

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.

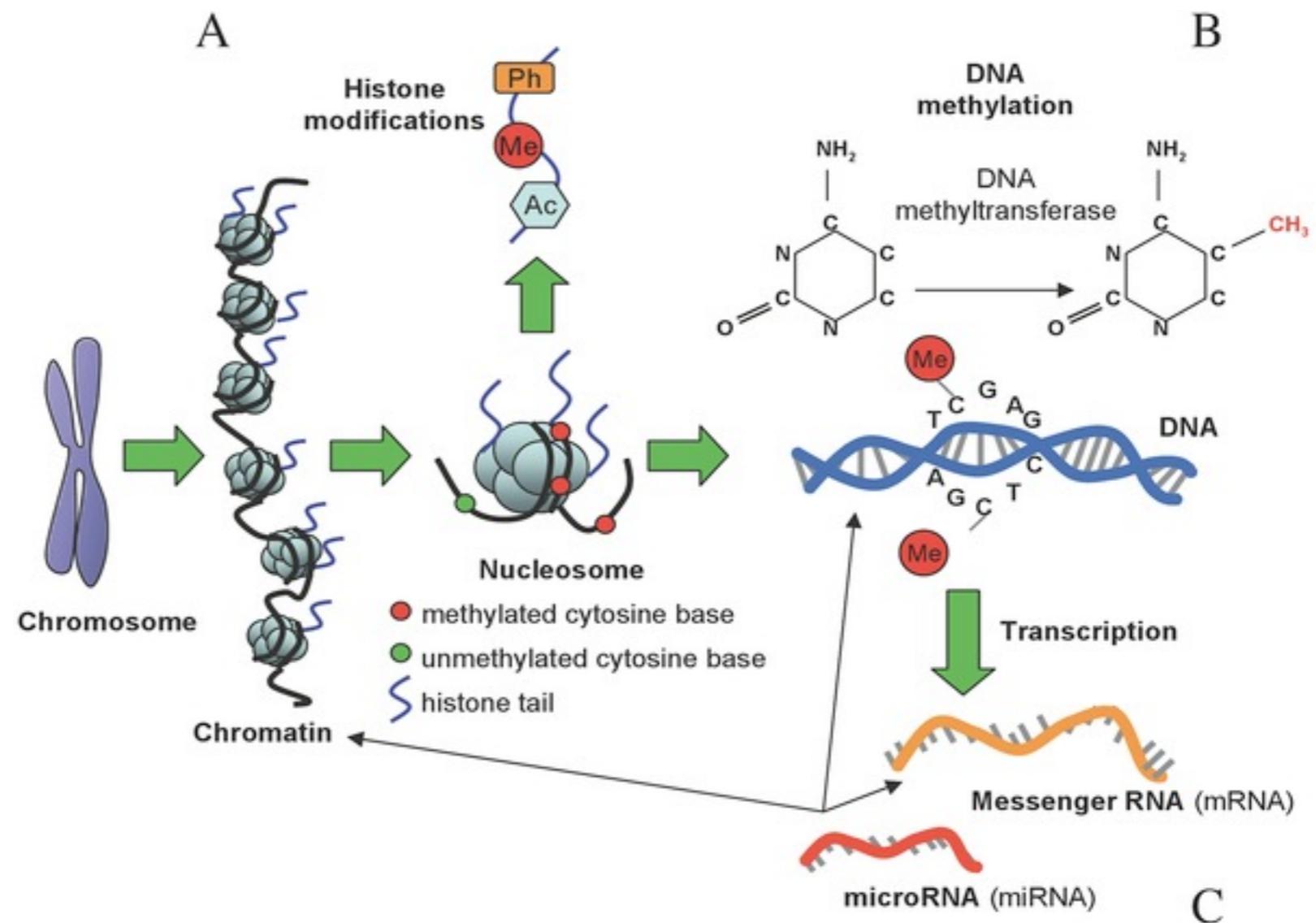
Innate immunity is classically defined as unable to build up immunological memory. Recently however, the assumption of the lack of immunological memory within innate immune responses has been reconsidered. Plants and invertebrates lacking adaptive immune system can be protected against secondary infections.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

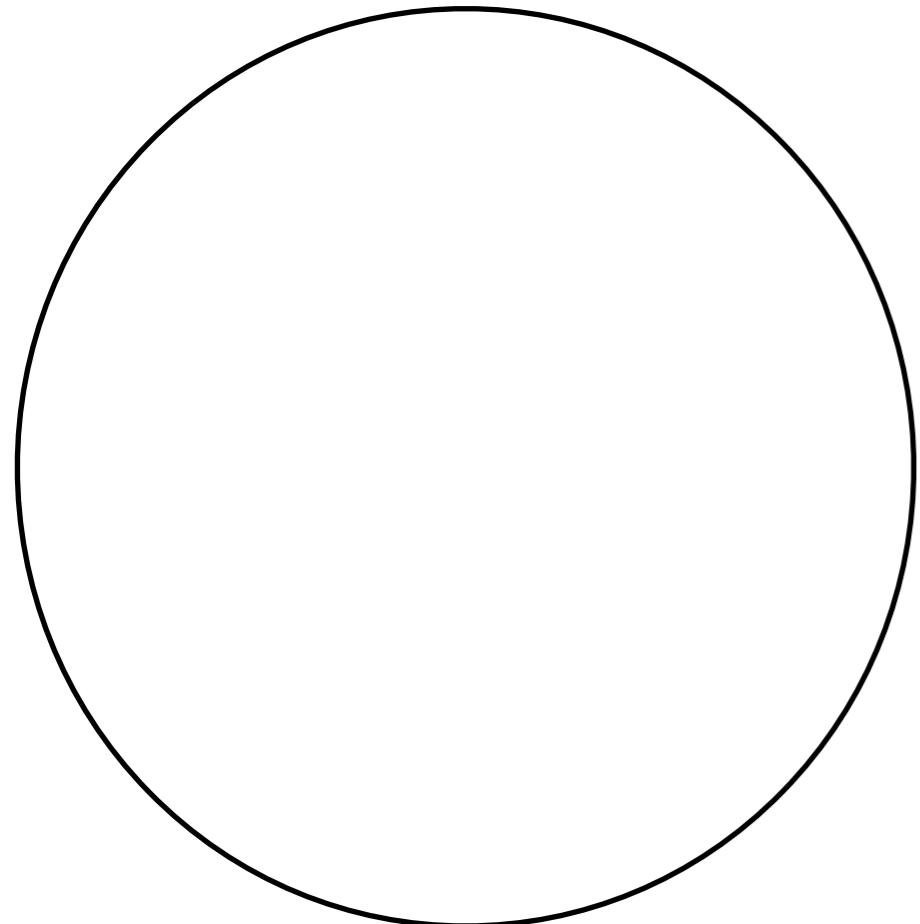
Anatomic Features



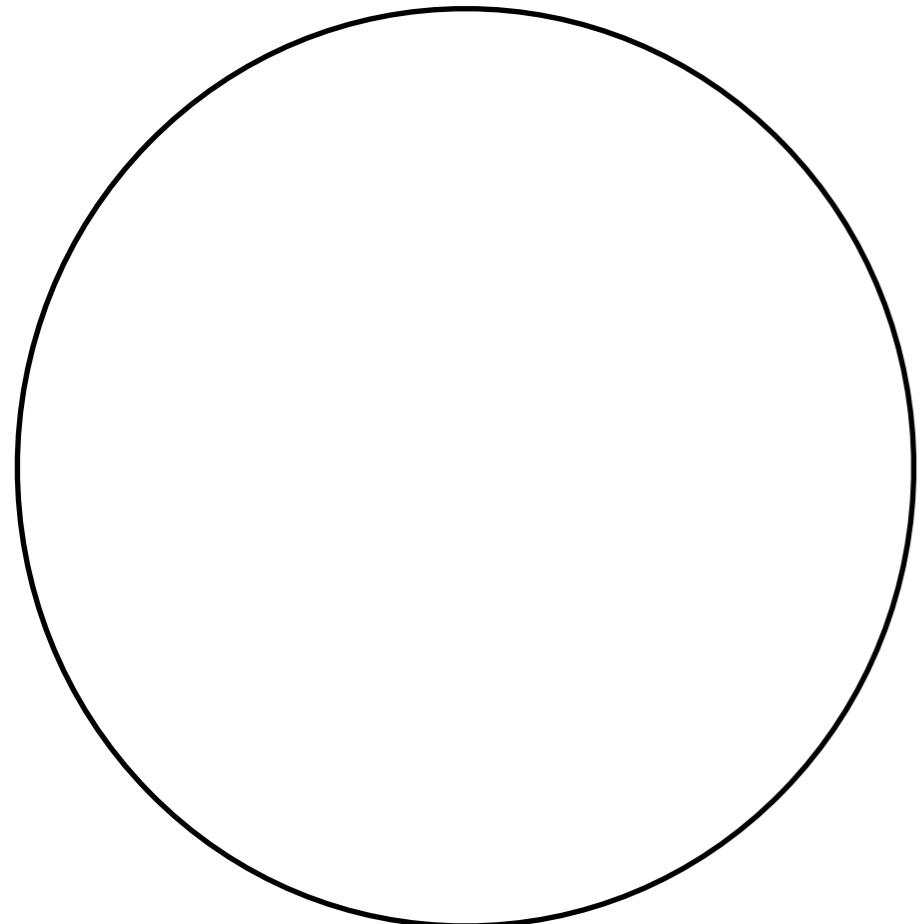
tinyurl.com/cgbso7

What is the overarching fear in those three examples?

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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

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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)

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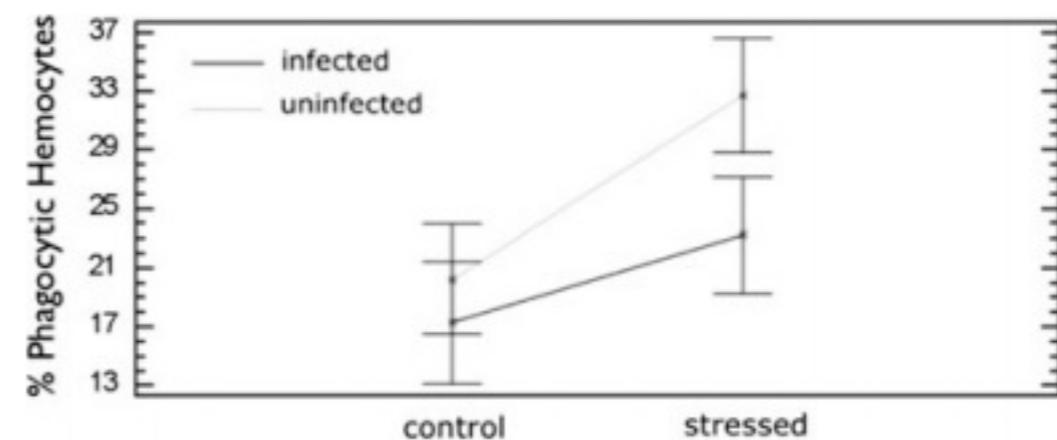
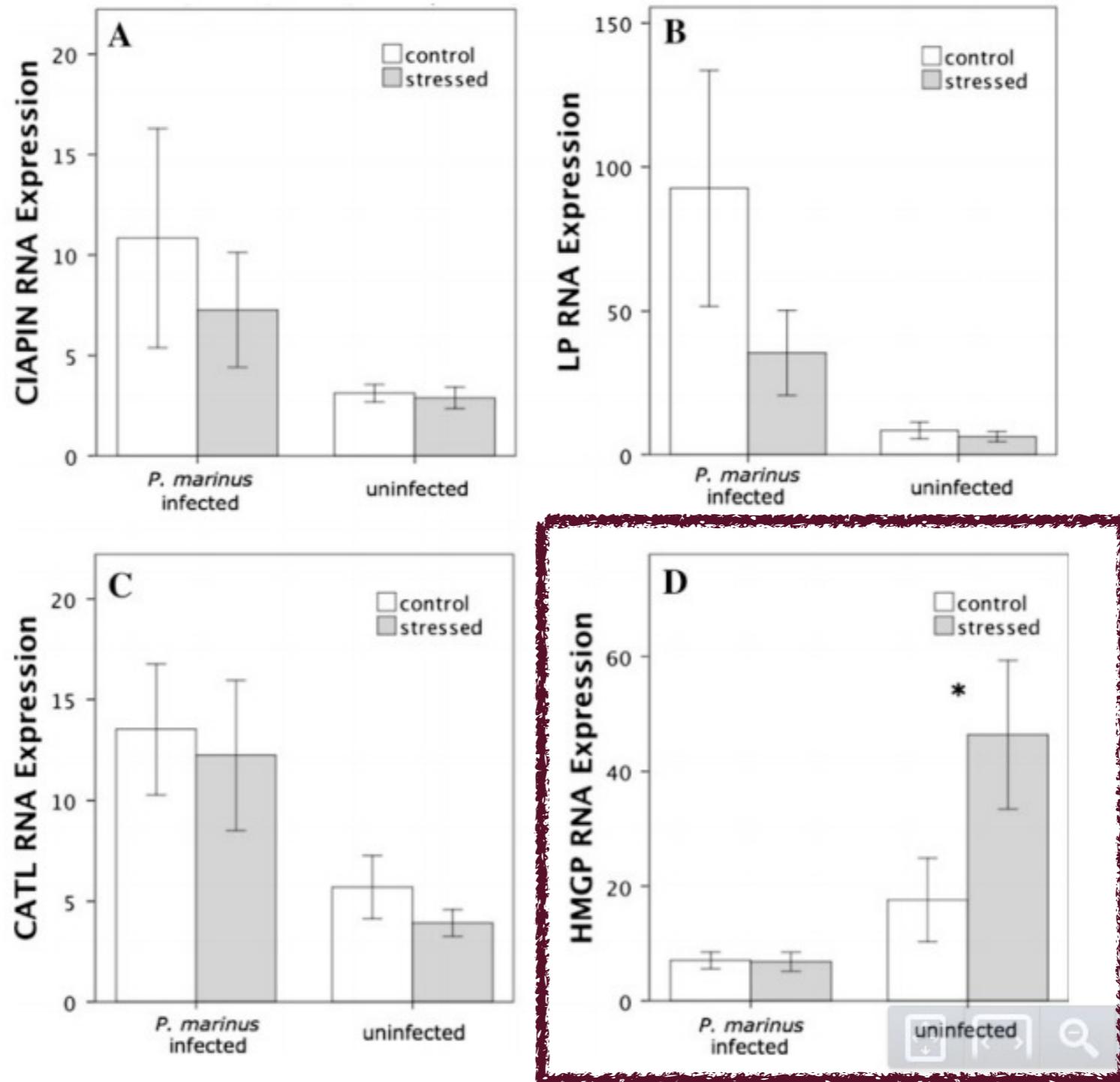


Fig. 2 Percentage of phagocytic hemocytes in *P. marinus*-infected ($n = 17$) and uninfected oysters ($n = 19$). A significant difference was observed after mechanical stress only in uninfected oysters (ANOVA $p < 0.05$)

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

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

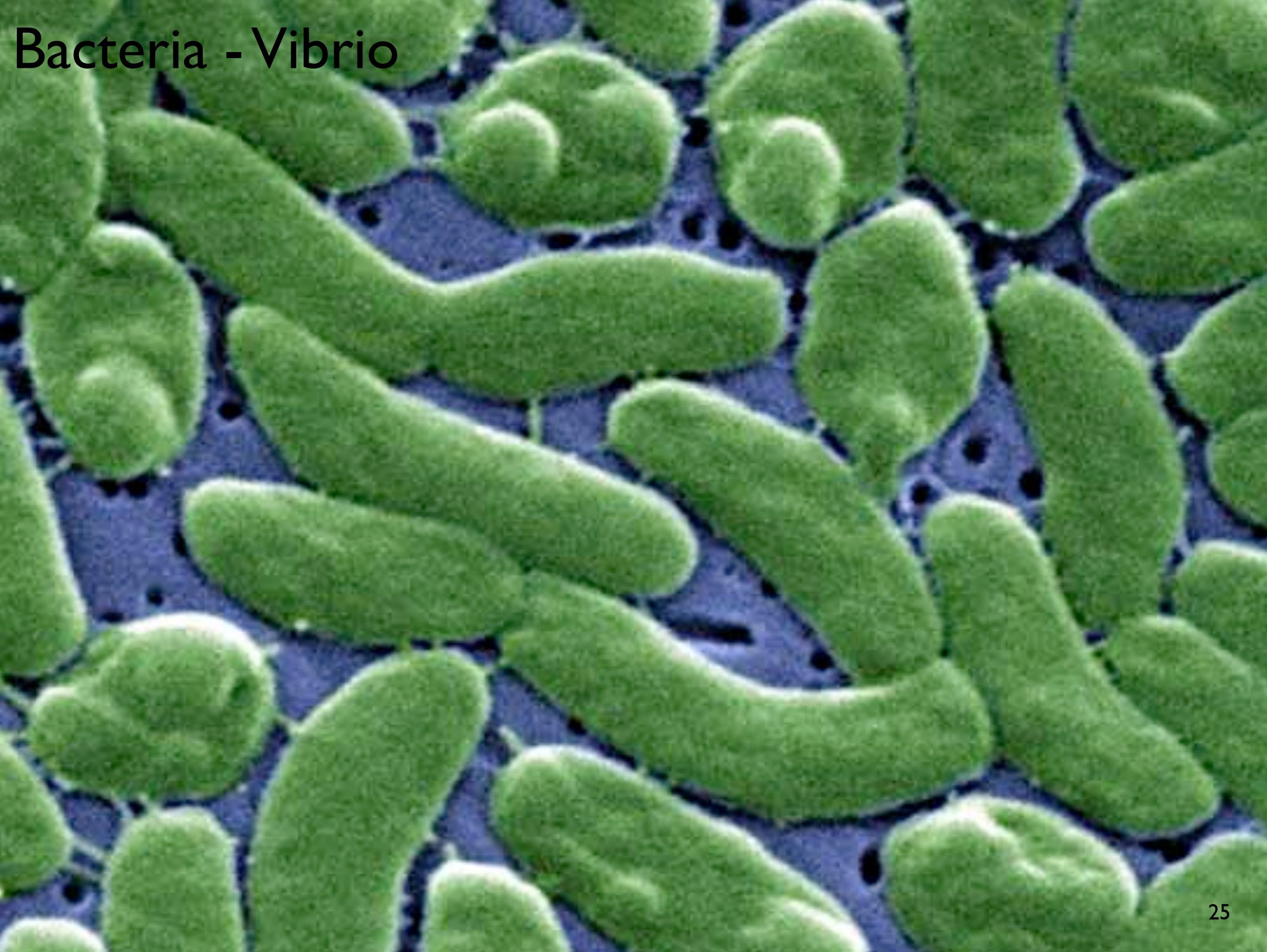


resource
allocation

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

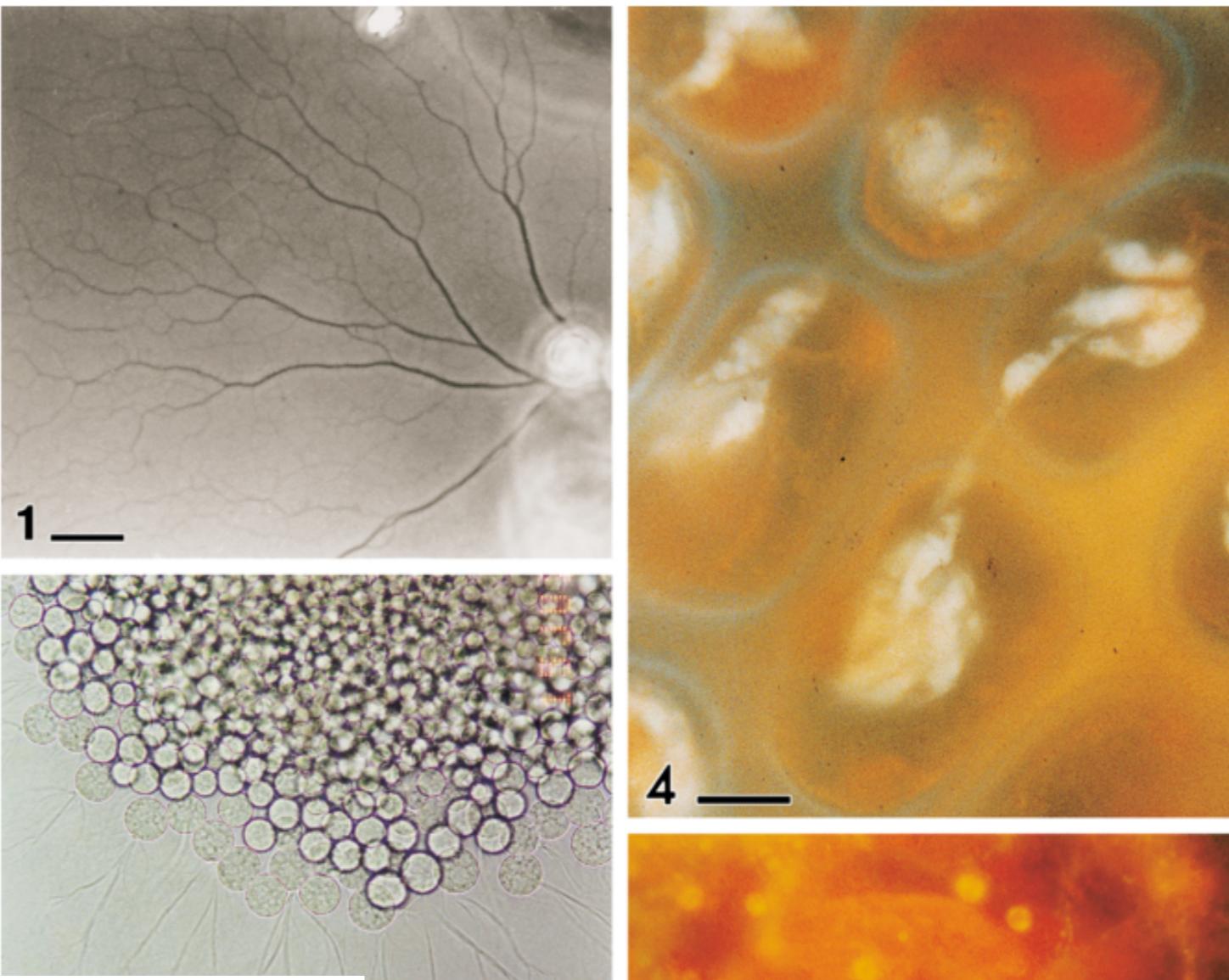


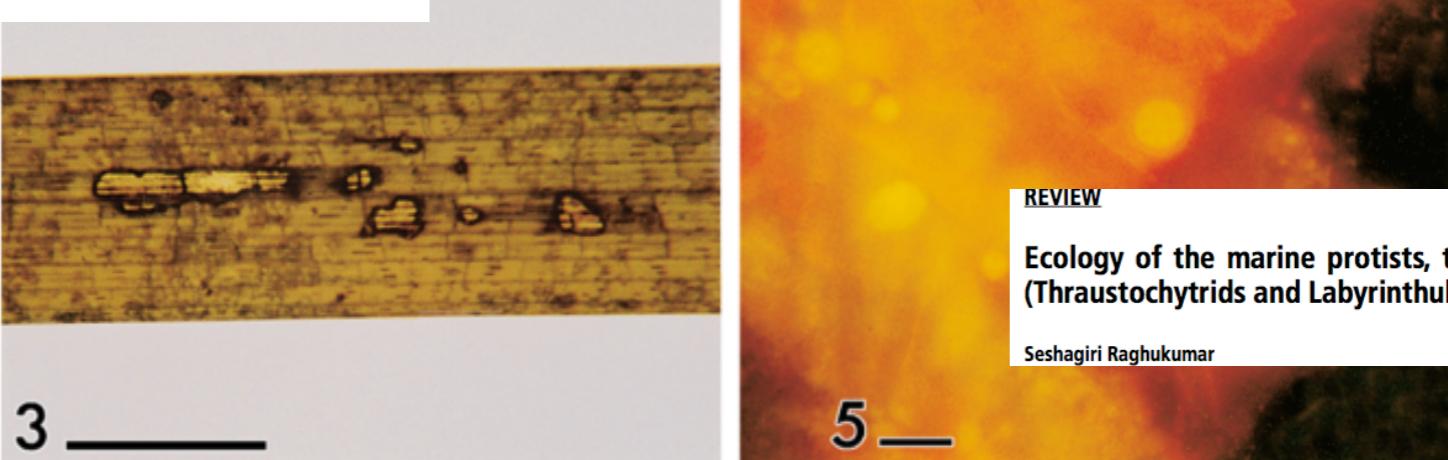
Fig. 1. Cells of a thraustochytrid growing on a nutrient agar medium. Bar represents 50 µm.

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.



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

Seshagiri RaghuKumar

Fungi - QPX

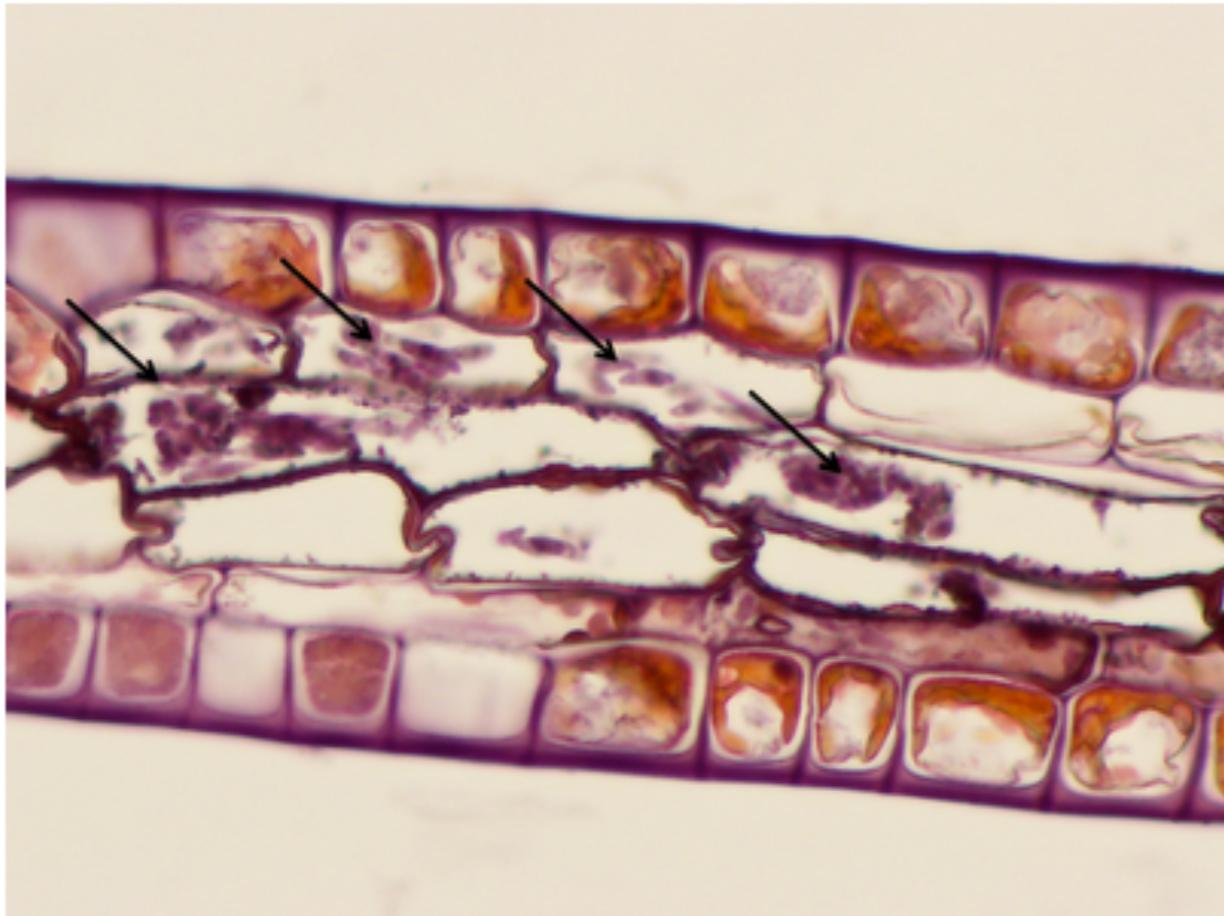


Roxanna Smolowitz



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](#)

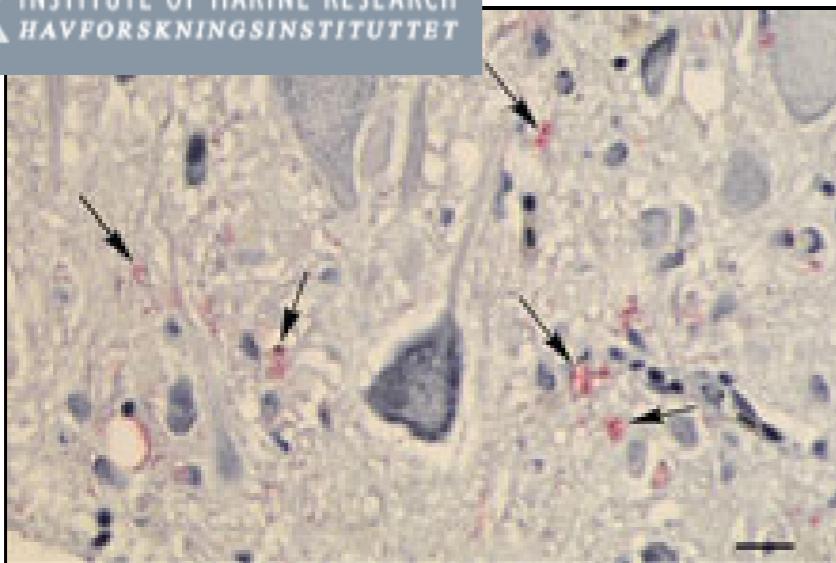


Colleen Burge - Sep 28, 2011 - Mobile - Limited

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



Phage



Abalone

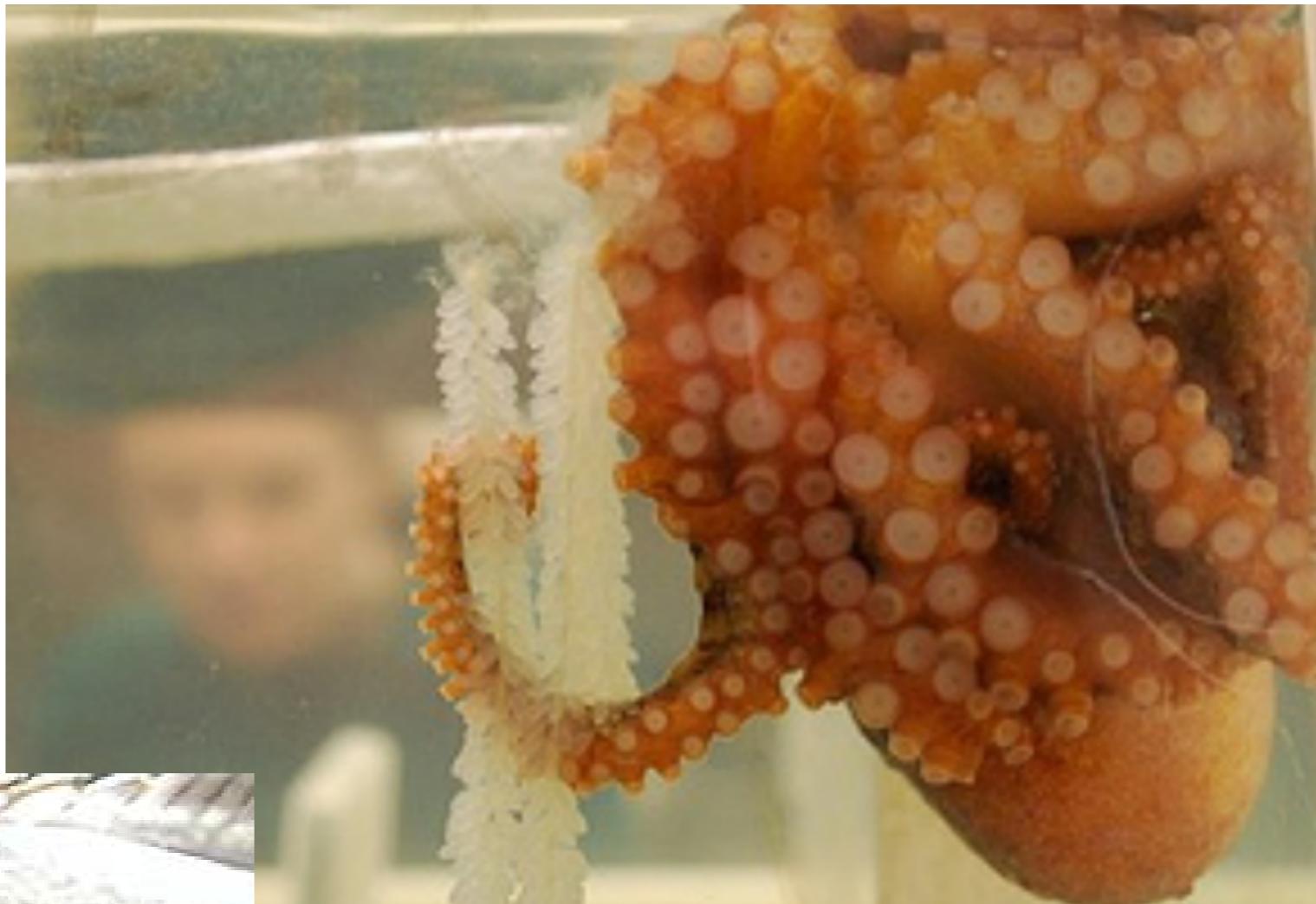


Caused by a bacteria..

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





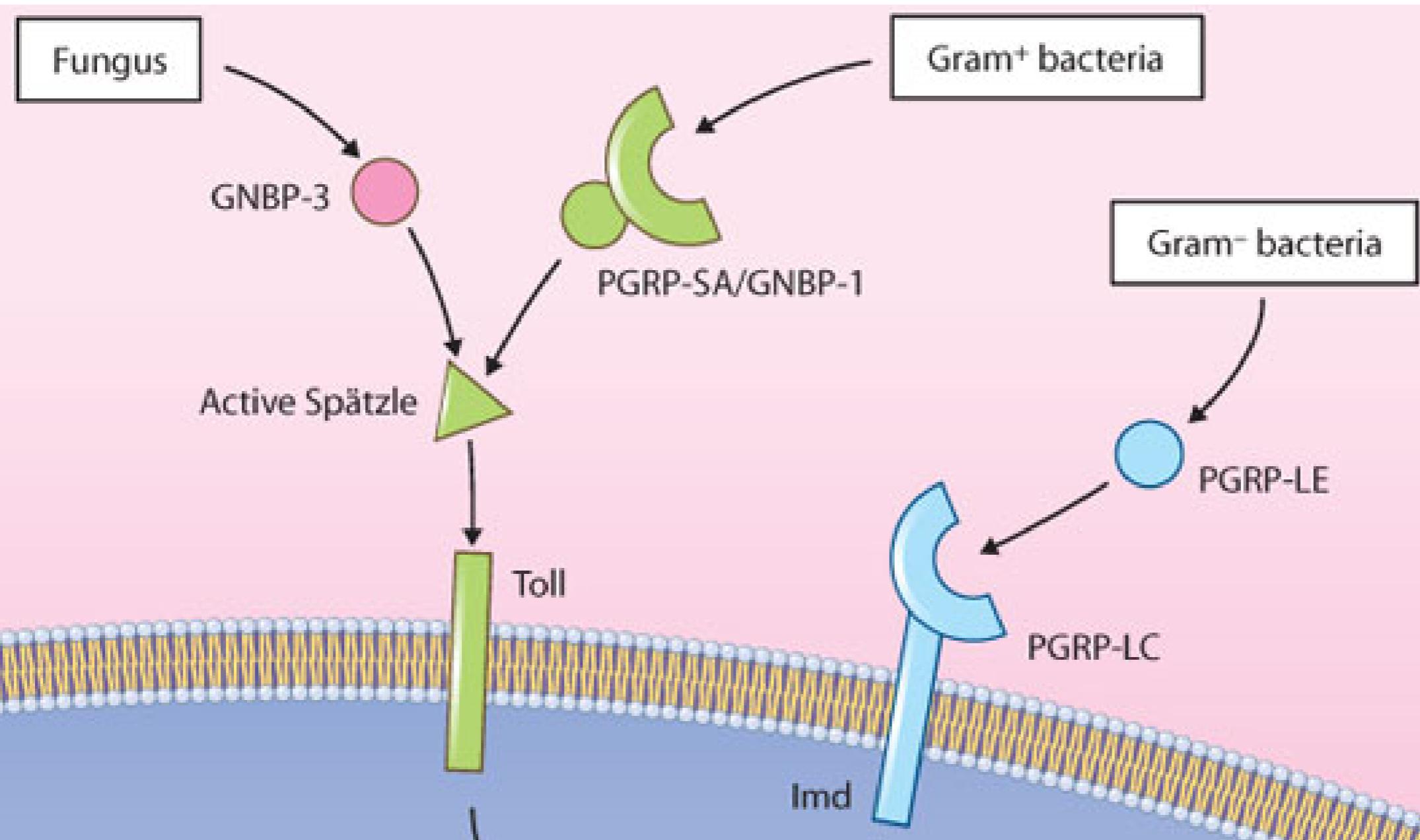
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This is a picture of two *A. elegantissima* or *A. sola* fighting with acrorhagia. Taken at San Simeon, CA by Dave Cowles

How do organisms distinguish self from non-self?

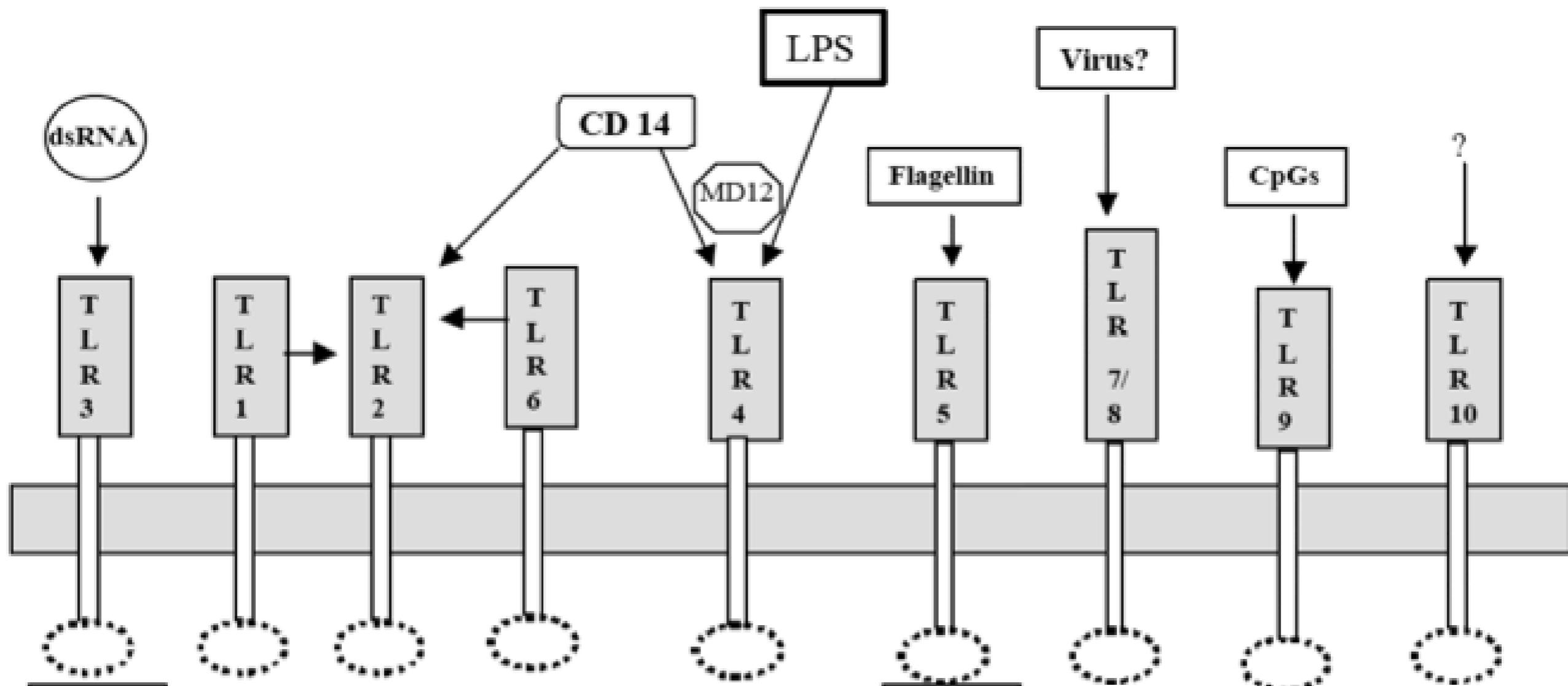
pattern recognitions proteins (PRPs)

PRPs



Toll-like Receptors
Peptidoglycan recognition proteins

PRPs - Toll-like Receptors

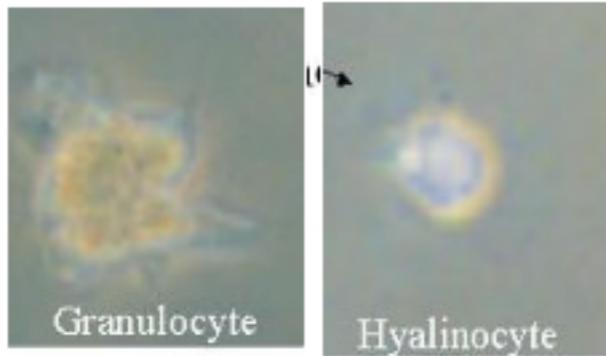


That's how the immune system
knows bad things are there...

Innate Immunity

Chemico-physical barrier (shell, mucus)

CELLS:



Hemolymph

SERUM:

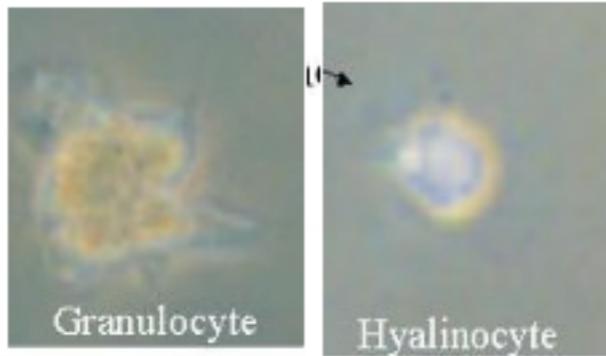
soluble lectins
hydrolytic enzymes
antimicrobial peptides

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

Innate Immunity

Chemico-physical barrier (shell, mucus)

CELLS:



Hemolymph

SERUM:

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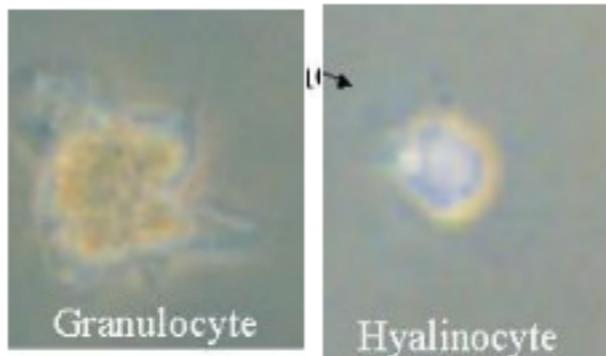
} chemokinesis
chemotaxis
binding and internalization
oxidative burst activation
lysosomal enzymes
antimicrobial peptides

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

Innate Immunity

Chemico-physical barrier (shell, mucus)

CELLS:



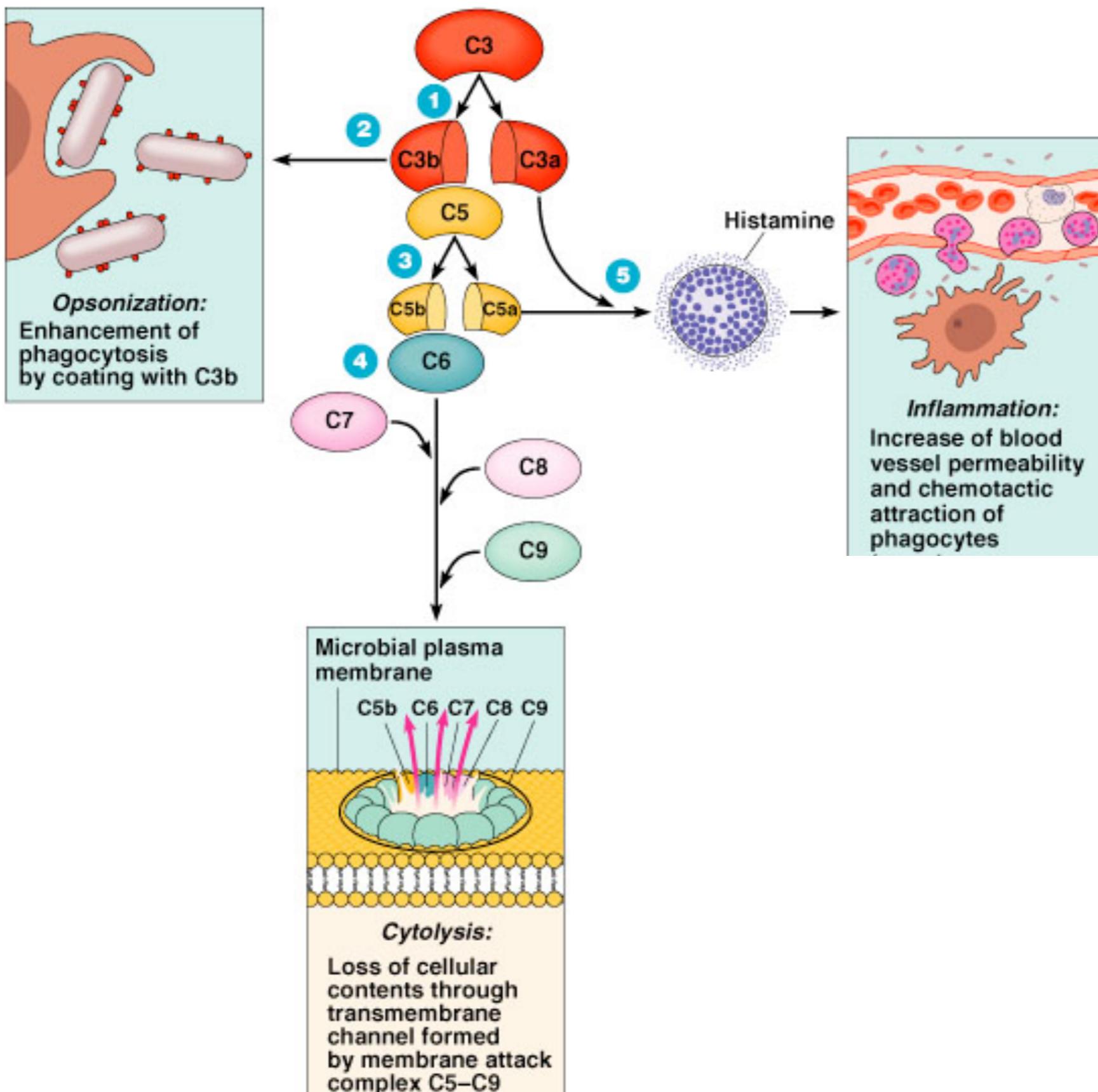
Hemolymph

SERUM:

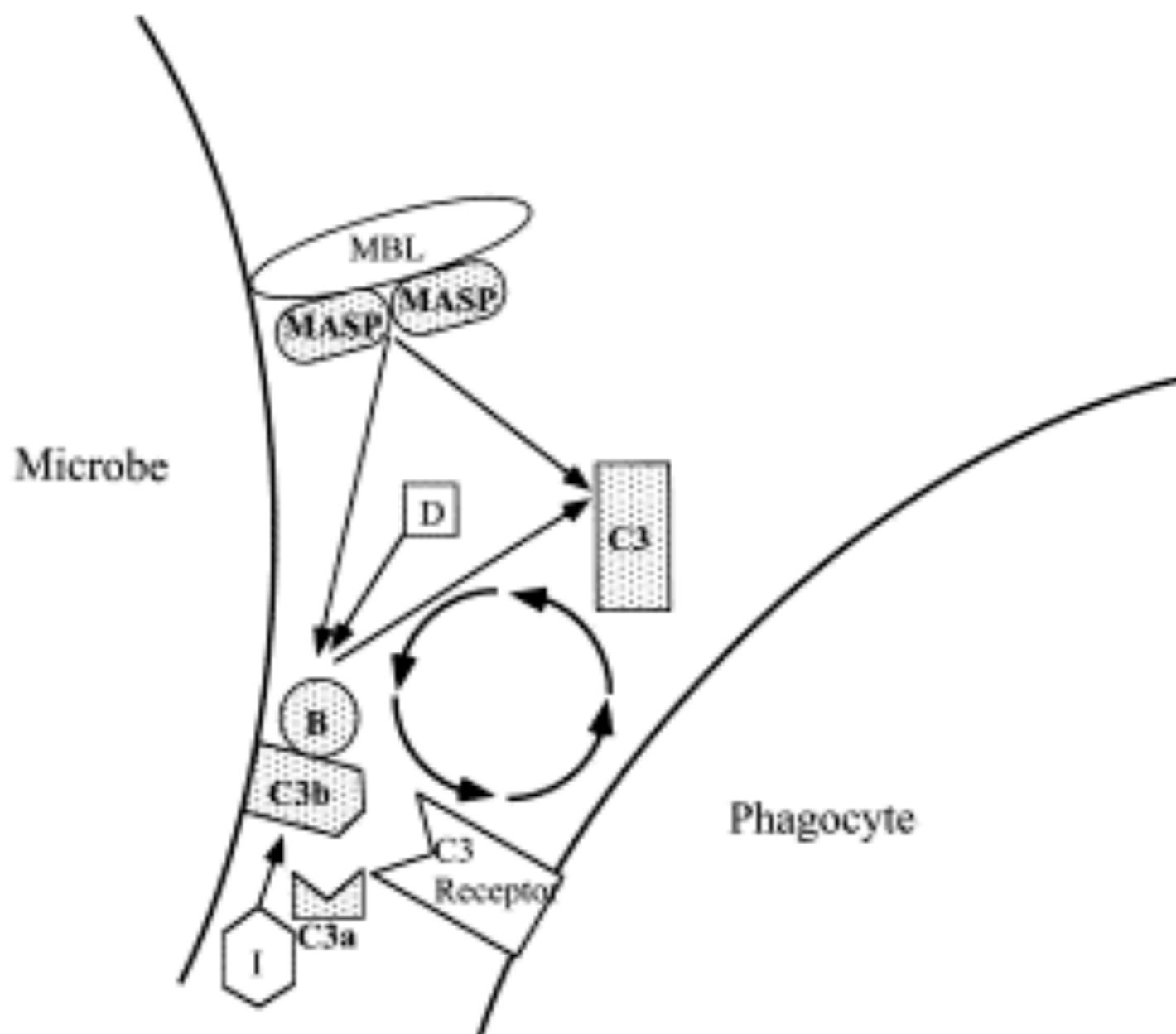
soluble lectins
hydrolytic enzymes
antimicrobial peptides

{ chemokinesis
chemotaxis
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oxidative burst activation
lysosomal enzymes
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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

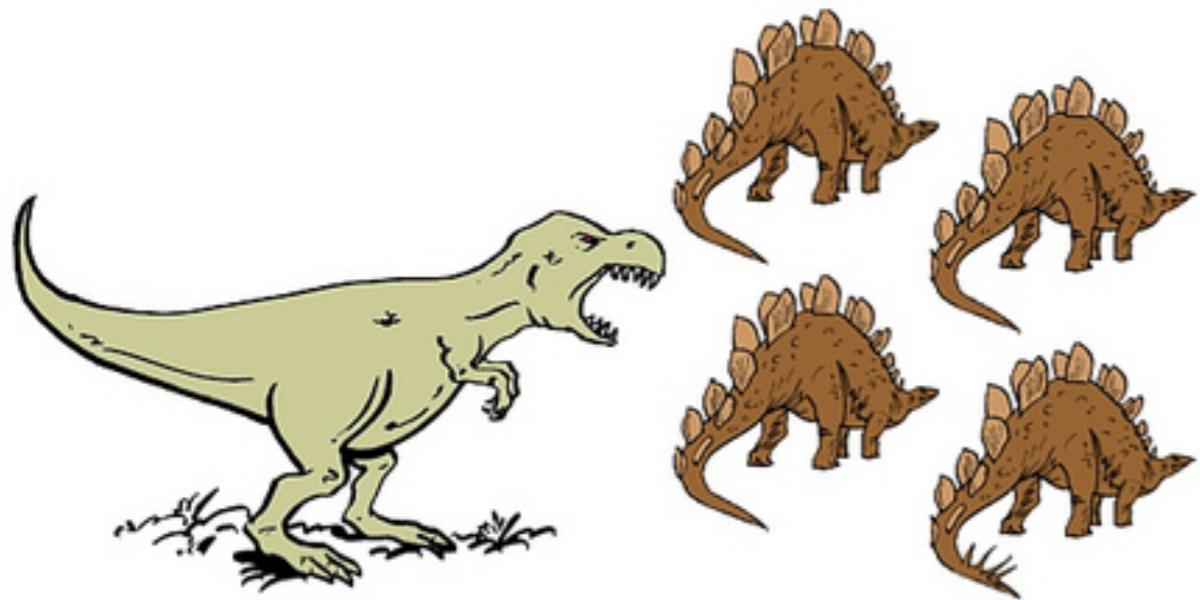
It is important to think about the big picture.

What else is going on with the critter...

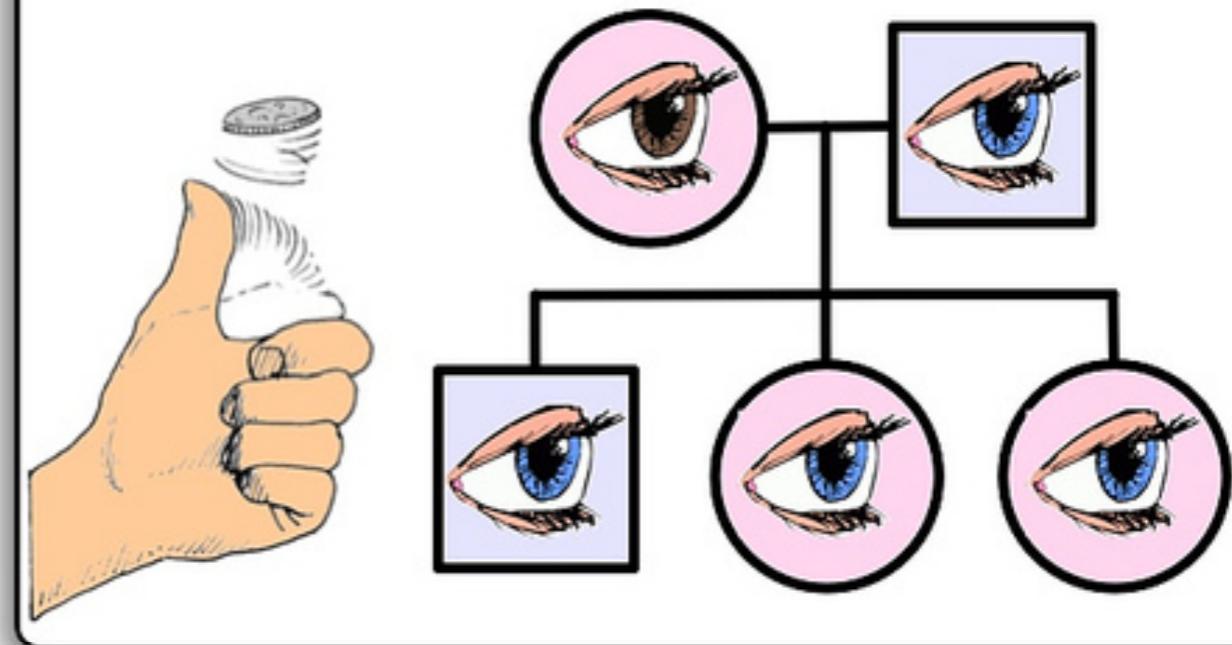
really big picture -

What has the population experienced.

NATURAL SELECTION



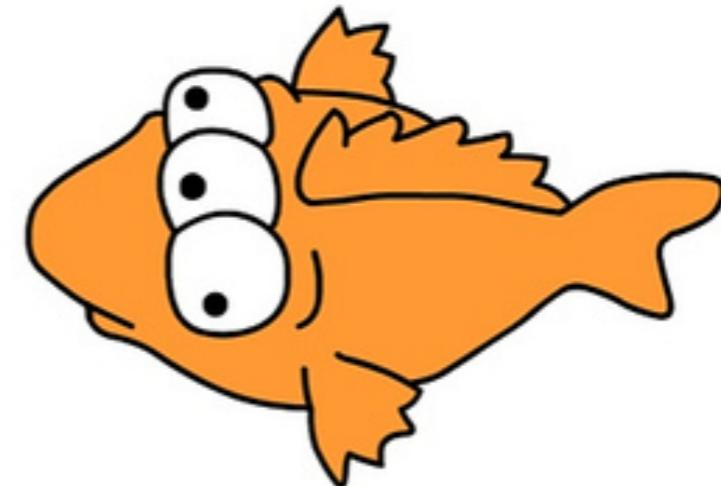
GENETIC DRIFT



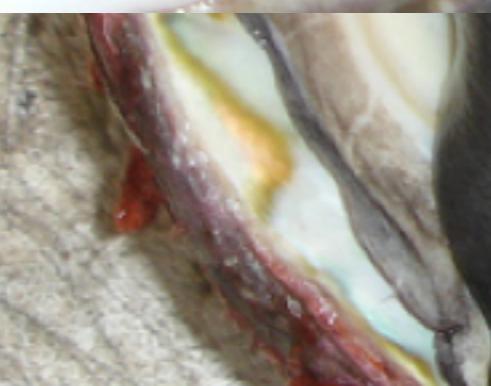
MIGRATION

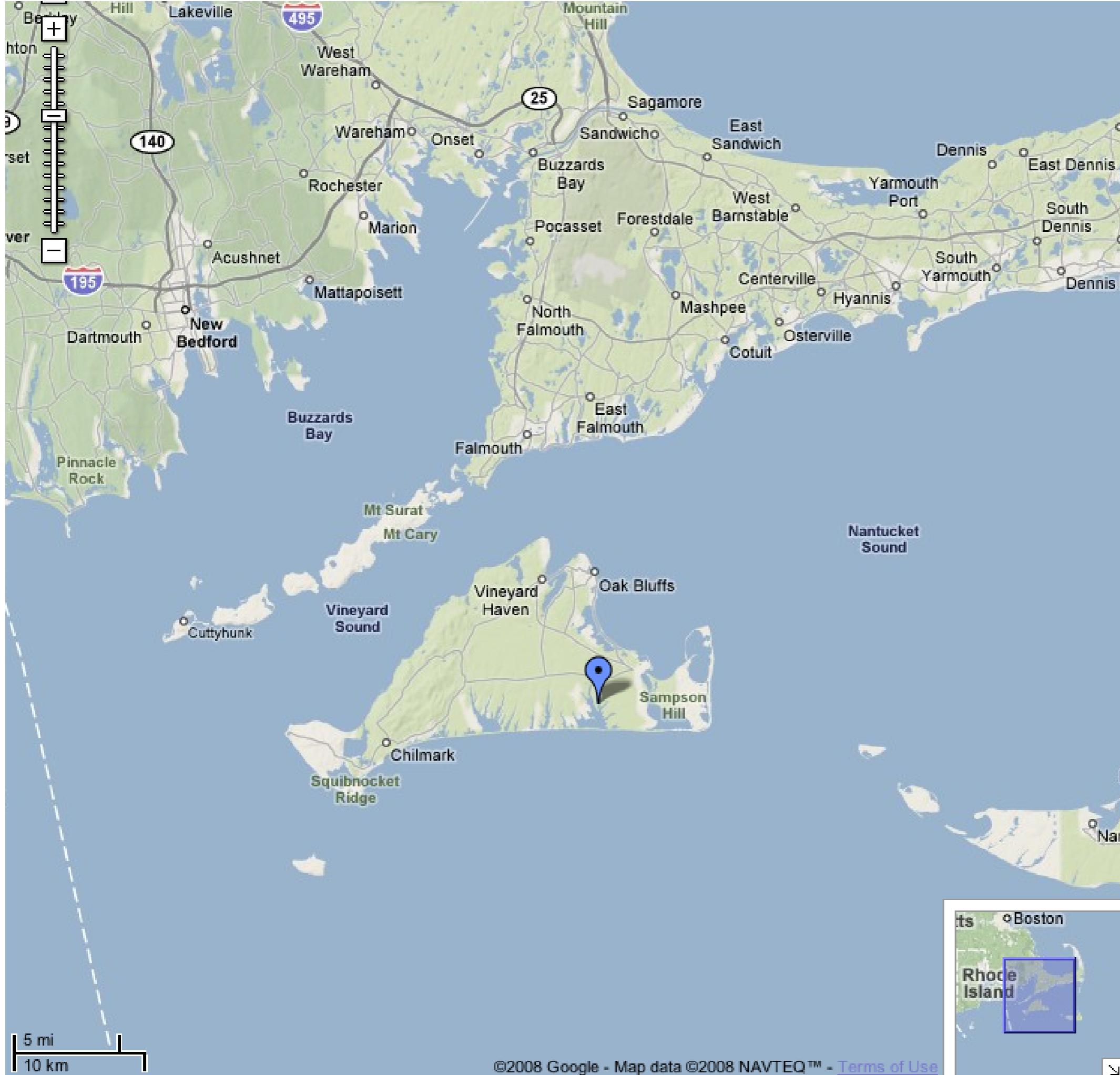


MUTATION

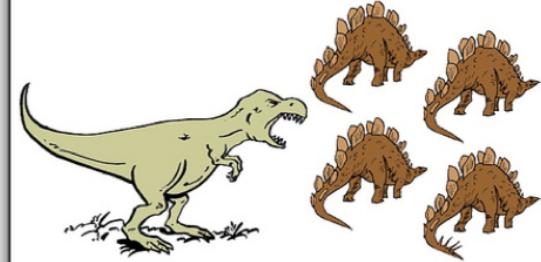


Two part story





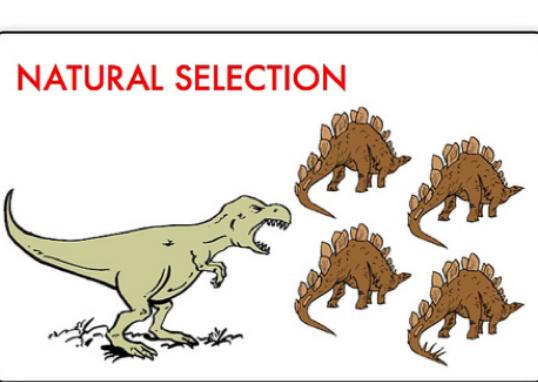
NATURAL SELECTION



flickr | cpurrin |



Roxanna Smolowitz
Rick Karney



flickr | cpurrin |

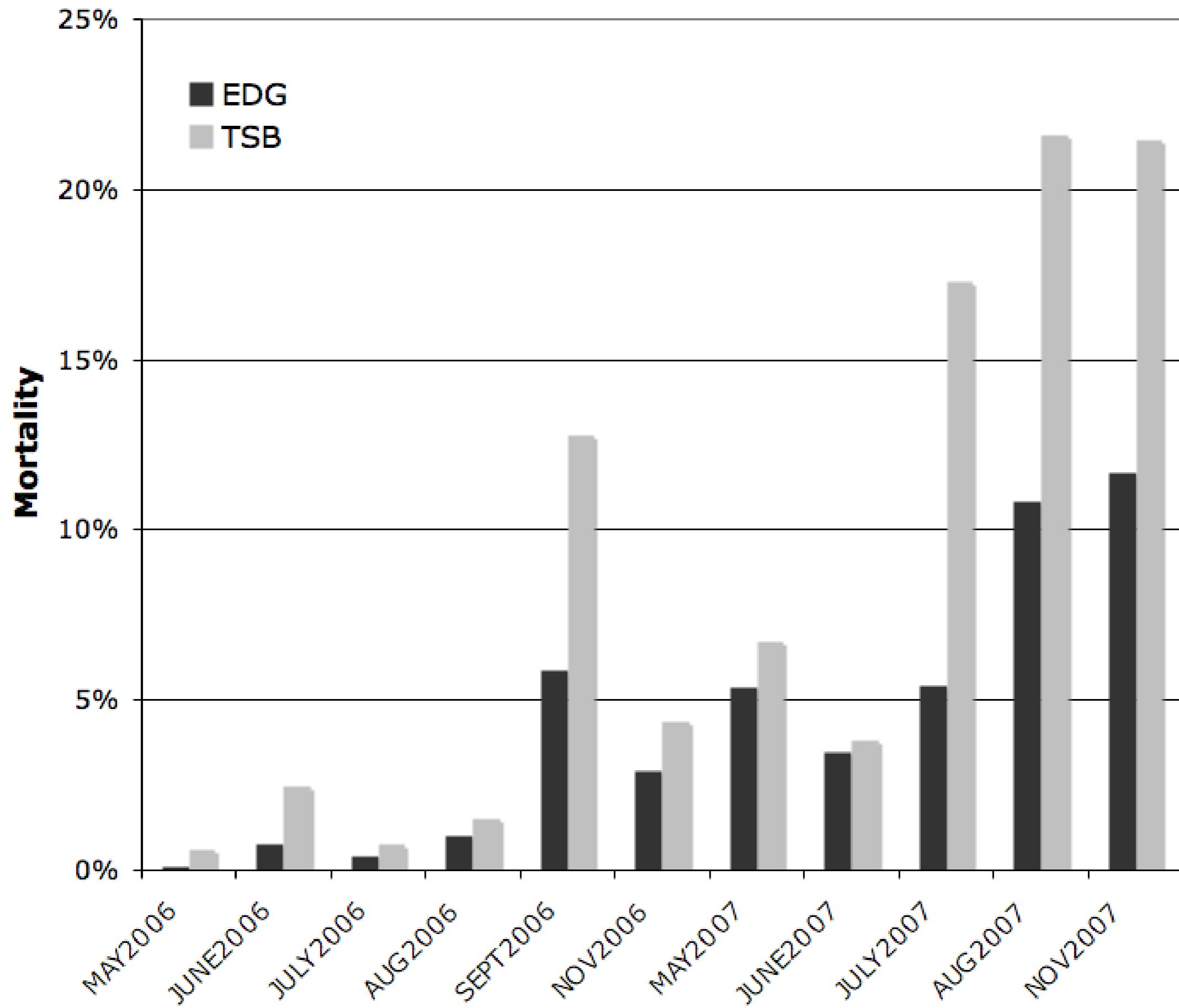
Roxanna Smolowitz
Rick Karney

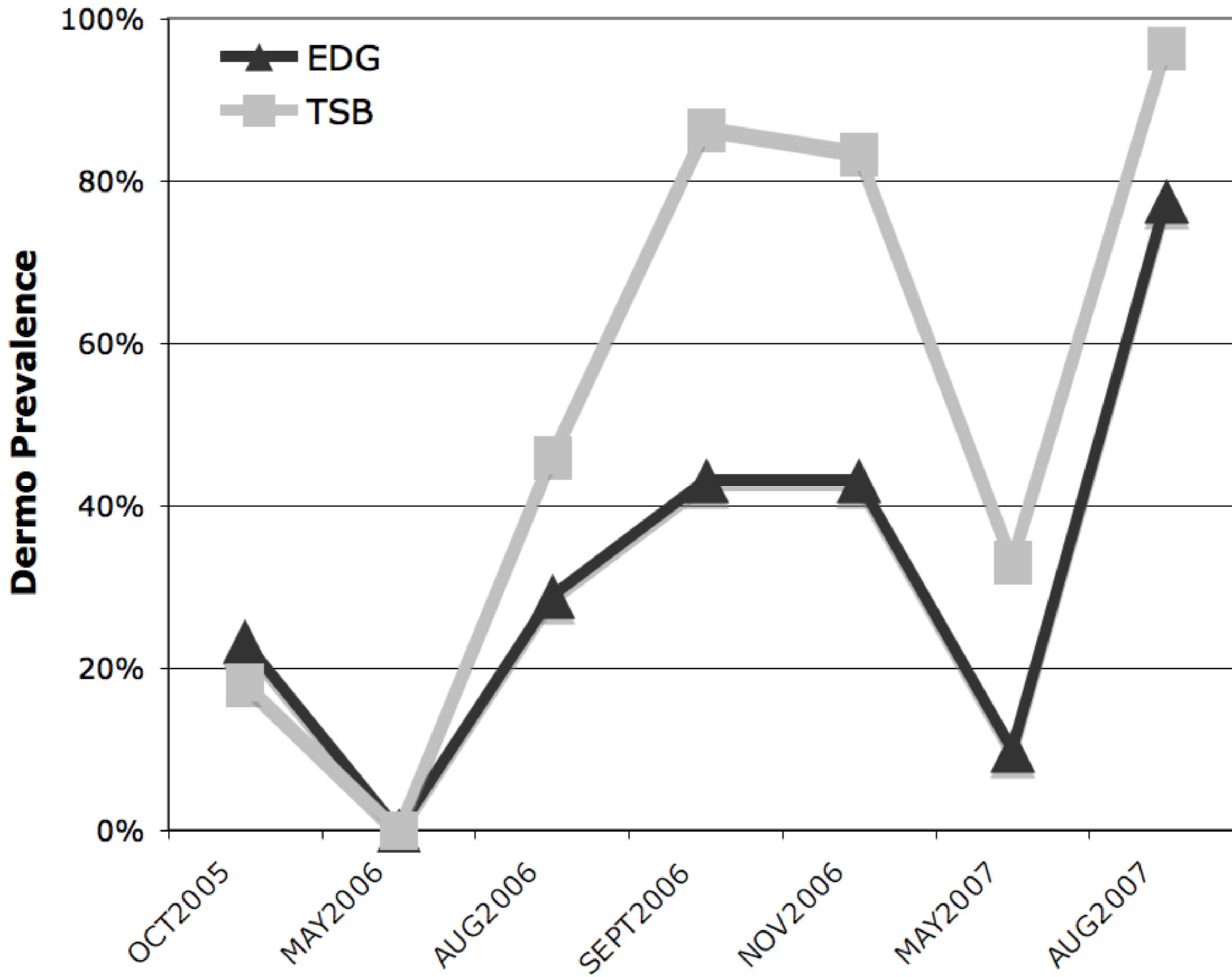




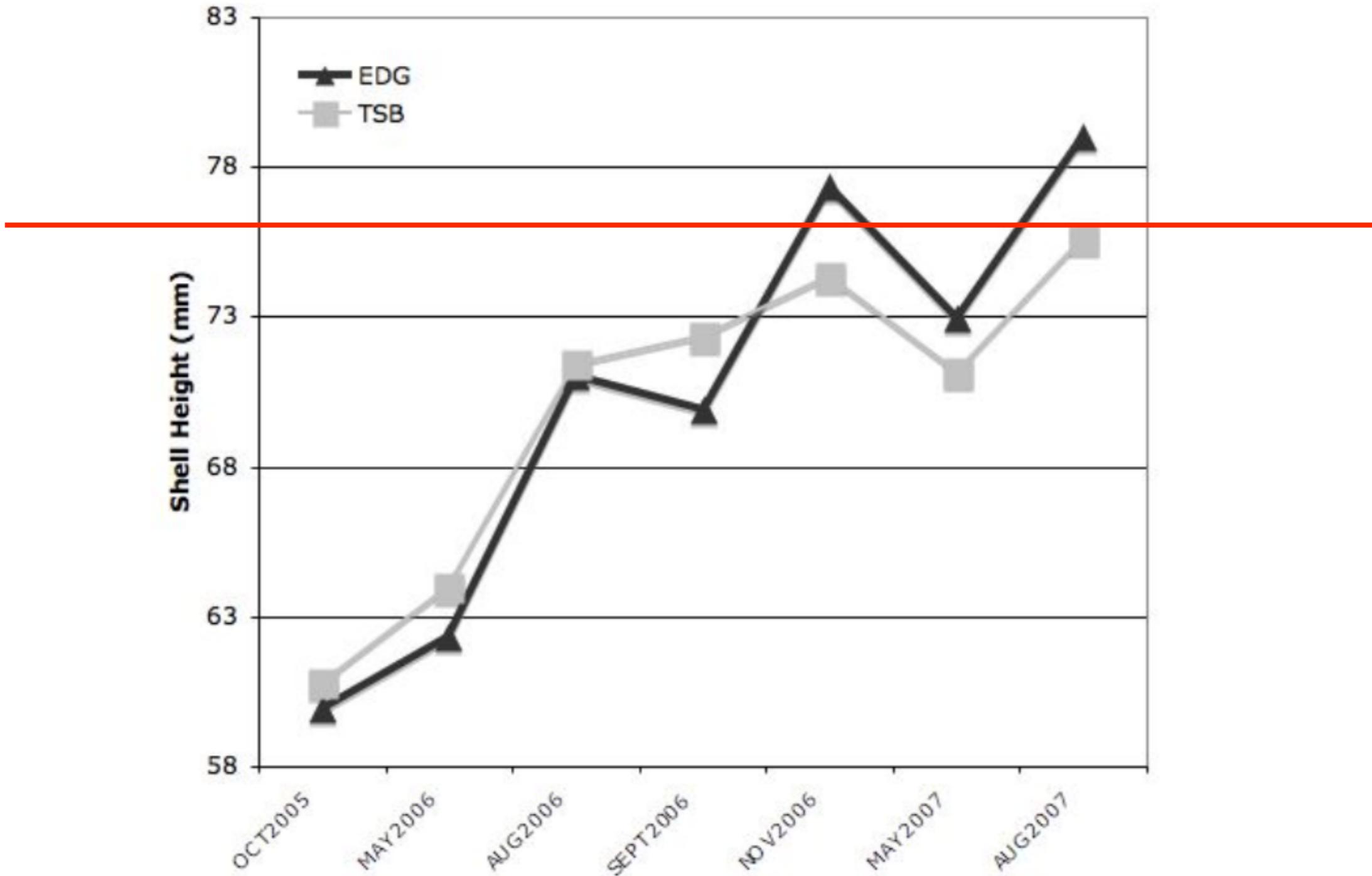








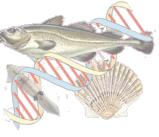
Market size



Mechanisms

They are different,
but how / why?



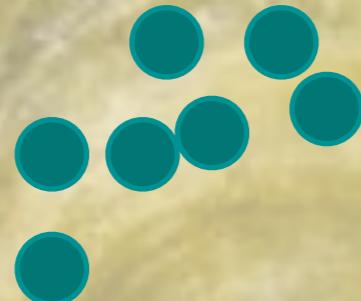


Schematic

Parasite



Hemocytes



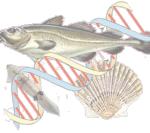
BCL-X

Resistant



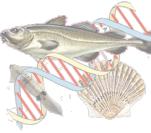
BCL-X

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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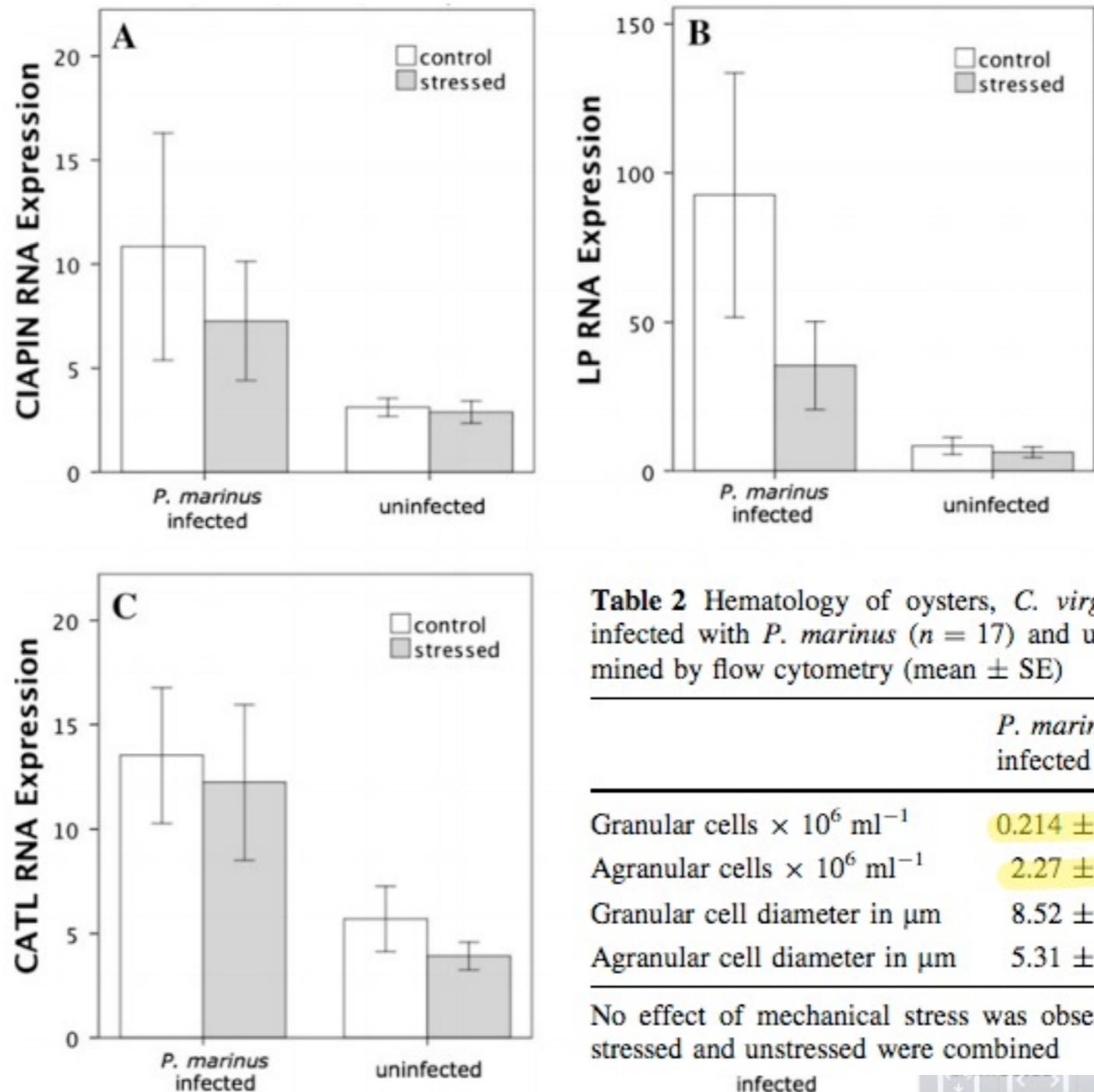


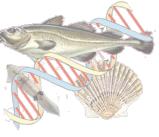
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infected





Schematic

Parasite



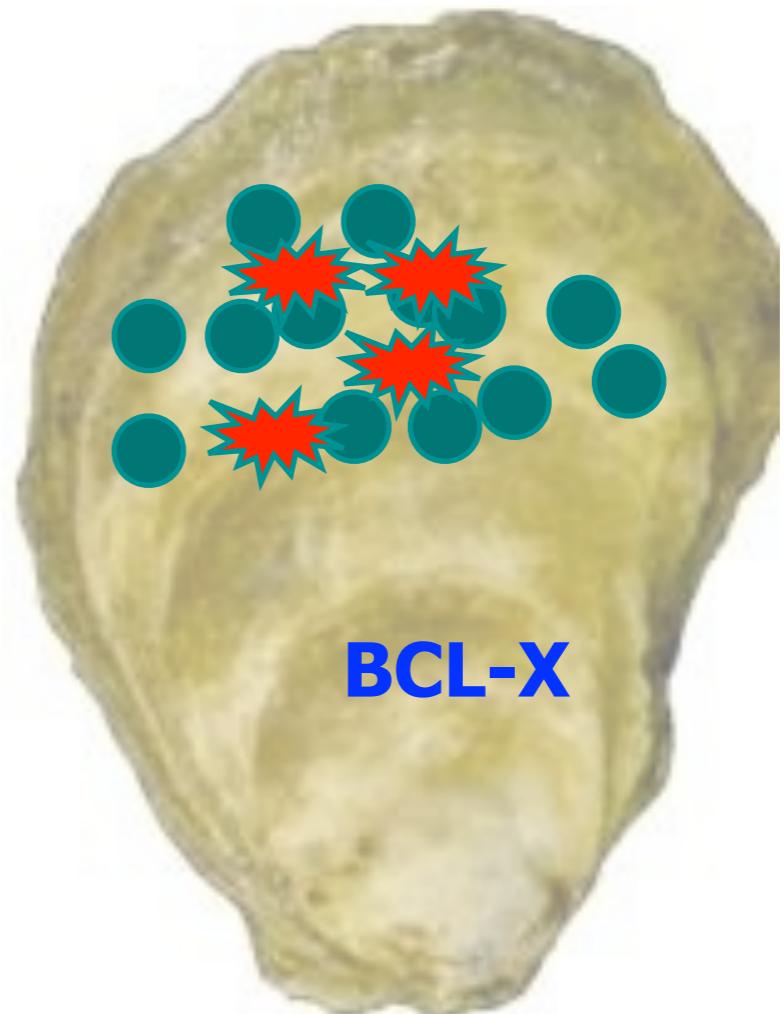
Hemocytes



Resistant



Epigenetic?



Wild-type

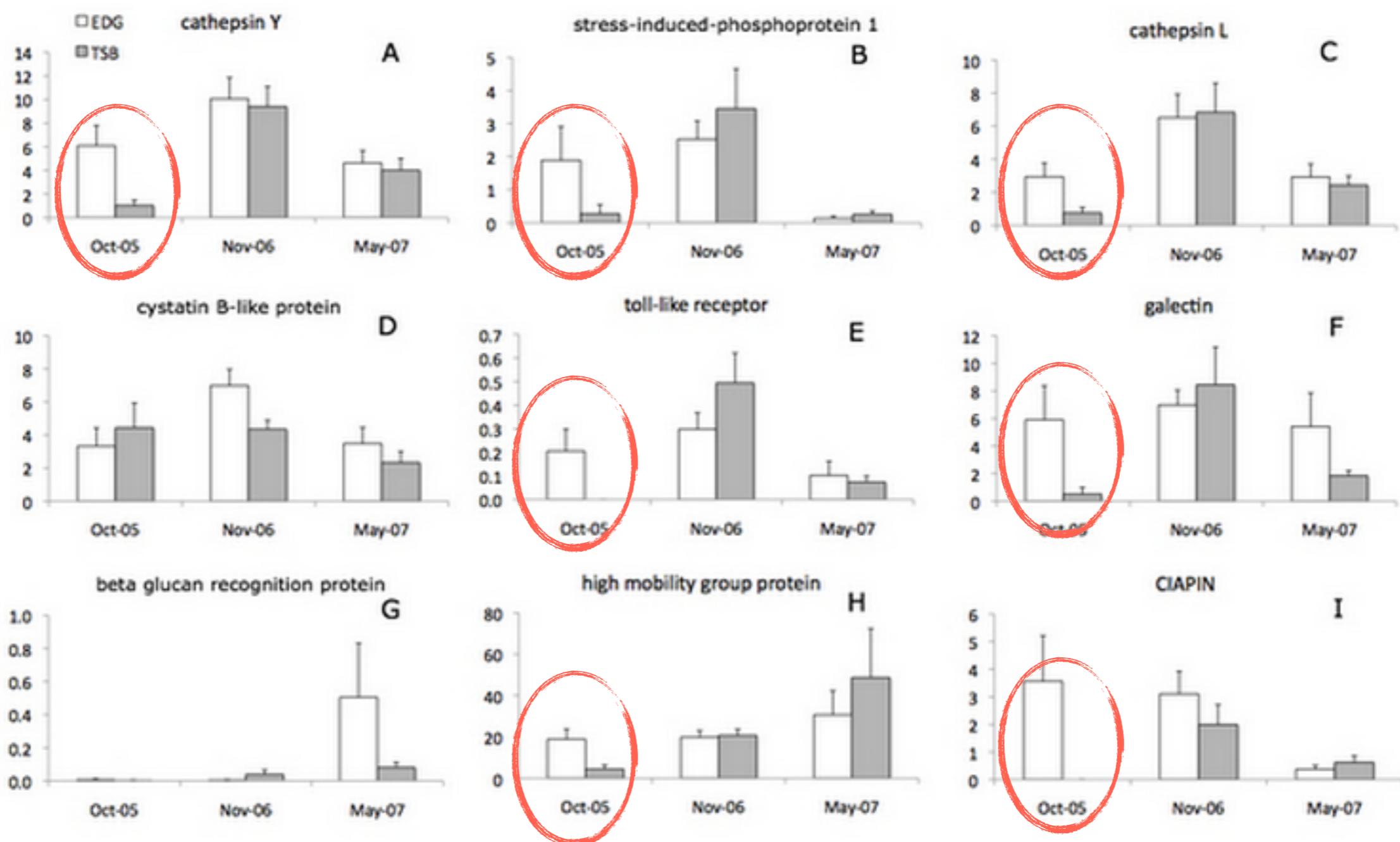
Summary - Oyster

- 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

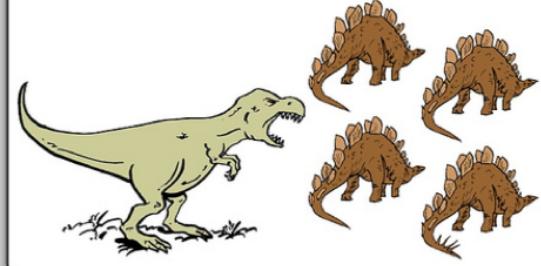
General Observation



Abalone



NATURAL SELECTION



Naive



California

Fresno

Visalia

Bakersfield

Santa
Maria

Santa
Barbara

Simi Valley

Oxnard

Glendale

Ontario

Los
Angeles

Riverside

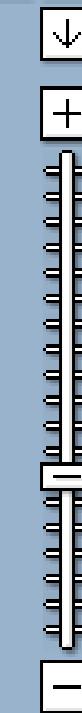
Corona

Huntington
Beach

Oceanside

Escondido

Disease Pressure



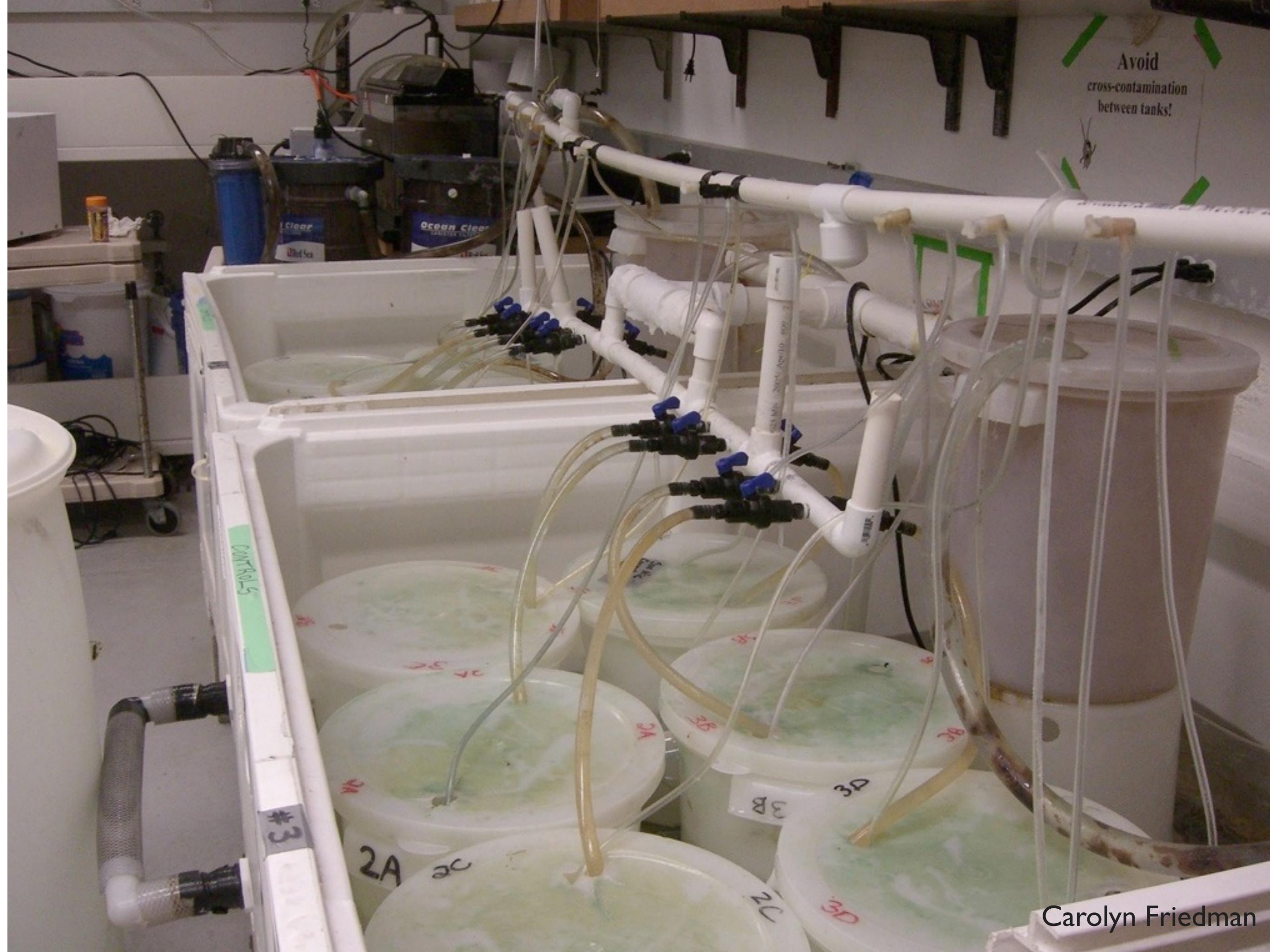
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Glenn VanBlaricom, Carolyn Friedman

Avoid
cross-contamination
between tanks!

Carolyn Friedman

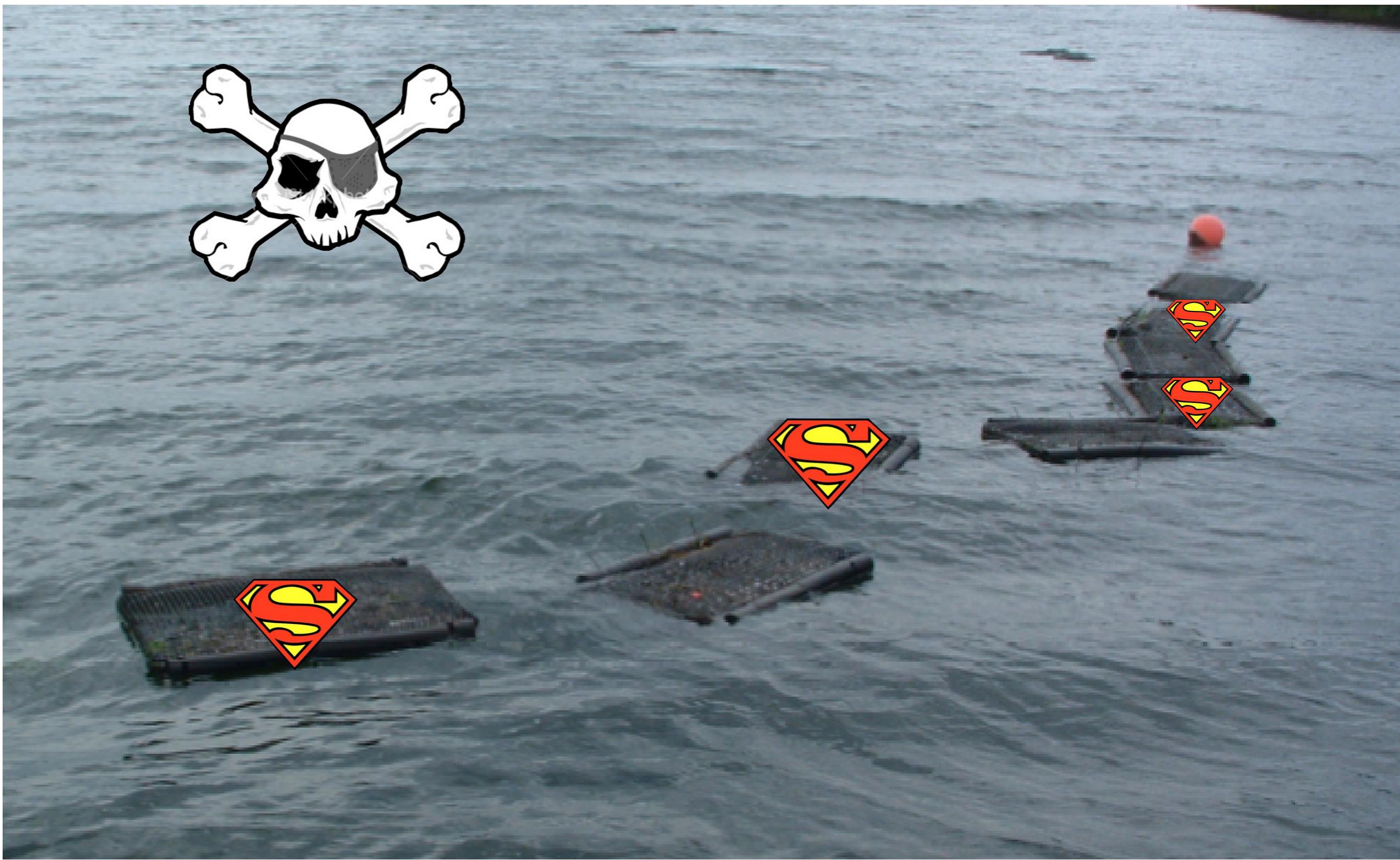


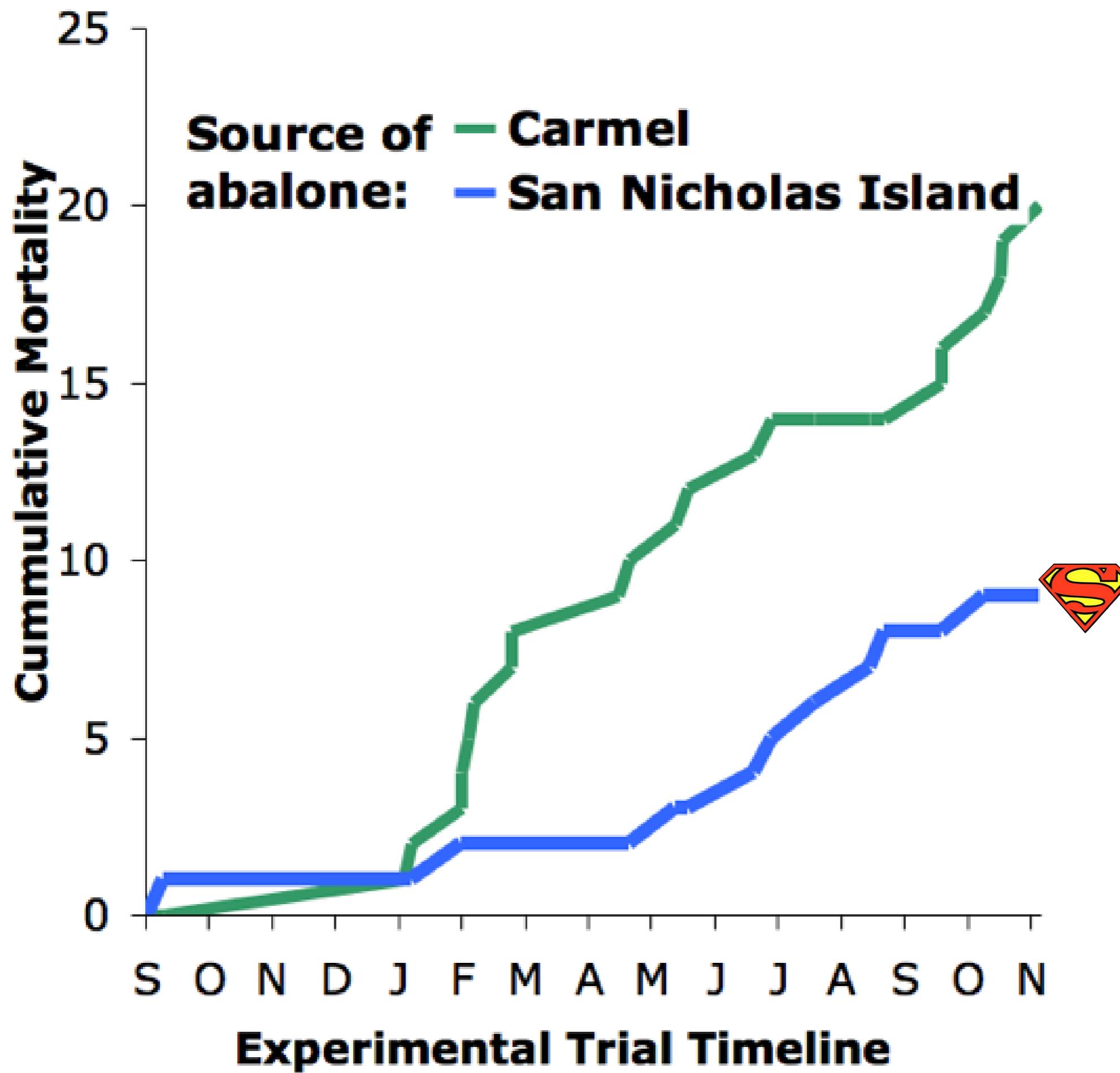
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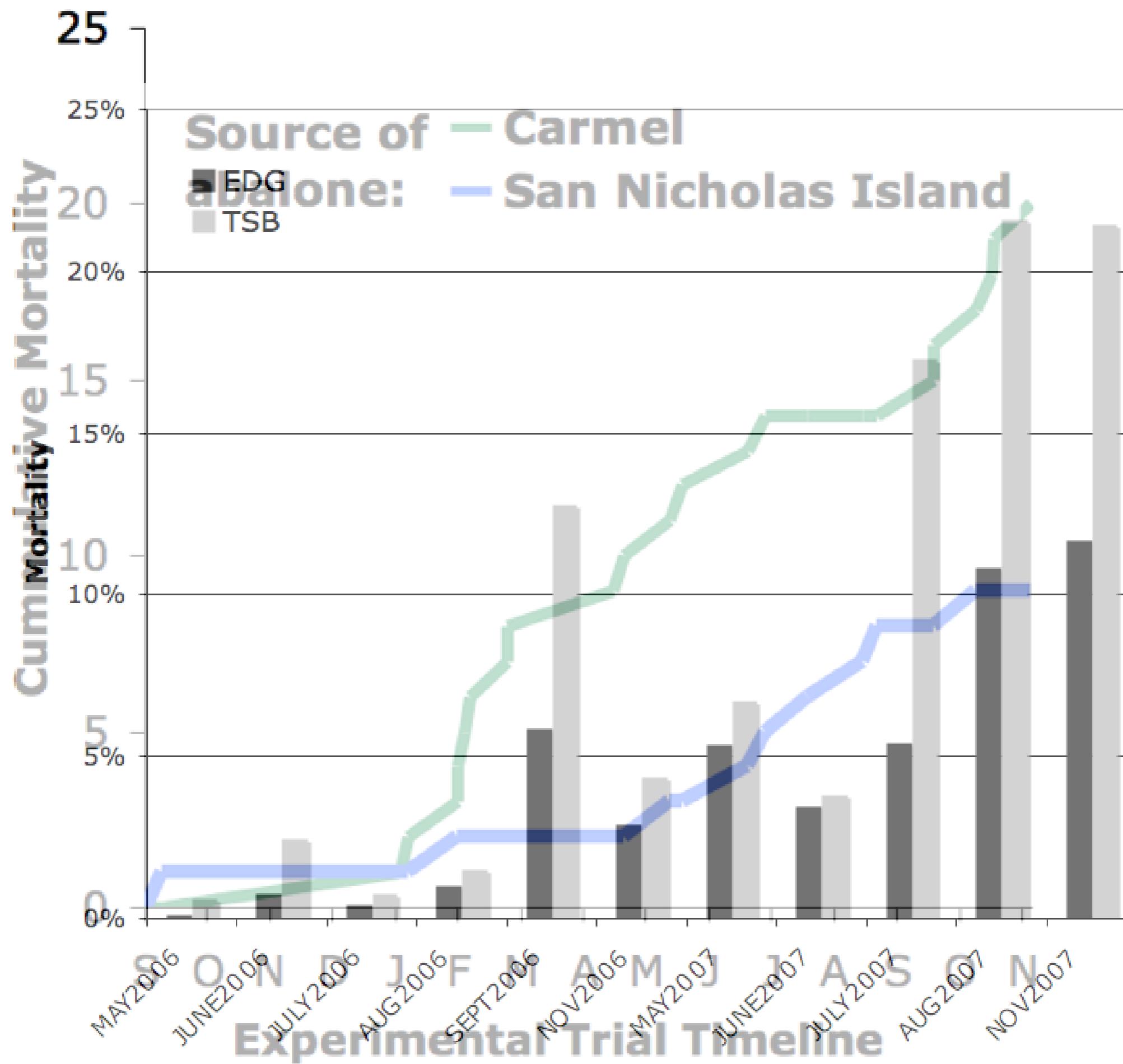


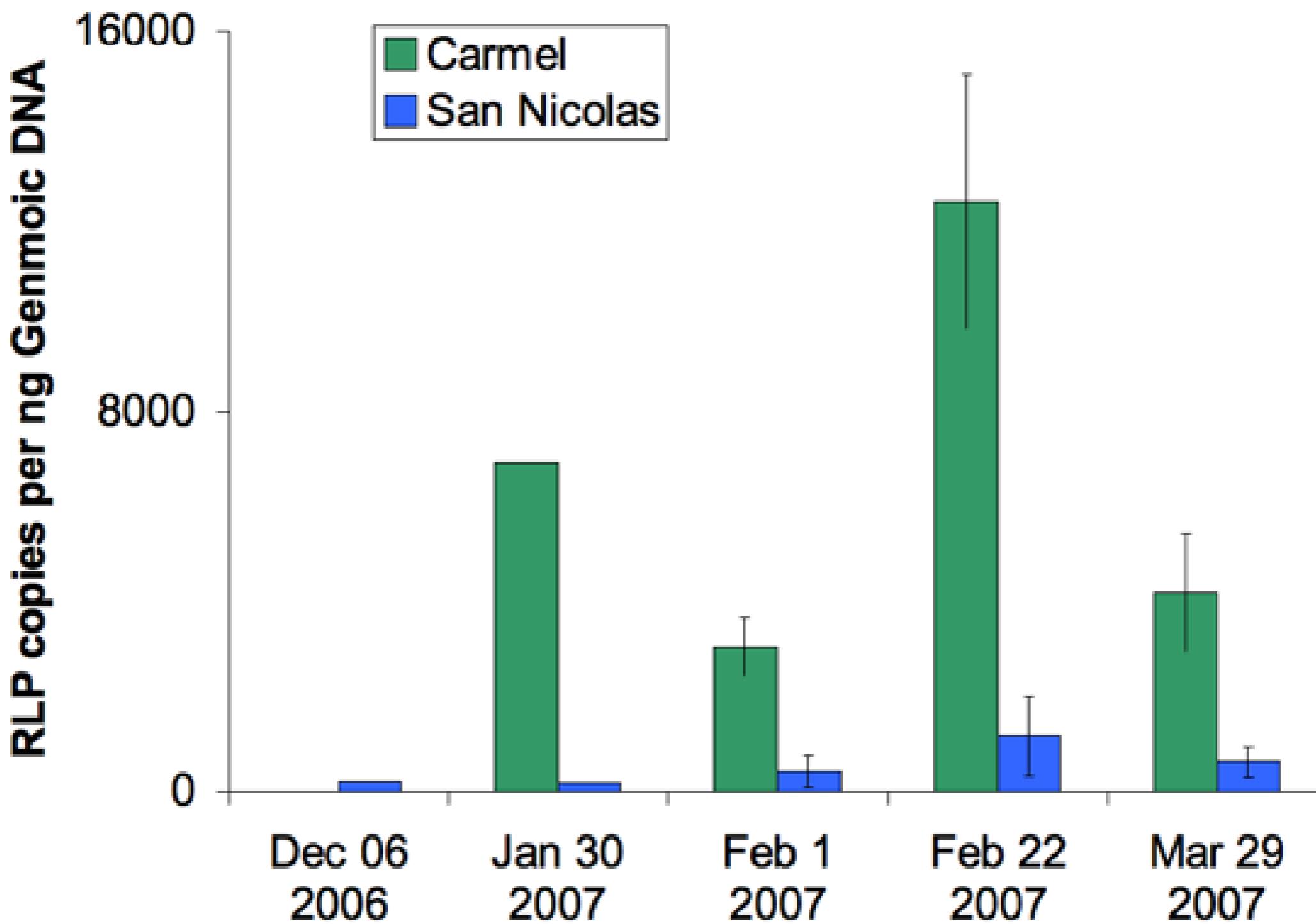
Carolyn Friedman

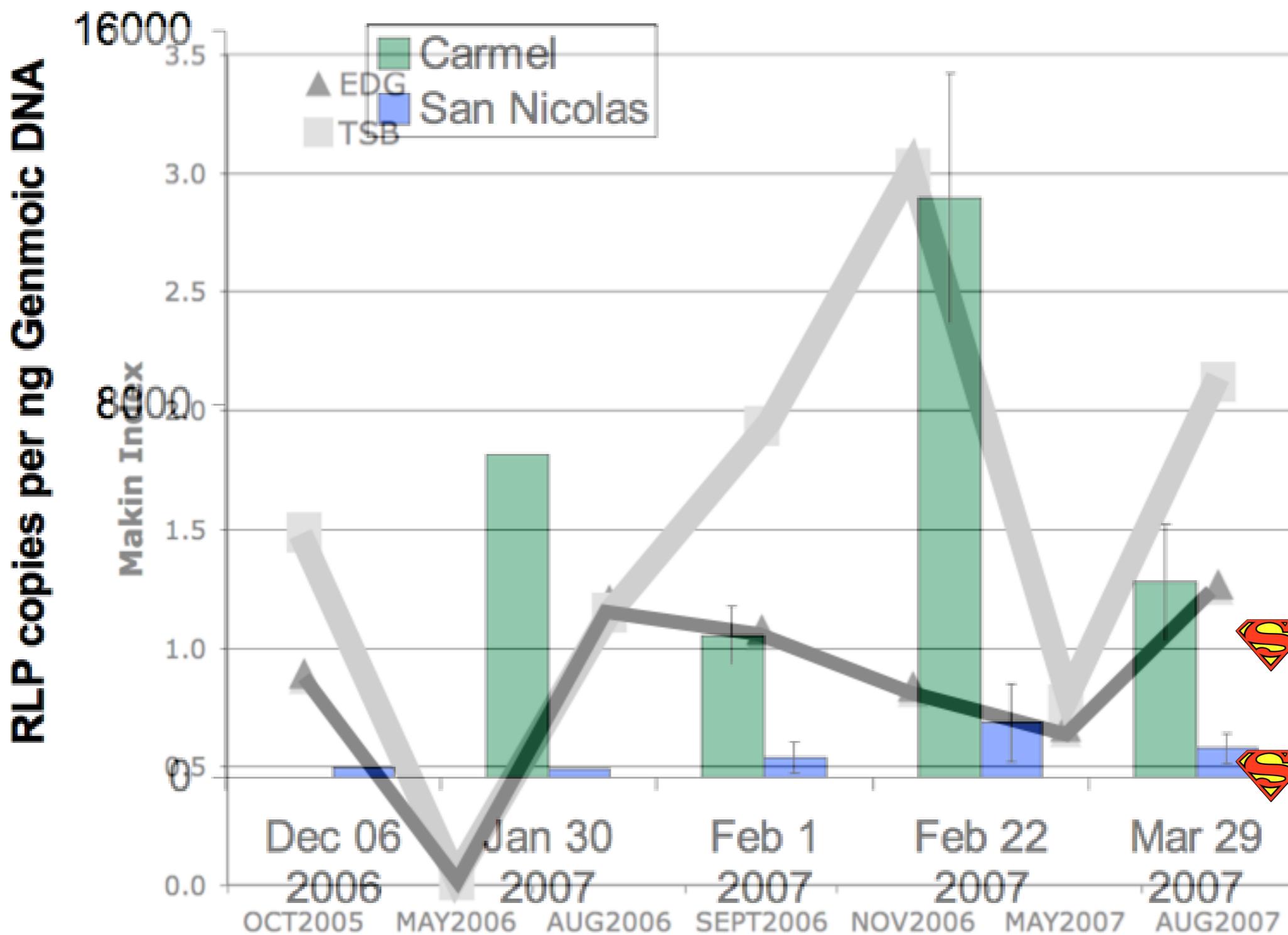
analagous to ...









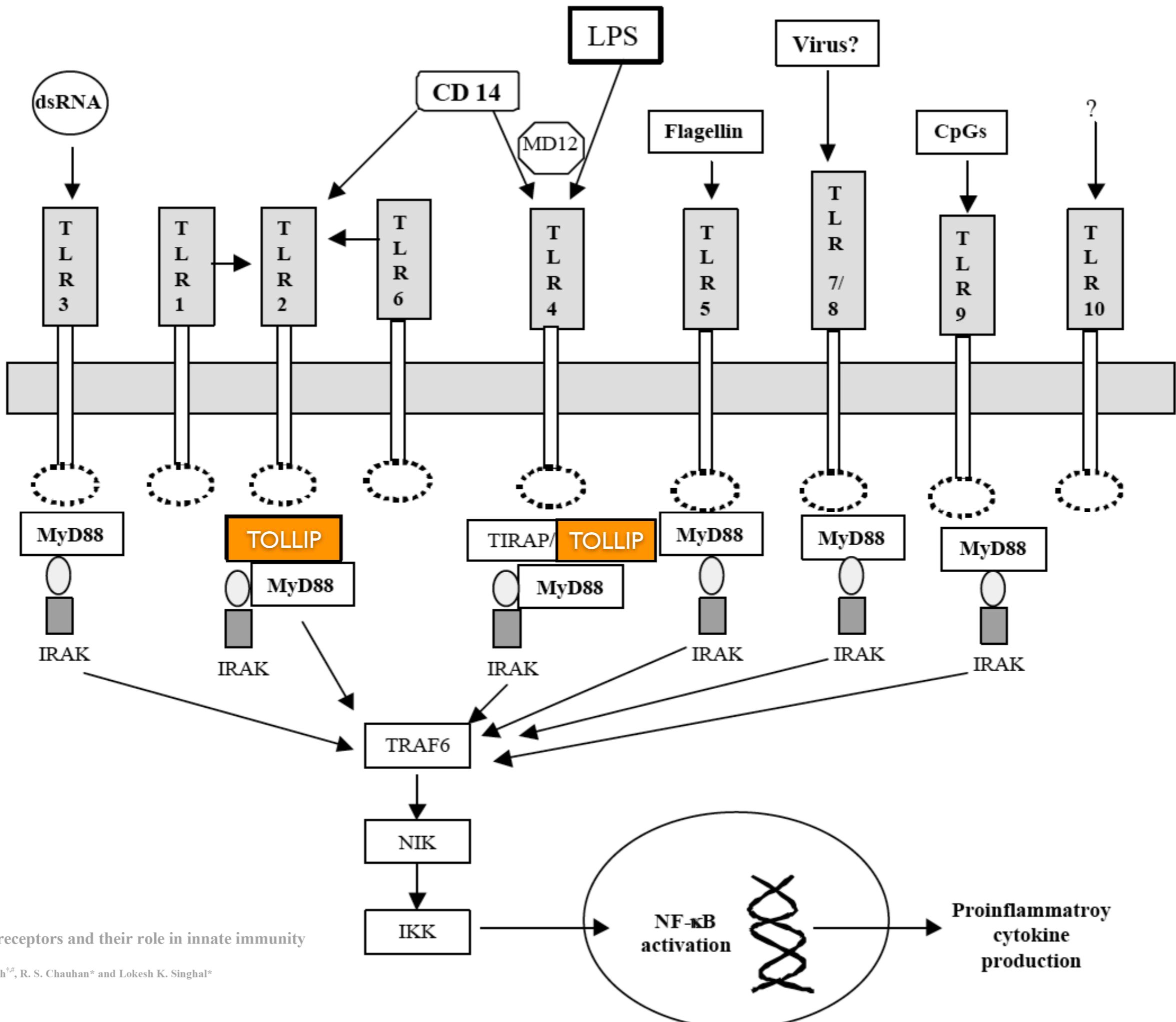


Increased Resistance

Better survival AND less pathogen load

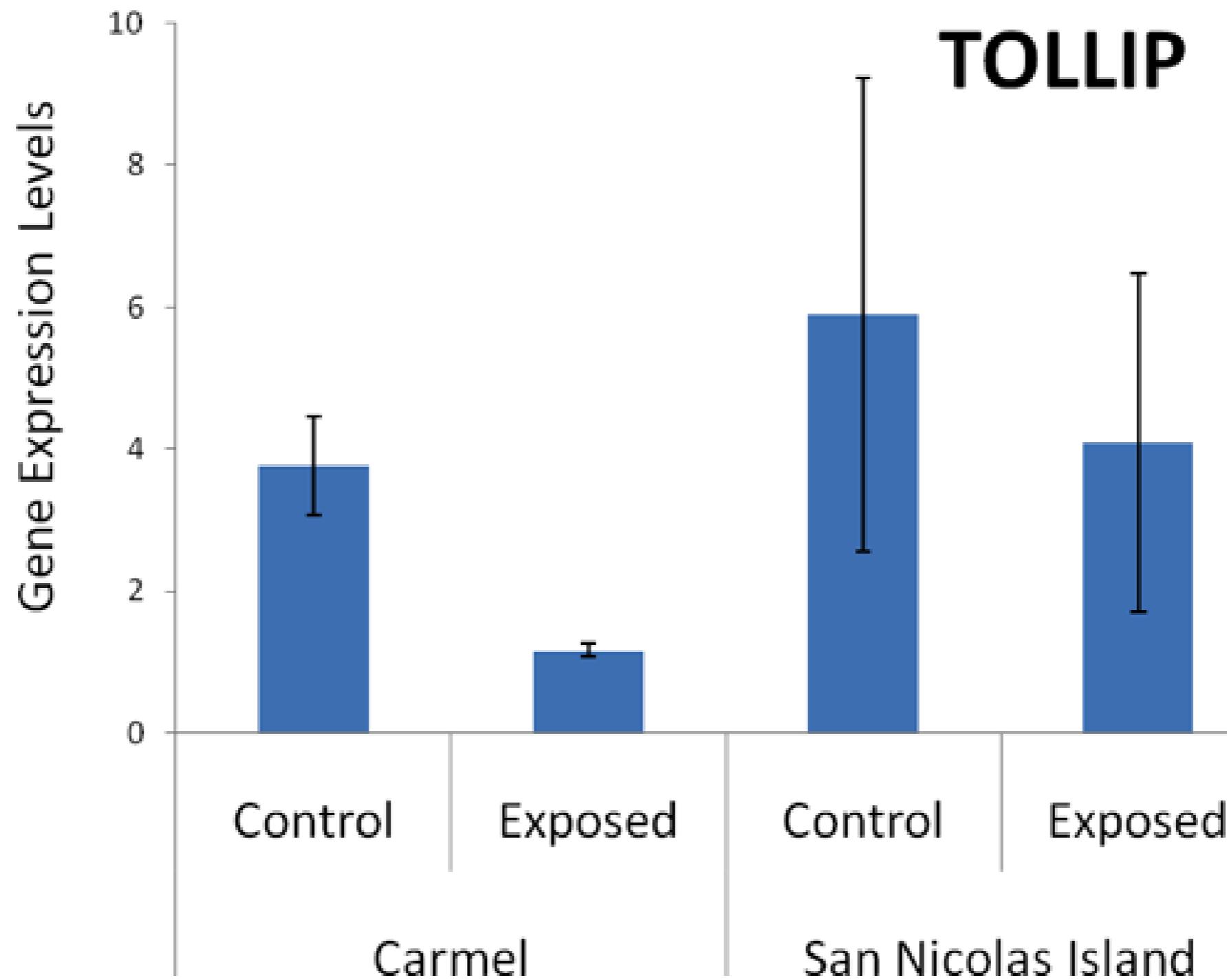
How?

Differences?



Toll-like receptors and their role in innate immunity

Bhanu P. Singh^{†#}, R. S. Chauhan* and Lokesh K. Singhal*



bacteria recognition protein

