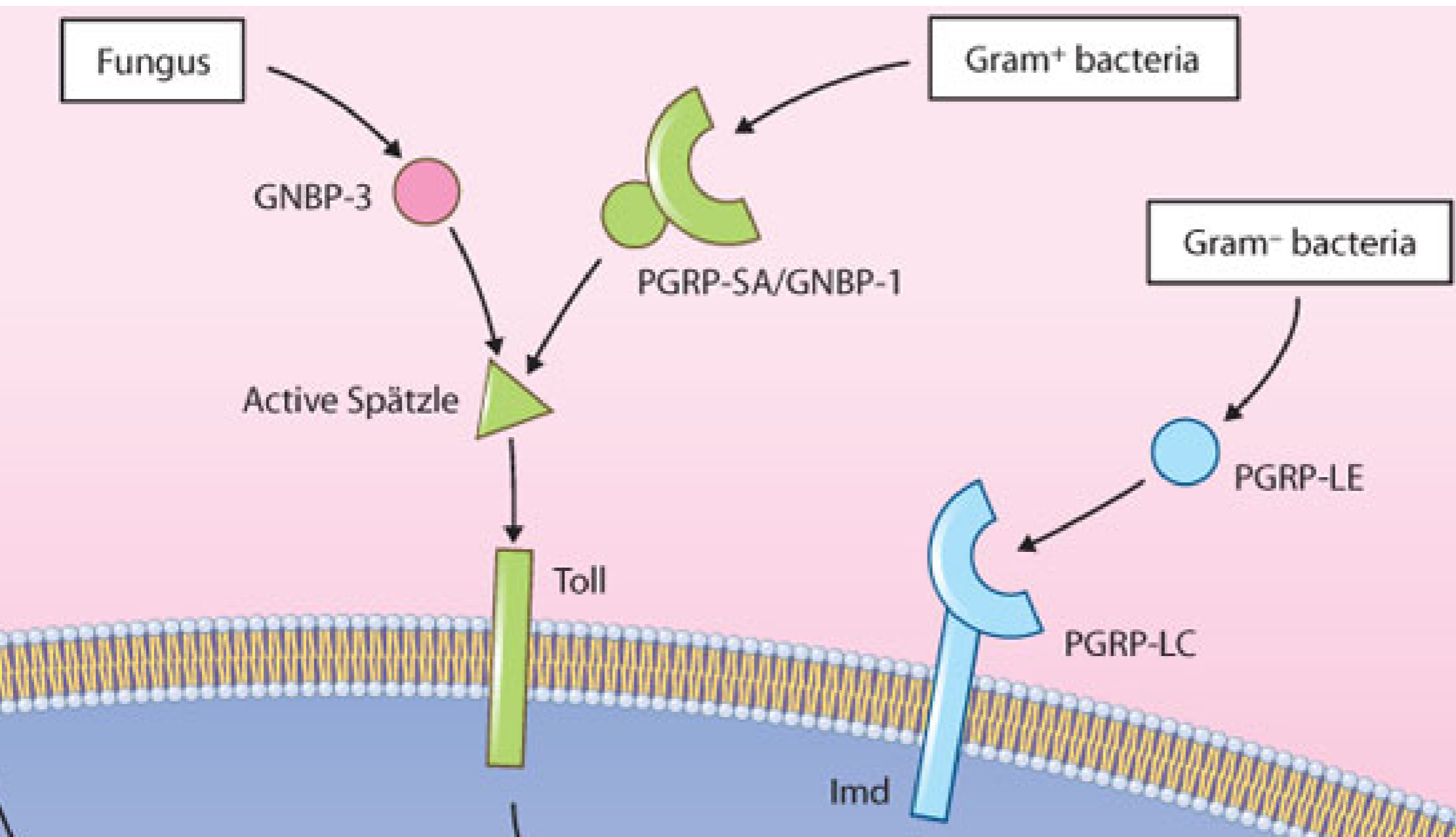


This is a picture of two *A. elegantissima* or *A. sola* fighting with acrorhagia. Taken at San Simeon, CA by Dave Cowles

How do organisms distinguish self from
non-self?

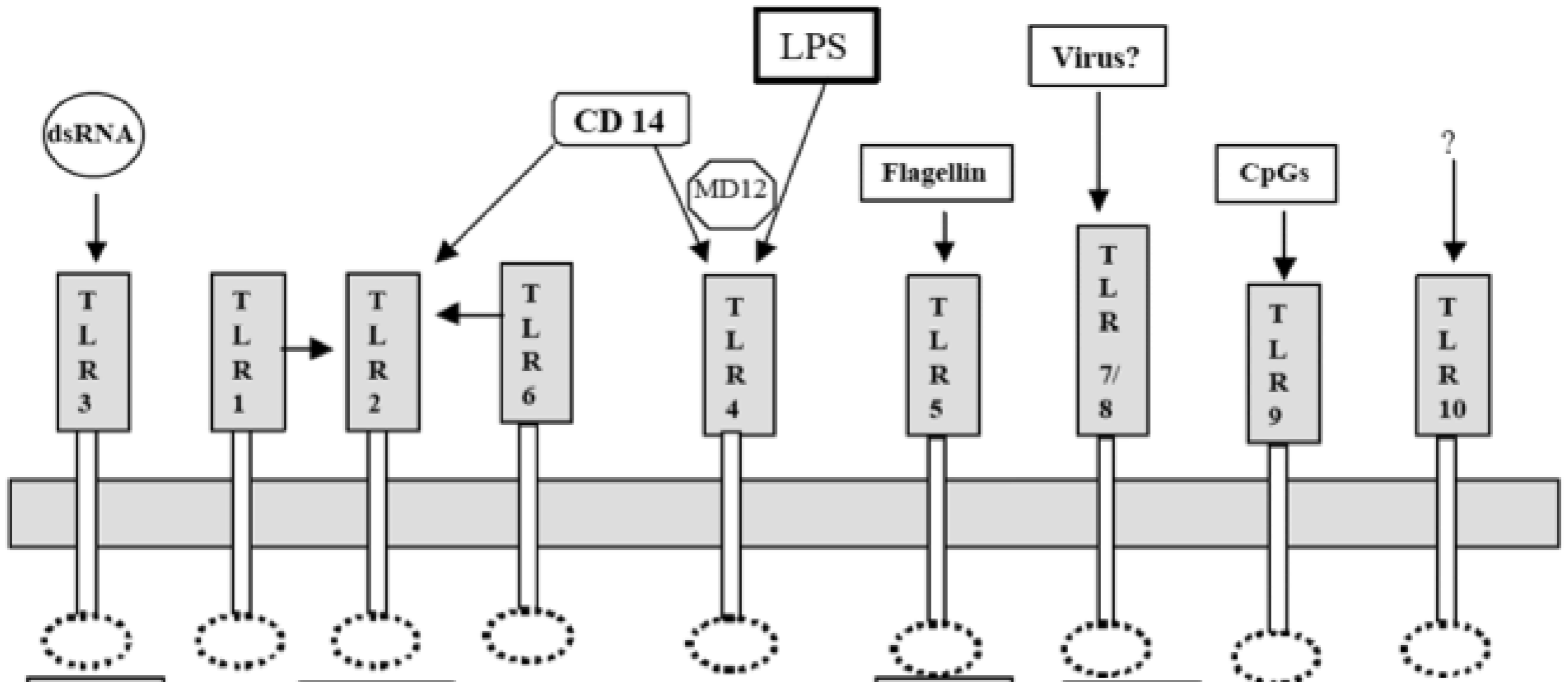
pattern recognition proteins (PRPs)

PRPs



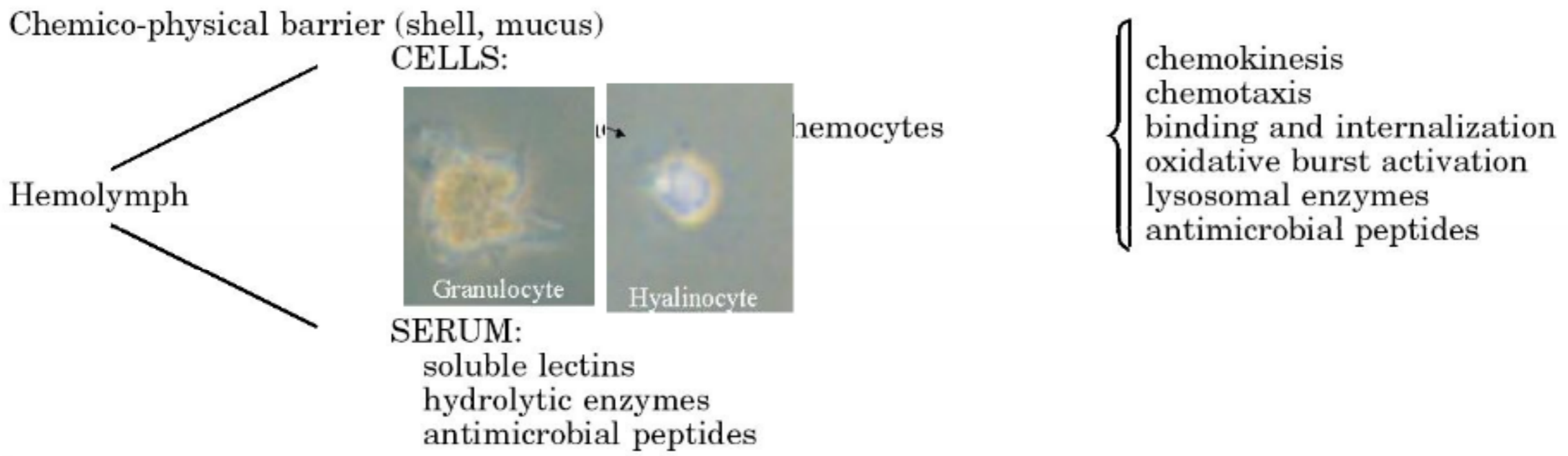
Toll-like Receptors
Peptidoglycan recognition proteins

PRPs - Toll-like Receptors



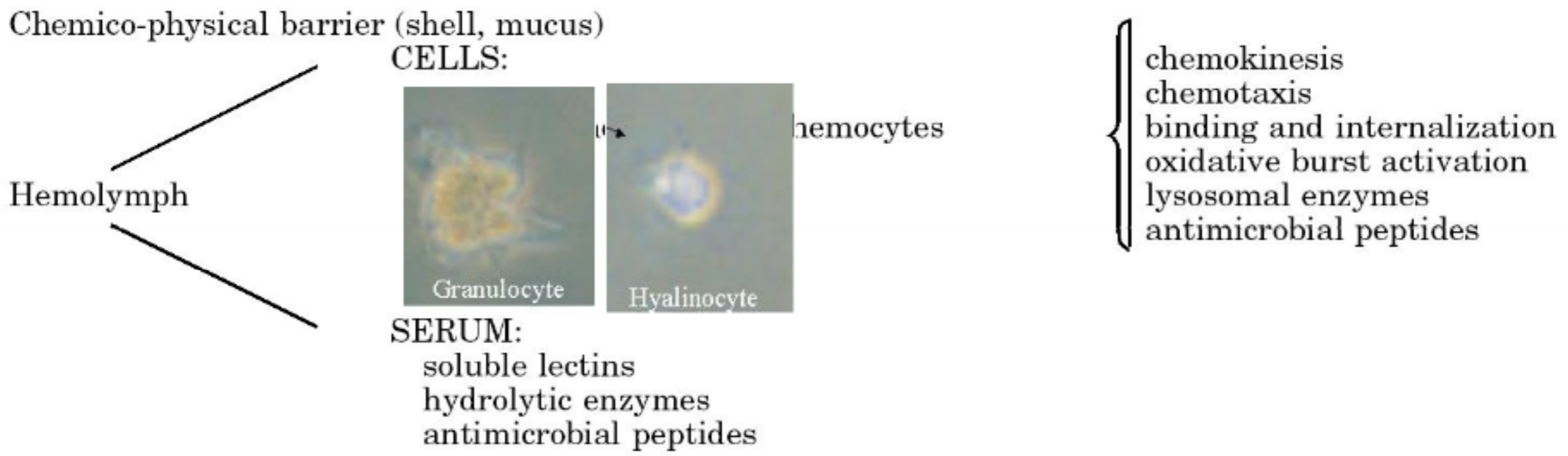
That's how the immune system
knows bad things are there...

Innate Immunity



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

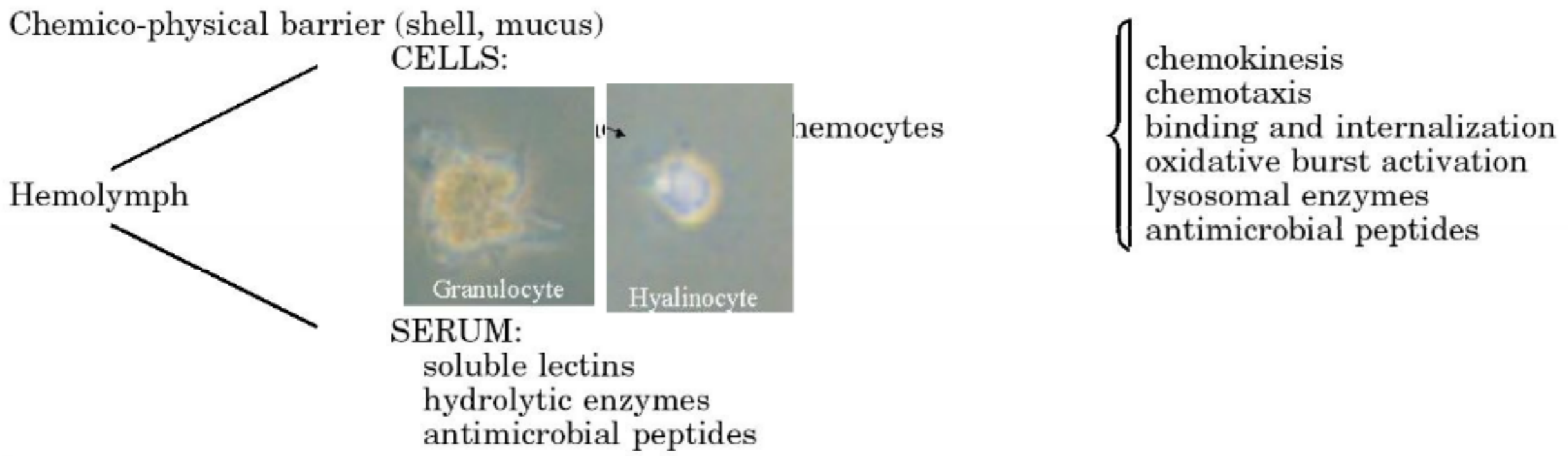
Innate Immunity



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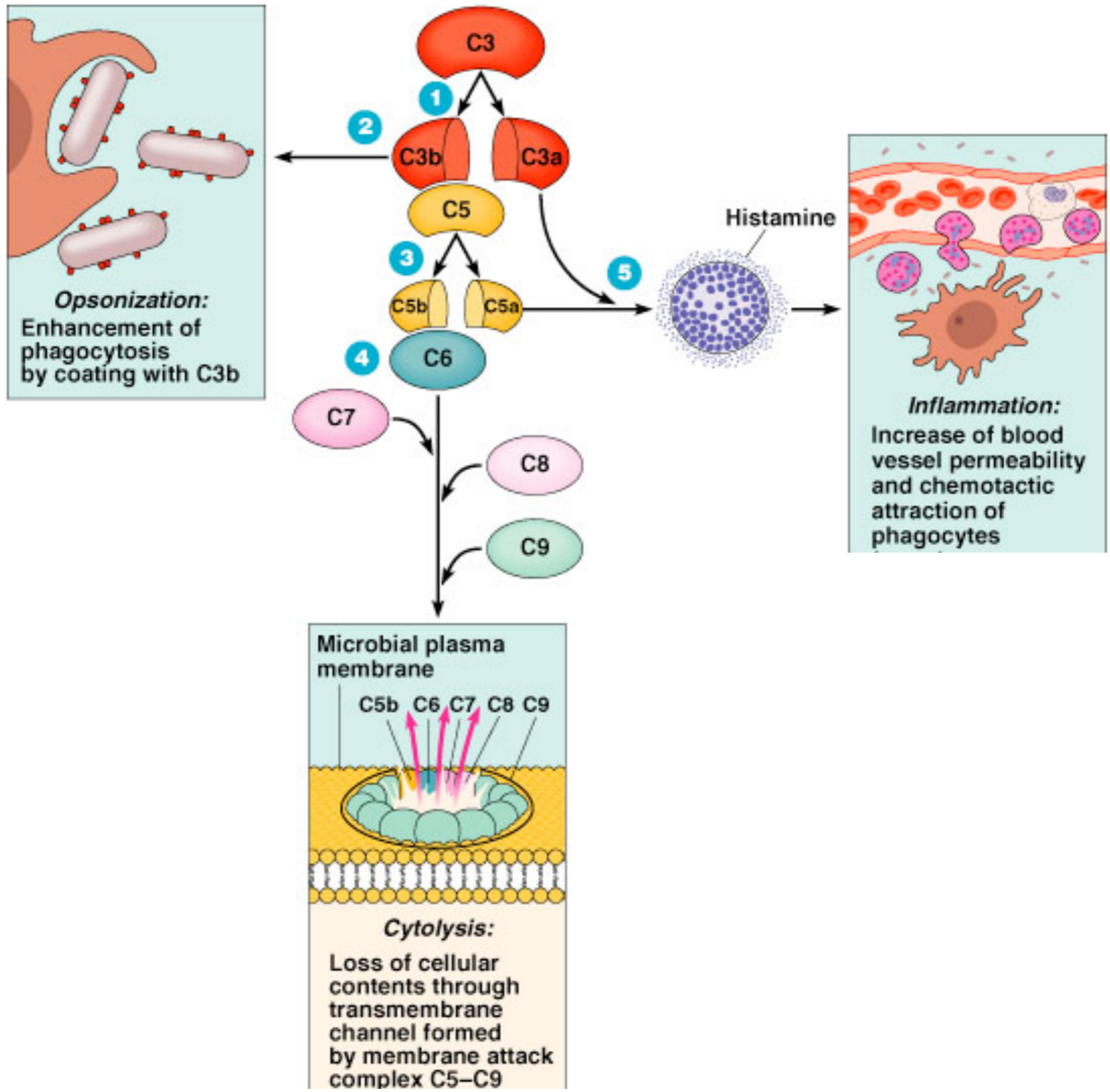
**BUT WAIT - How do these immune cells
know where to go?**

Innate Immunity

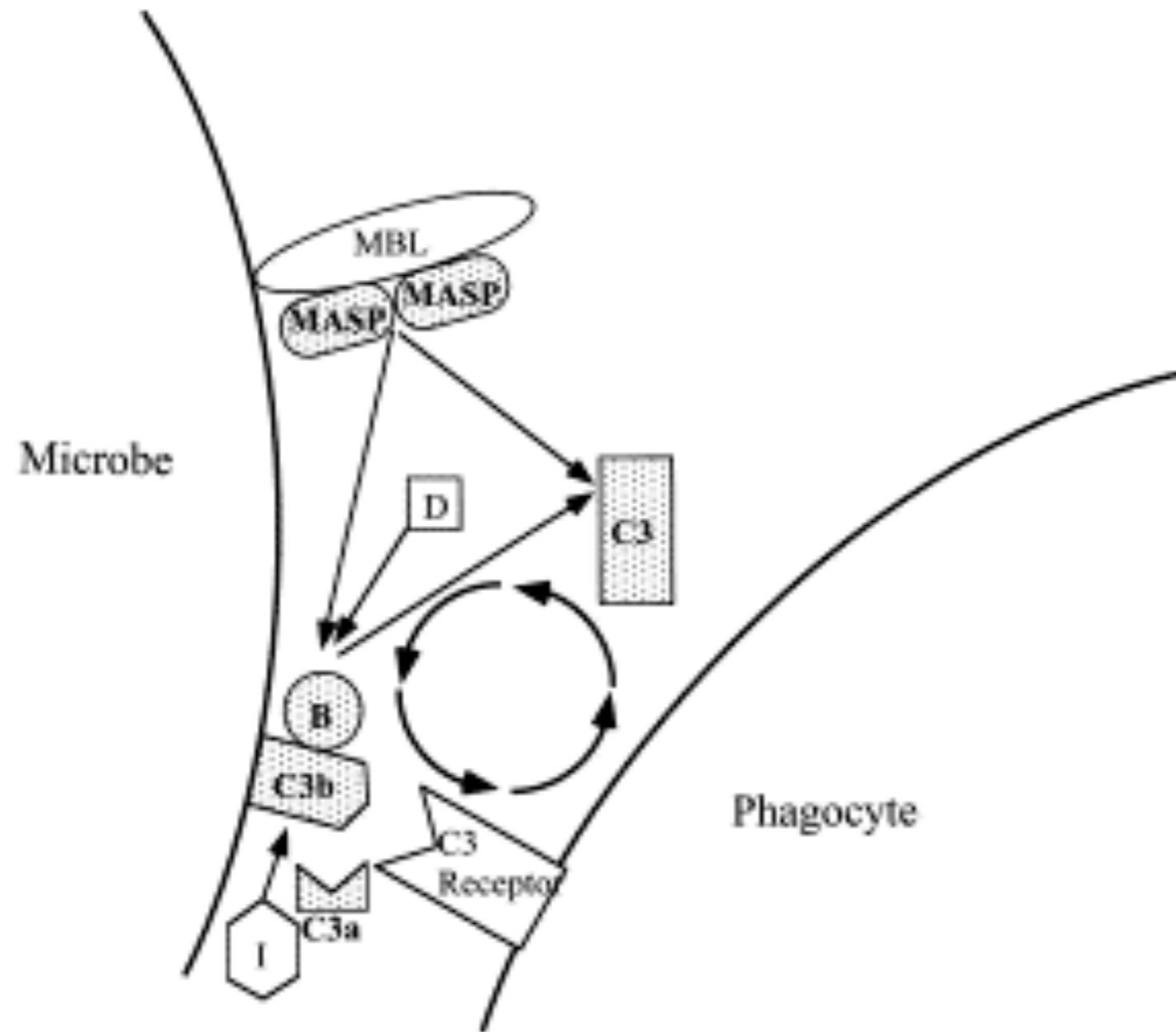


Laura Canesi, Gabriella Gallo, Miriam Gavioli, and Carla Pruzzo
Bacteria-hemocyte Interactions and Phagocytosis in Marine
Bivalves. 2002. Microscopy Research And Technique 57:469-476

Complement System



Complement System - Invertebrates



Complement systems in invertebrates. The ancient alternative and lectin pathways

Immune Response

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

Today: *Physiological Response* to things that are bad

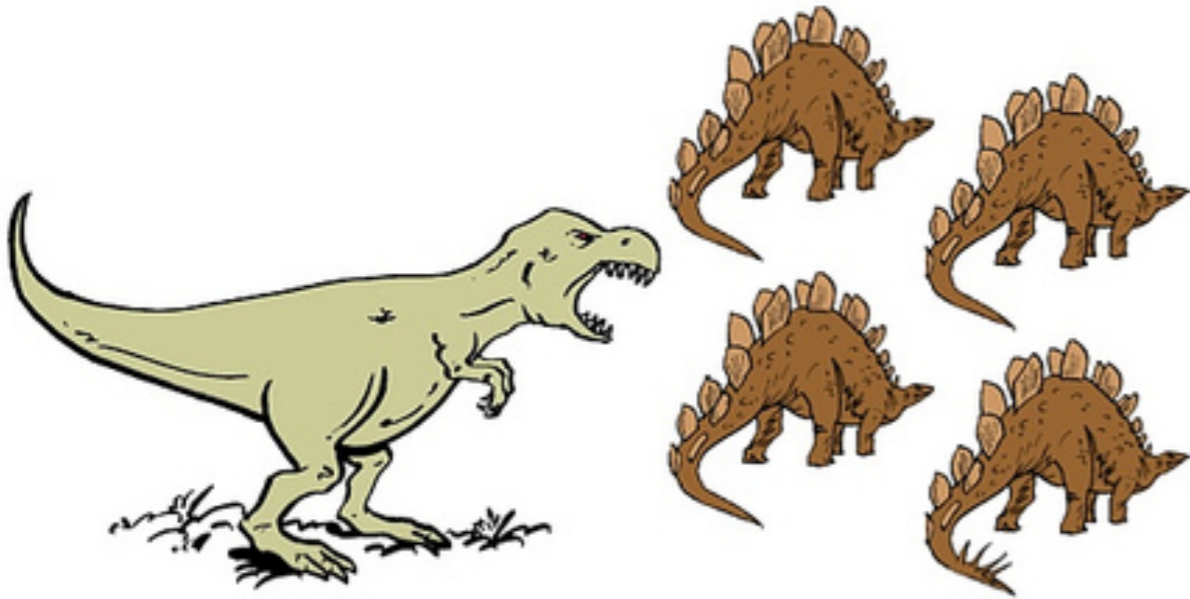
It is important to think about the big picture.

What else is going on with the critter..

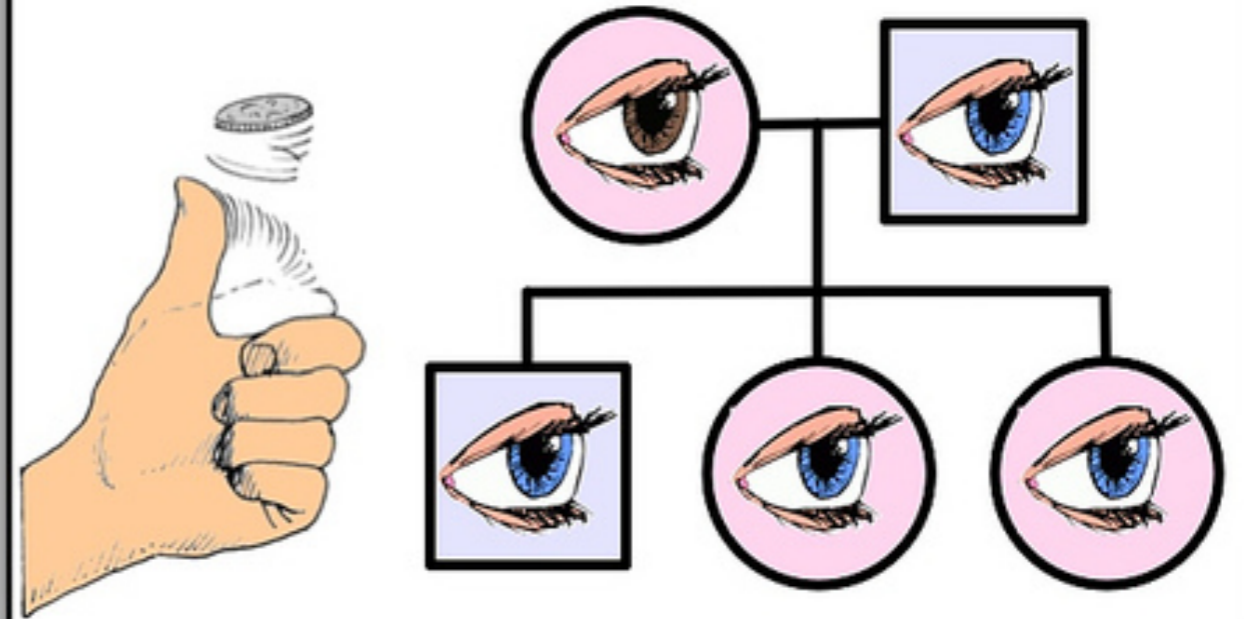
really big picture -

What has the population experienced.

NATURAL SELECTION



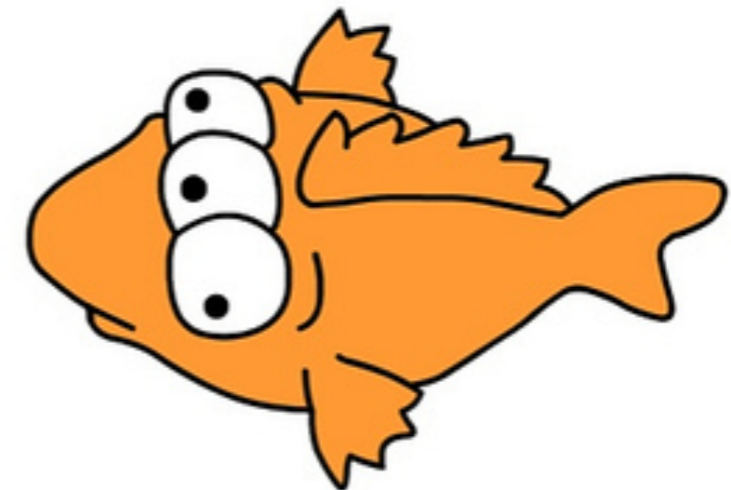
GENETIC DRIFT



MIGRATION

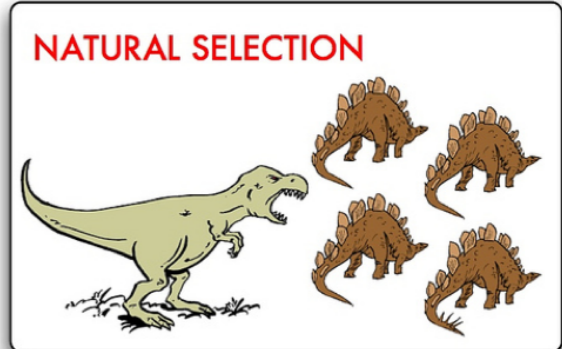
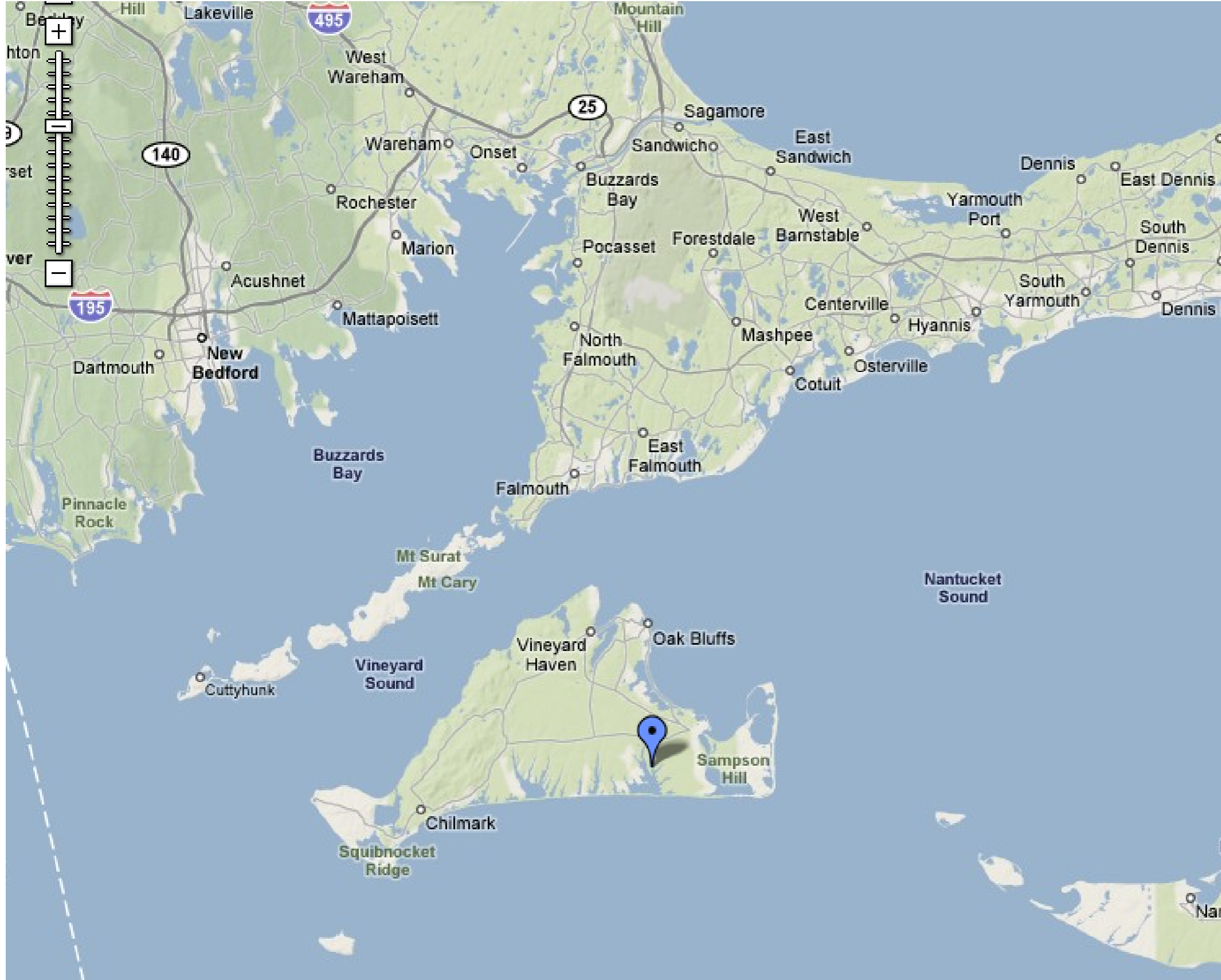


MUTATION



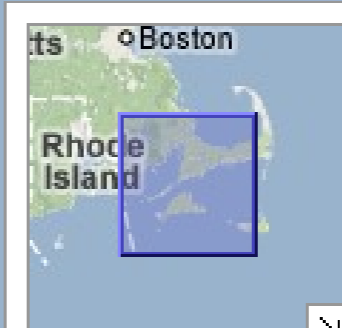
Two part story





flickr | cpurrin |

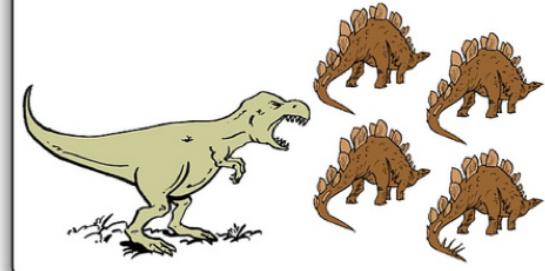
5 mi
10 km



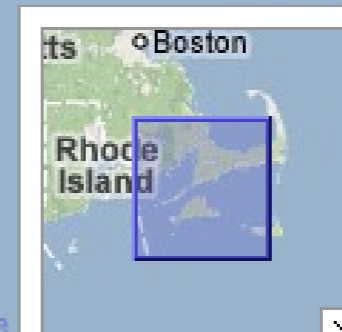
Roxanna Smolowitz
Rick Karney

Disease Resistance?

NATURAL SELECTION



flickr | cpurrin1



Roxanna Smolowitz
Rick Karney





Edgartown
Great Pond

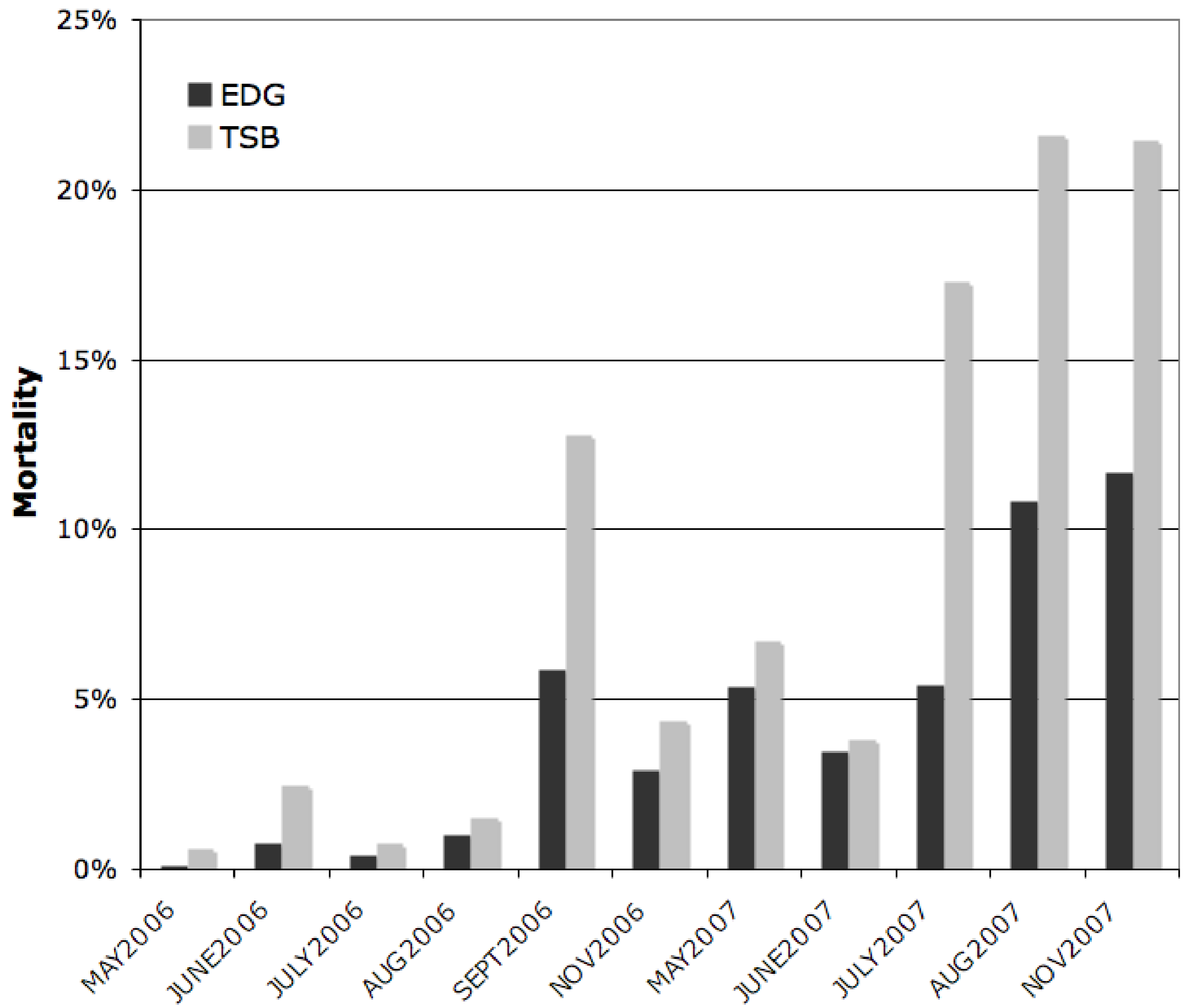
Crackatuxet
Cove

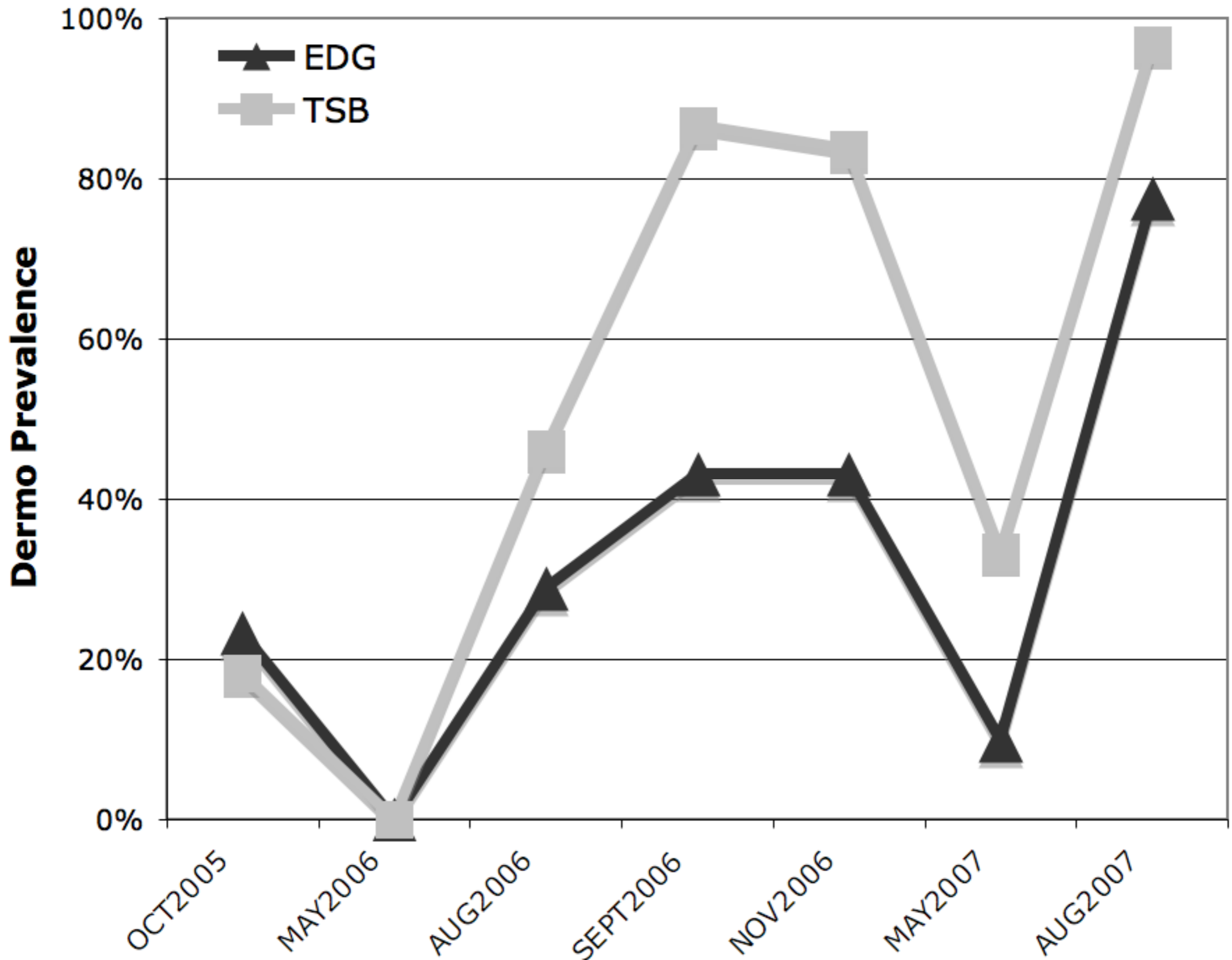
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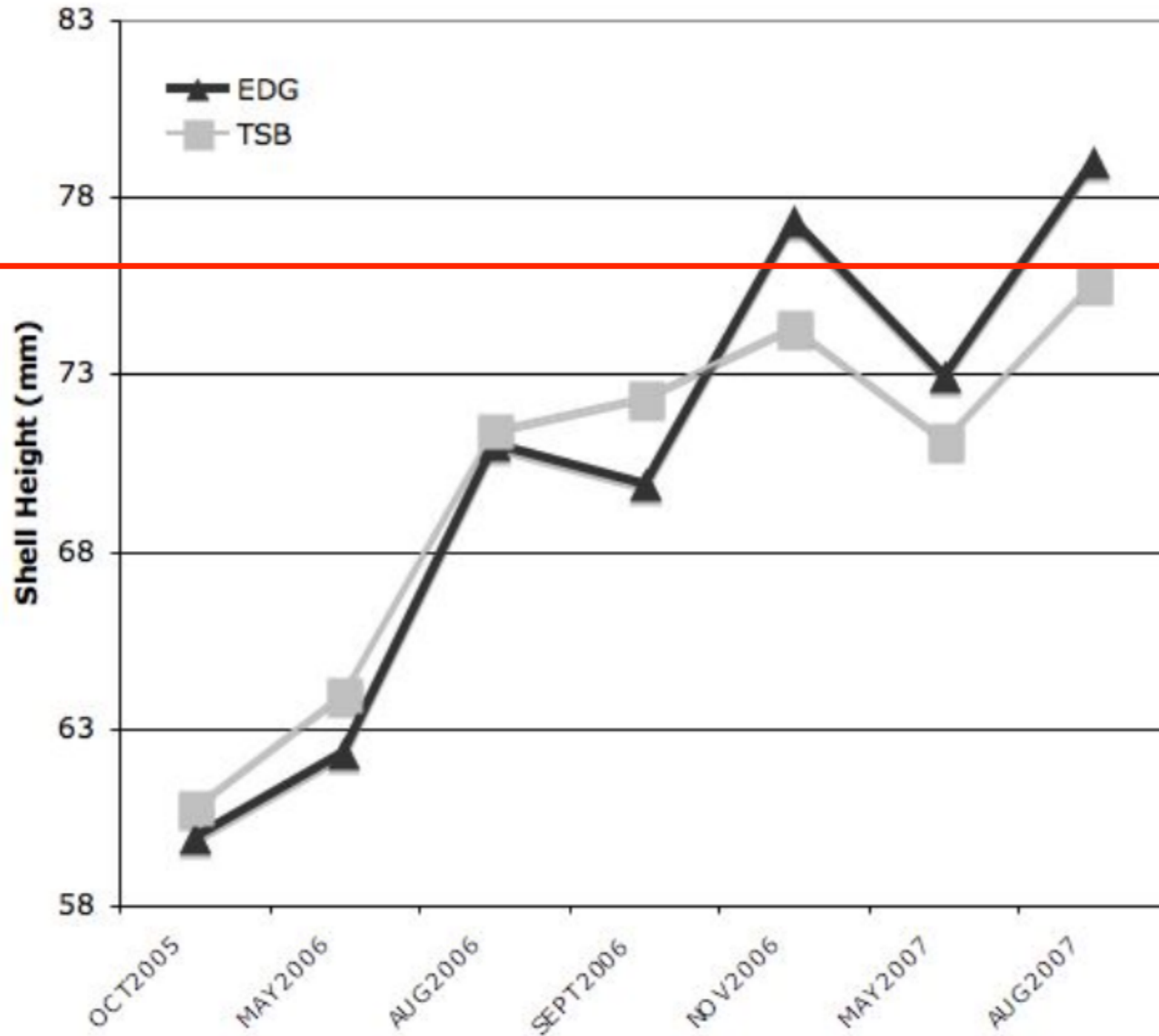








Market size



Mechanisms

They are different,
but how / why?



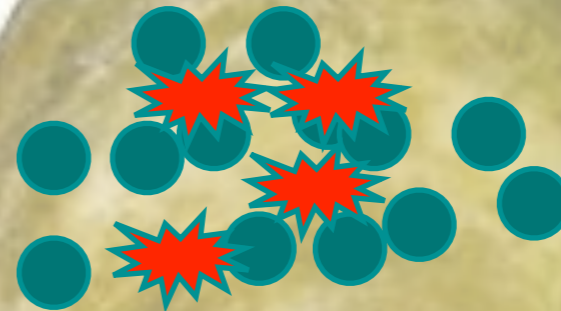


Schematic

Parasite



Hemocytes



BCL-X

BCL-X

Resistant

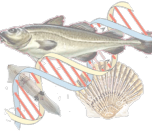
Wild-type





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*

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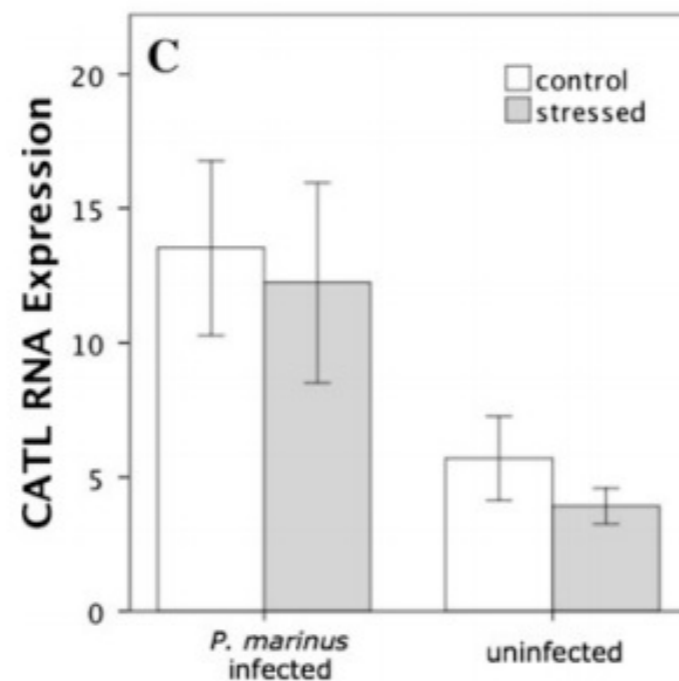
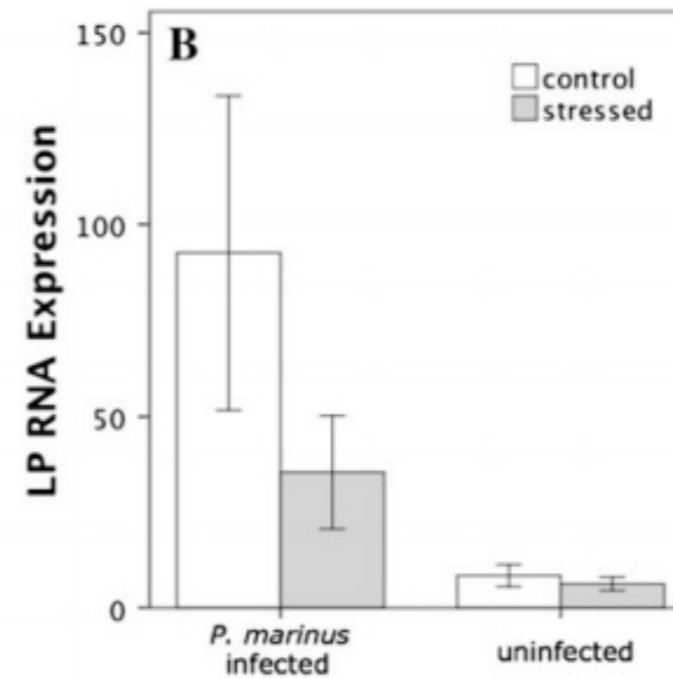
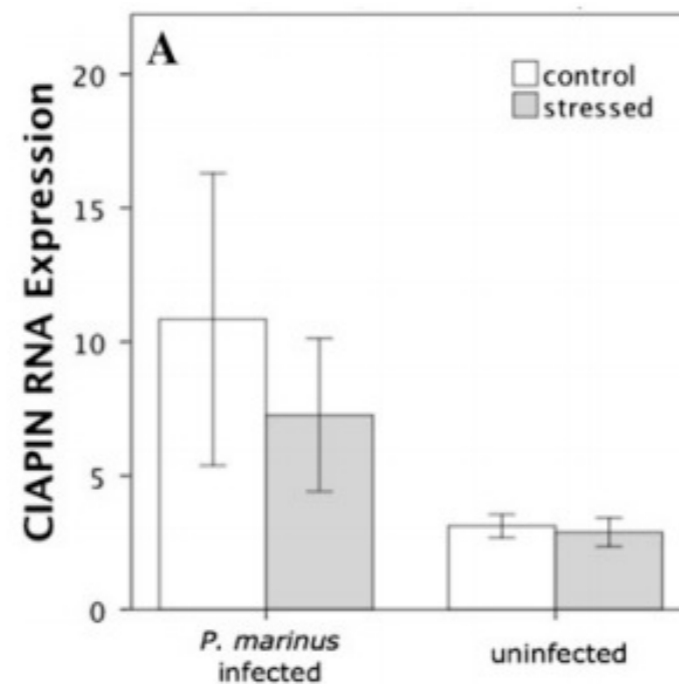


Table 2 Hematology of oysters, *C. virginica*, from two cohorts, infected with *P. marinus* ($n = 17$) and uninfected ($n = 19$), determined by flow cytometry (mean \pm SE)

	<i>P. marinus</i> infected	Uninfected
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infected

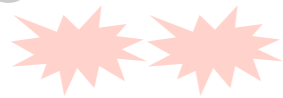




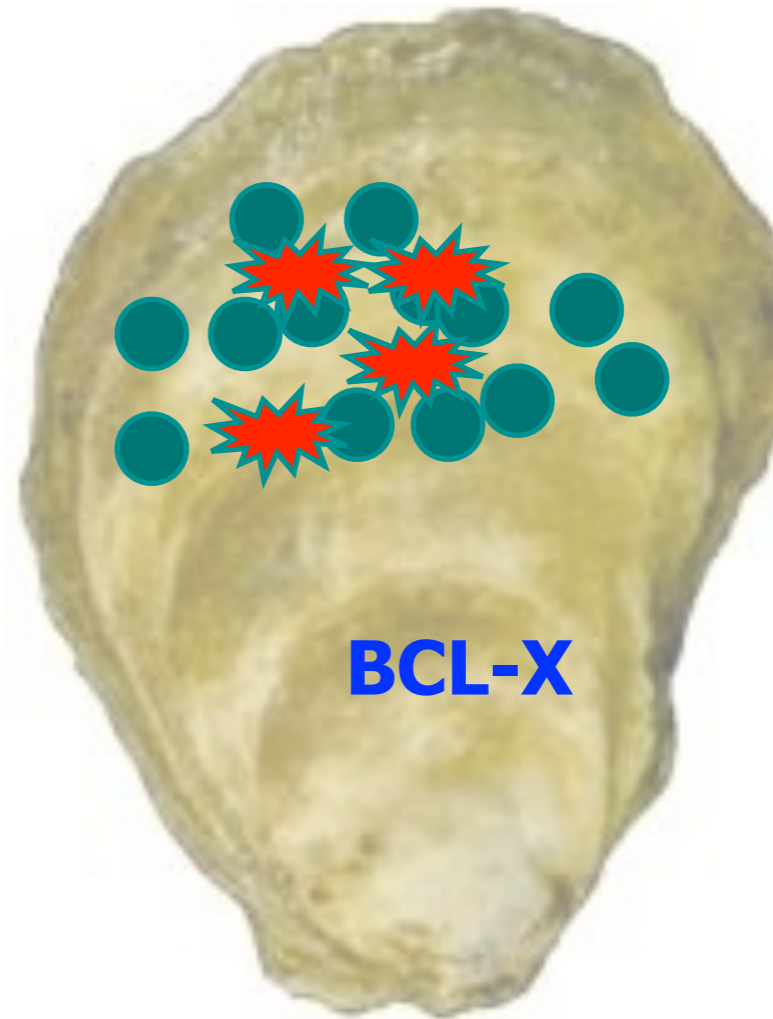
Schematic

Parasite

Epigenetic?



Hemocytes



Resistant

Wild-type



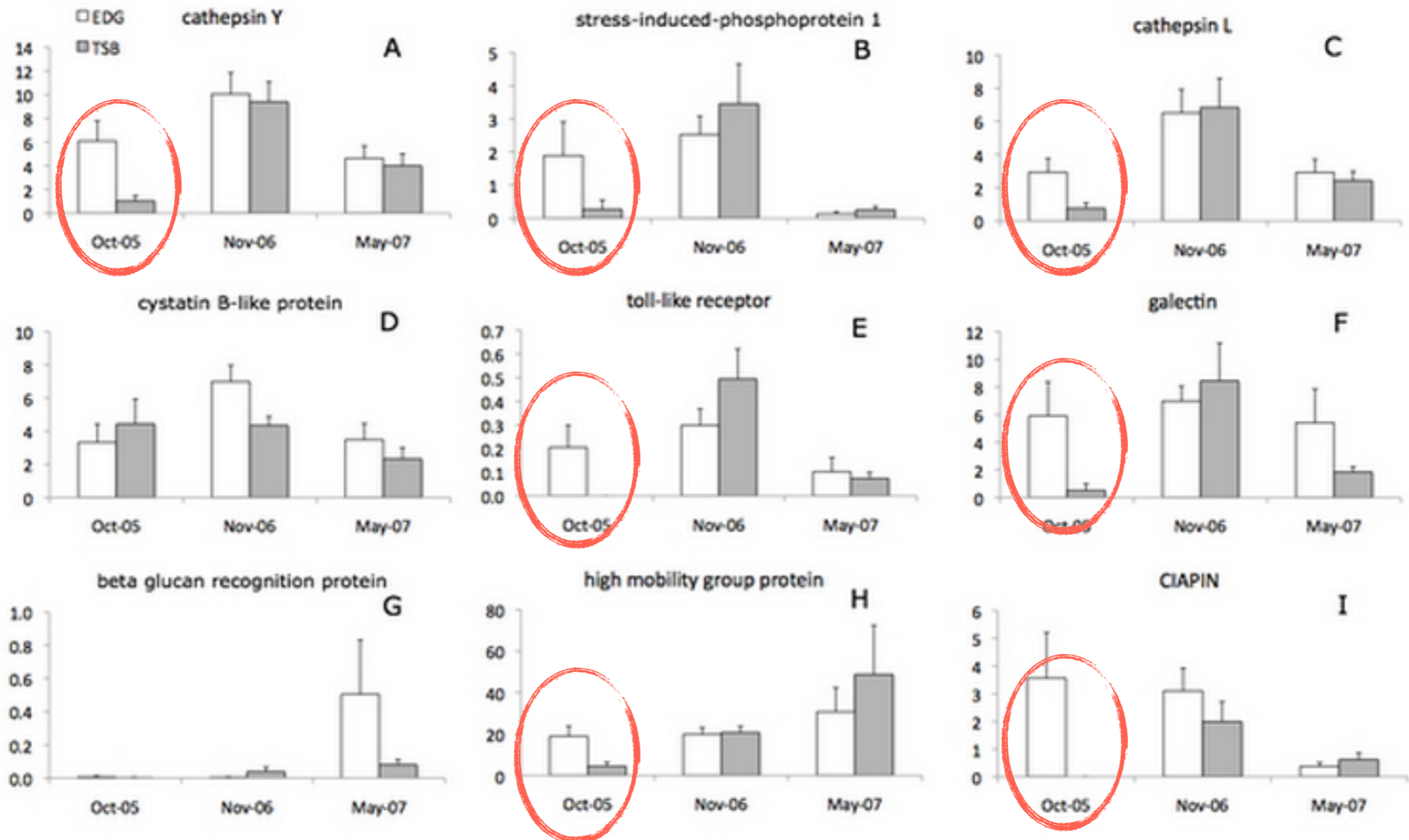
Summary - Oyster

- 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

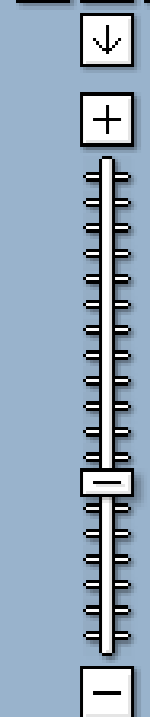
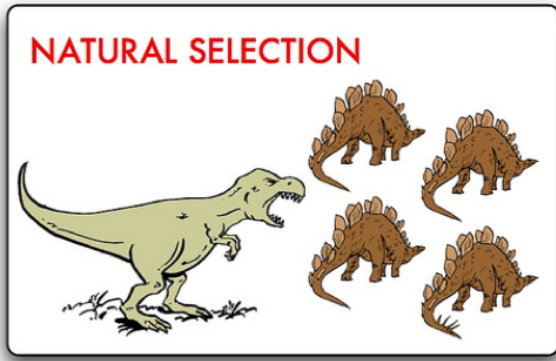
on selection

General Observation



Abalone

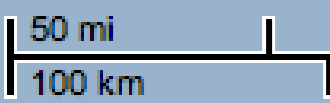




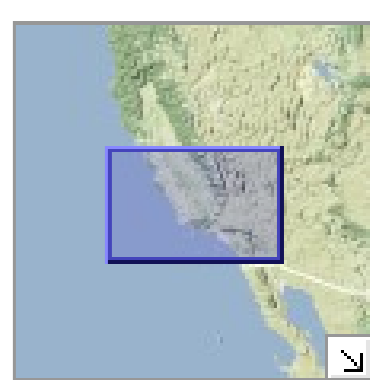
Naive

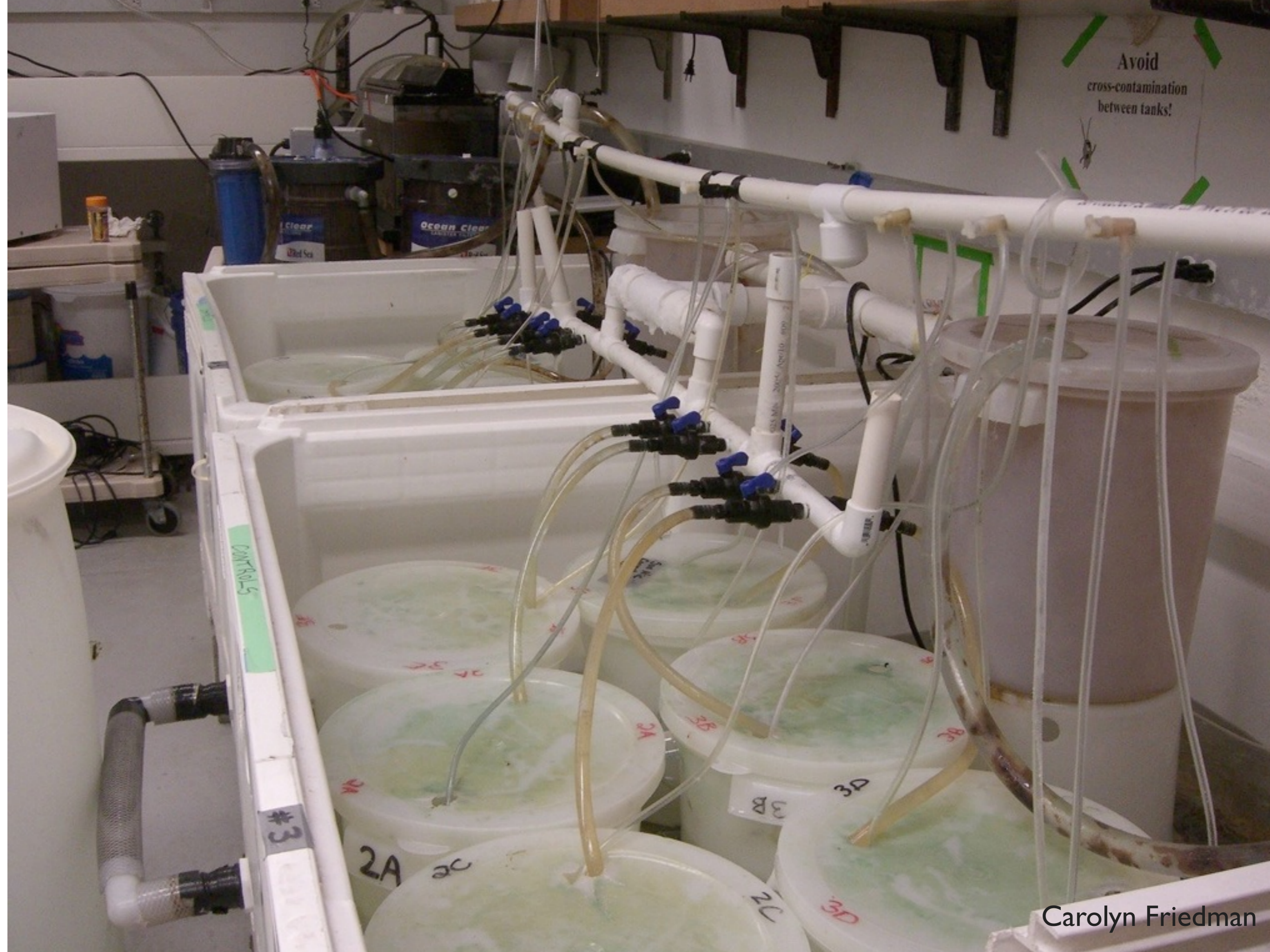


Disease Pressure



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Avoid
cross-contamination
between tanks!

CONTROLS

#3

2A

2B

3B

3D

Carolyn Friedman

Avoid
cross-contamination
between tanks!



CONTROLS

#3

2A

2C

3B

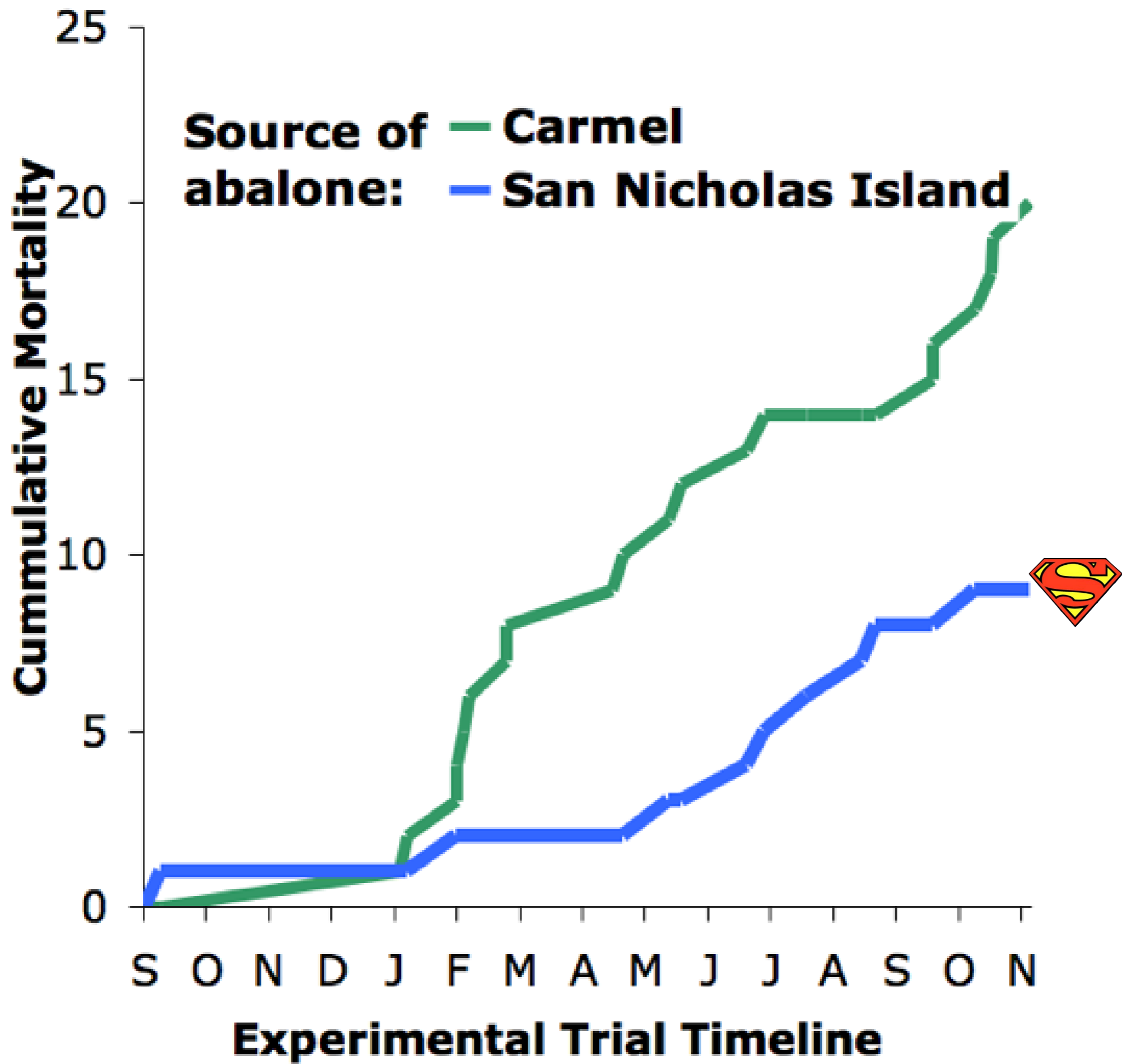
3D

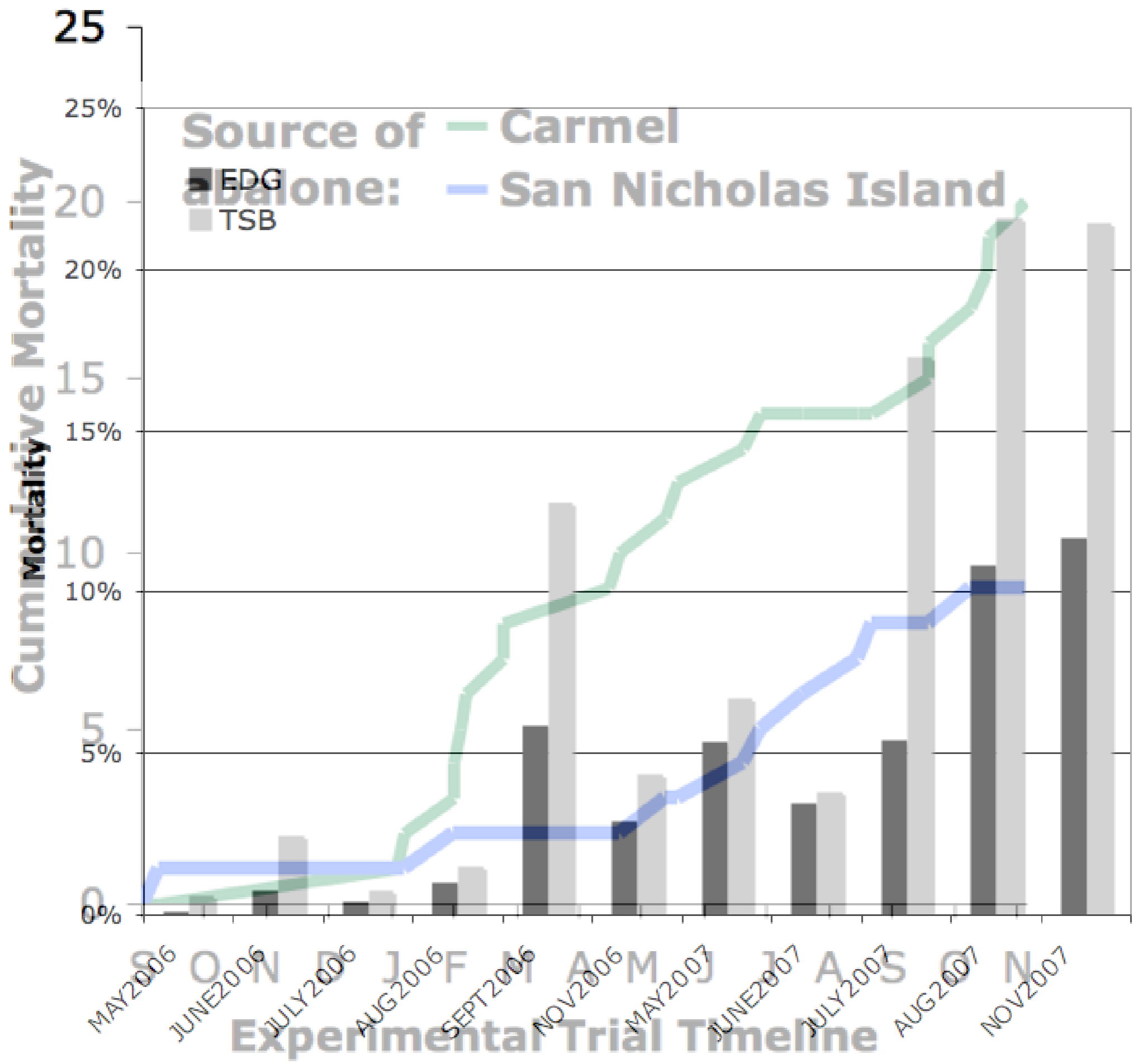
3D

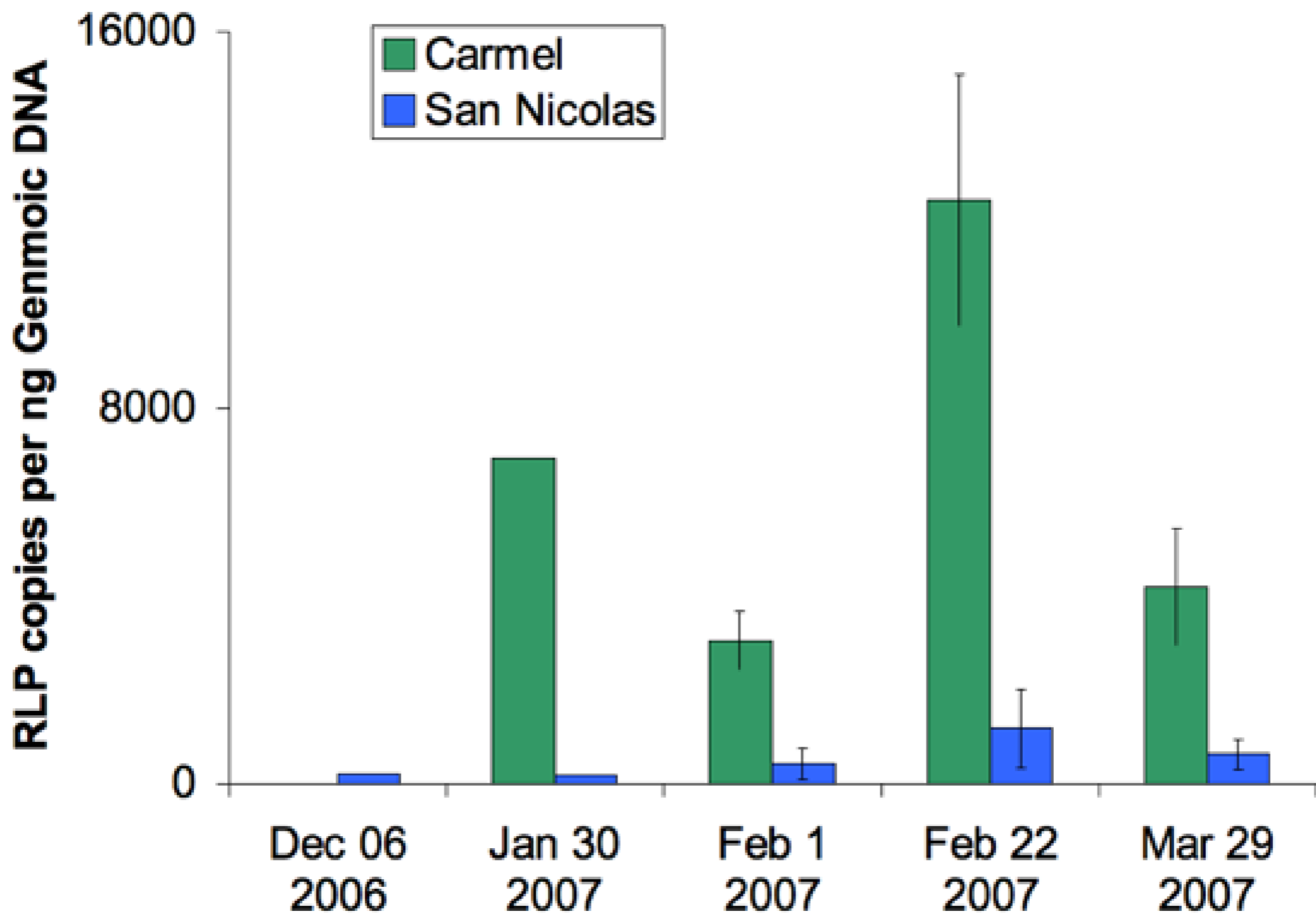
Carolyn Friedman

analogous to ...

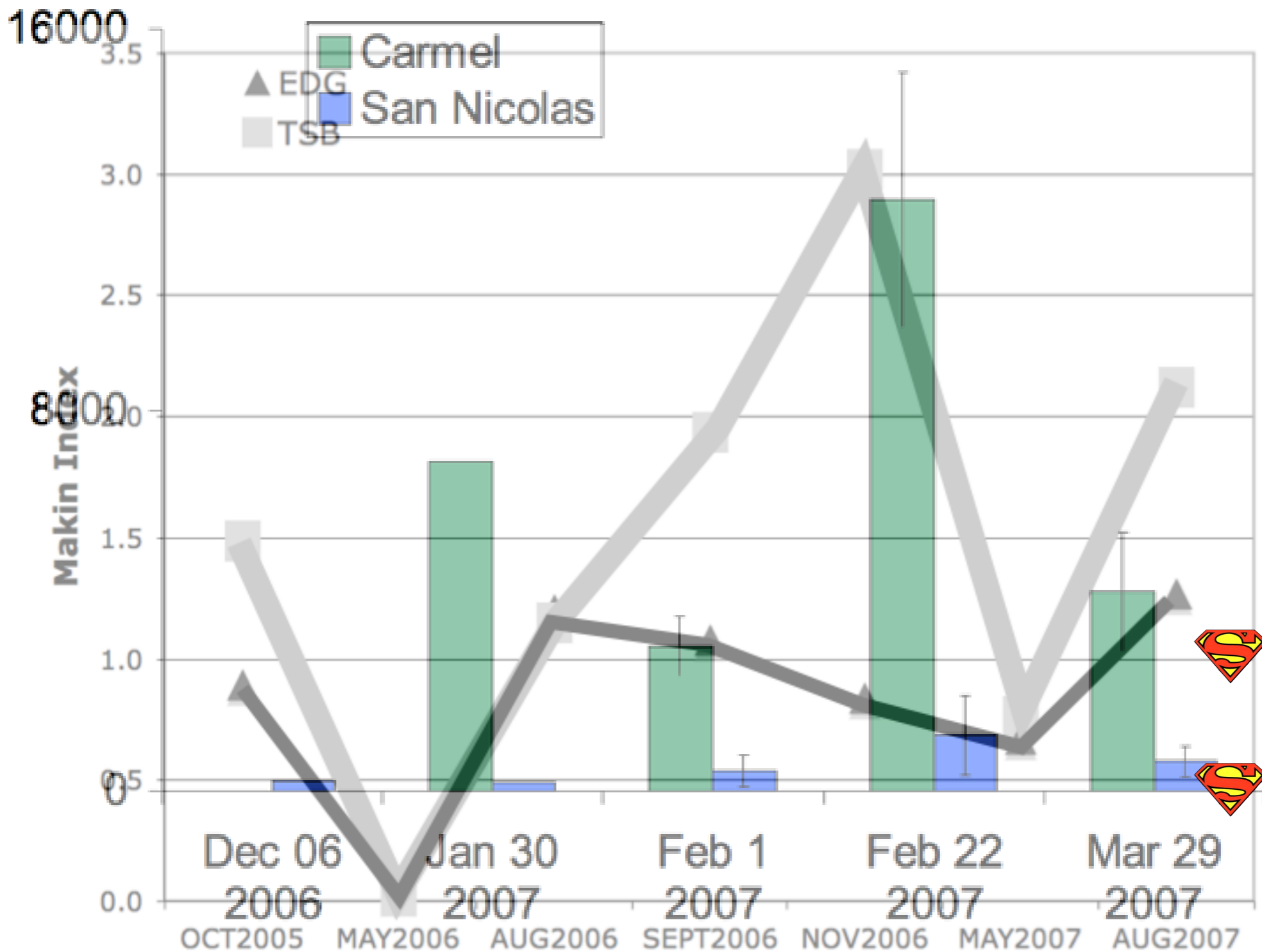








RLP copies per ng Genmoic DNA

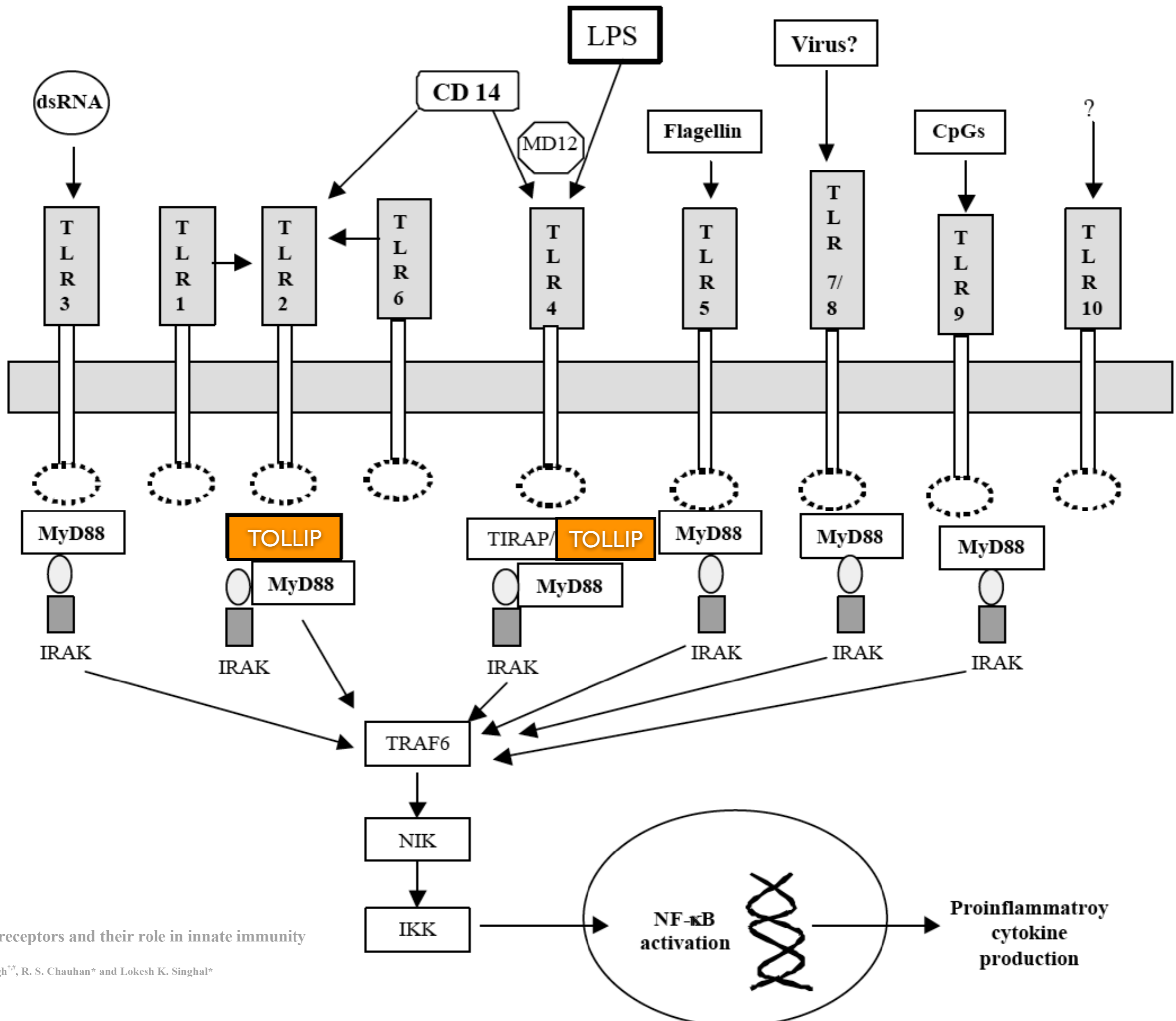


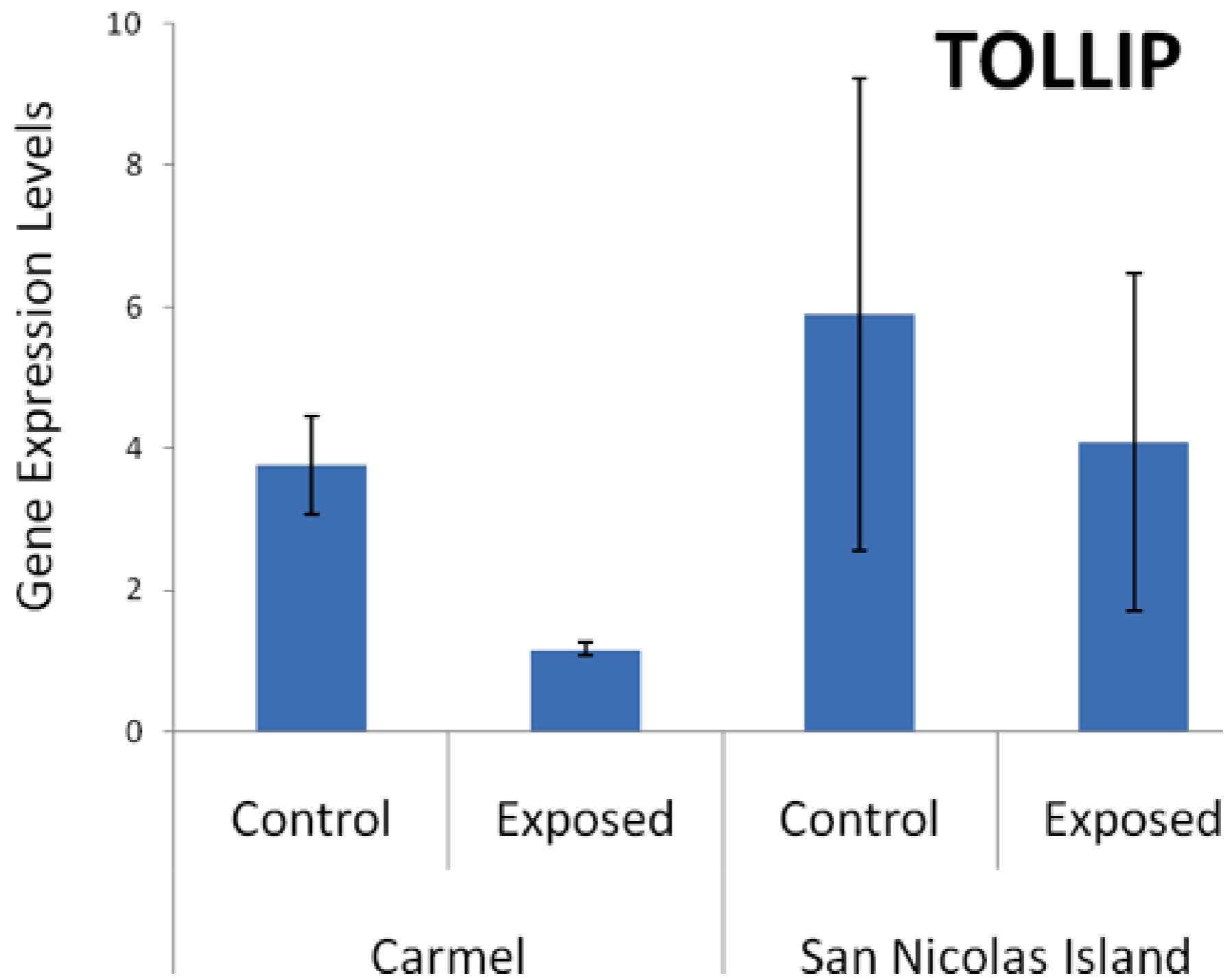
Increased Resistance

Better survival AND less pathogen load

How?

Differences?





bacteria recognition protein

