Protecting oneself from invaders

An invader is someone who enters into, and takes control of, someone else's territory (or domain, area, etc.)

https://www.wallpaperflare.com/viking-clip-art-asterix-le-domaine-des-dieux-roger-karelia-wallpaper-qvne

Defense mechanisms against infection

- **Pathogens** are “agents" that cause disease
  - Pathogens are known to exist for a wide range of organisms including plants, animals, bacteria, and.... even viruses!
- Target (or host) organisms have defense mechanisms to protect themselves from pathogens
  - Immune system: comprises of different types of cells, cellular components, pathways, etc.
  - Recognize “foreign agents” and respond to eliminate such agents

Invasion versus infection!

Immune system

Innate immunity

Generic
First line of defence
Immediate response

Pretty ubiquitous i.e., found in animals, plants, and bacteria

Innate = inborn, natural

Acquired immunity

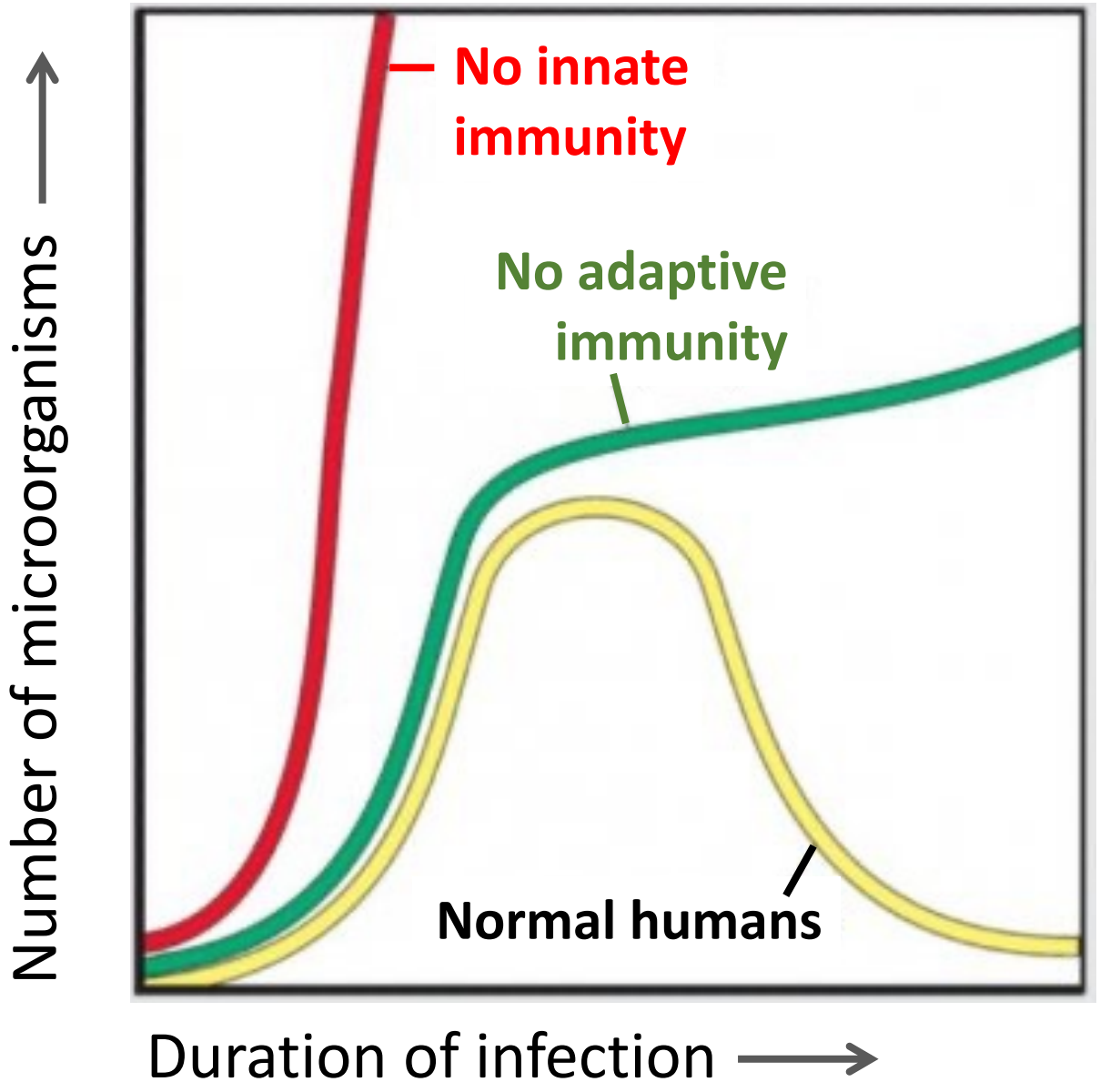
Specific to a pathogen

In vertebrates, plants, and bacteria; in addition to innate immunity

Acquired immunity is also called as adaptive immunity

Figure 43.2 in Campbell Biology (10th edition)

Synergy between innate and adaptive immunities



http://www.glycopedia.eu/e-chapters/chapter-1/article/introduction

Today's topics

- Innate immunity
- Adaptive immunity
- How do plants protect themselves?
- Bacterial defense mechanisms

Innate immunity

- Present before any exposure to pathogens
- Found in animals, plants, and bacteria
- Is effective from the time of birth
- First response to infections
  - **Serves as the foundation of adaptive immunity**

What innate immunity does to us...

The fact that most people are not perpetually sick is testament to innate immunity squelching (= suppressing) most of the infections that we contract

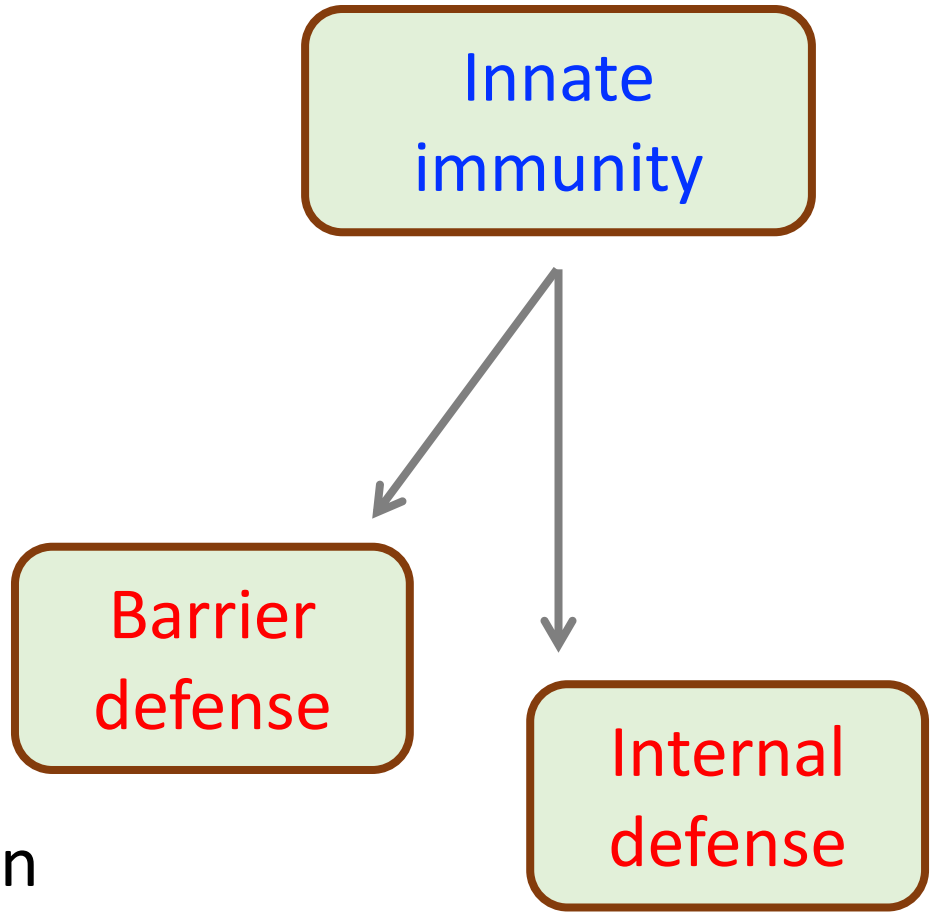
Peter Parham
Stanford U School of Medicine

Nature (2009) 423:20

Innate immunity is “generic”

- Responds to a broad range of pathogens
  - Recognition of “foreign” particles or organisms relies on common traits
  - Typically uses cell surface structures (e.g., polysaccharides)
  - Different responses for different classes of pathogens

Components of innate immunity in animals



- Skin
- Mucous linings
- Secretions

Phago-: from Greek *phagein* to eat

Cyto- or -cyte: cell

Inflammation is body's reaction to injury

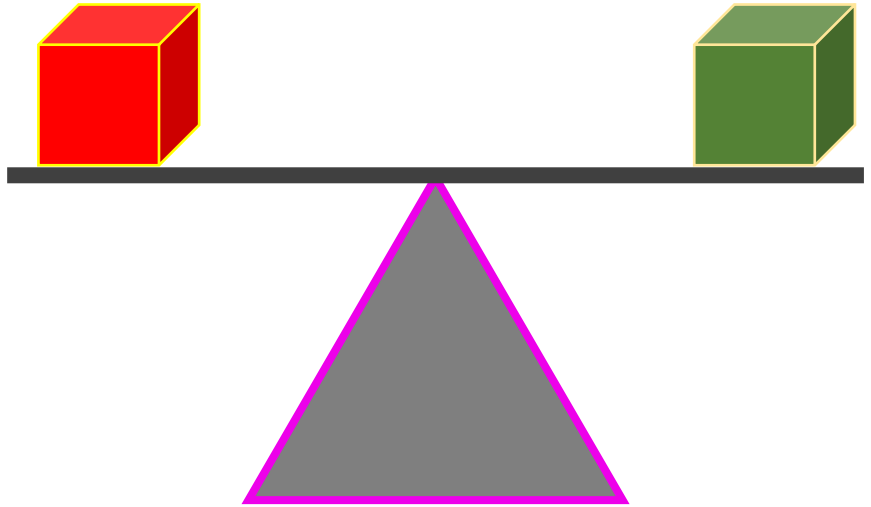
- Phagocytes
- Natural killer cells
- Anti-microbial peptides / proteins
- Inflammatory response
- Complement system

Figure 43.2 in Campbell Biology (10th edition)

Infection versus innate immunity

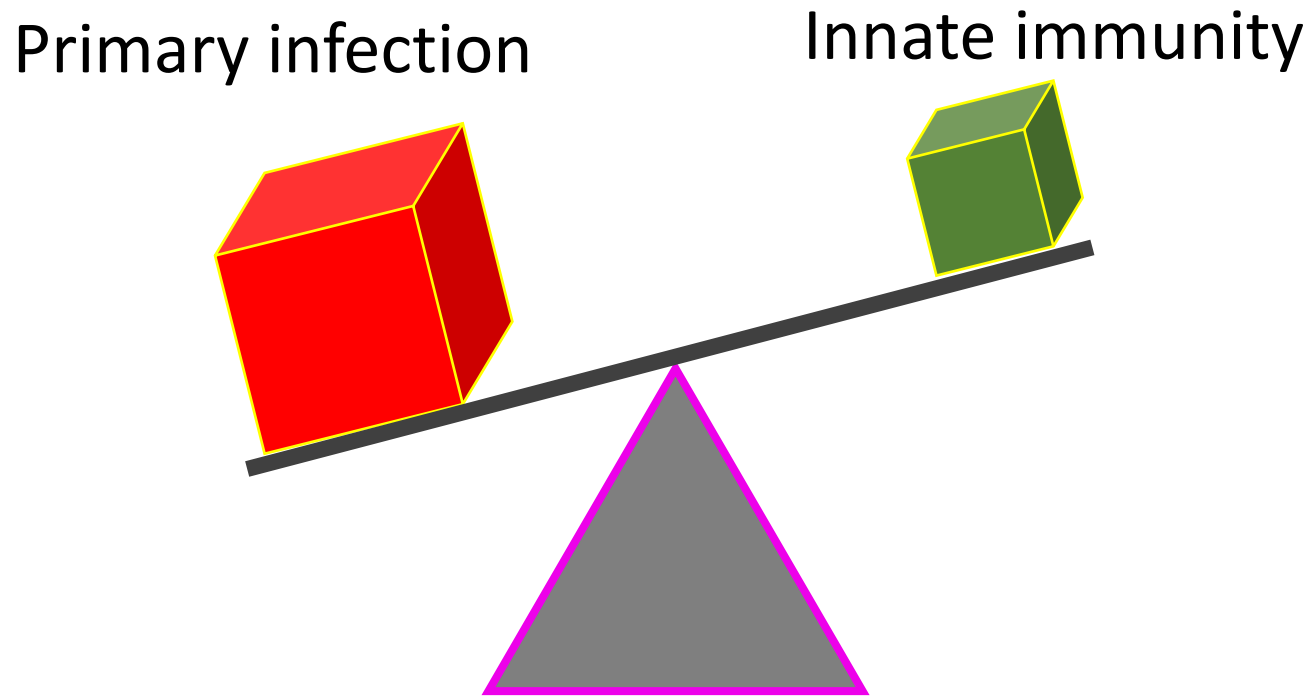
Primary infection

Innate immunity



Nature (2009) 423:20

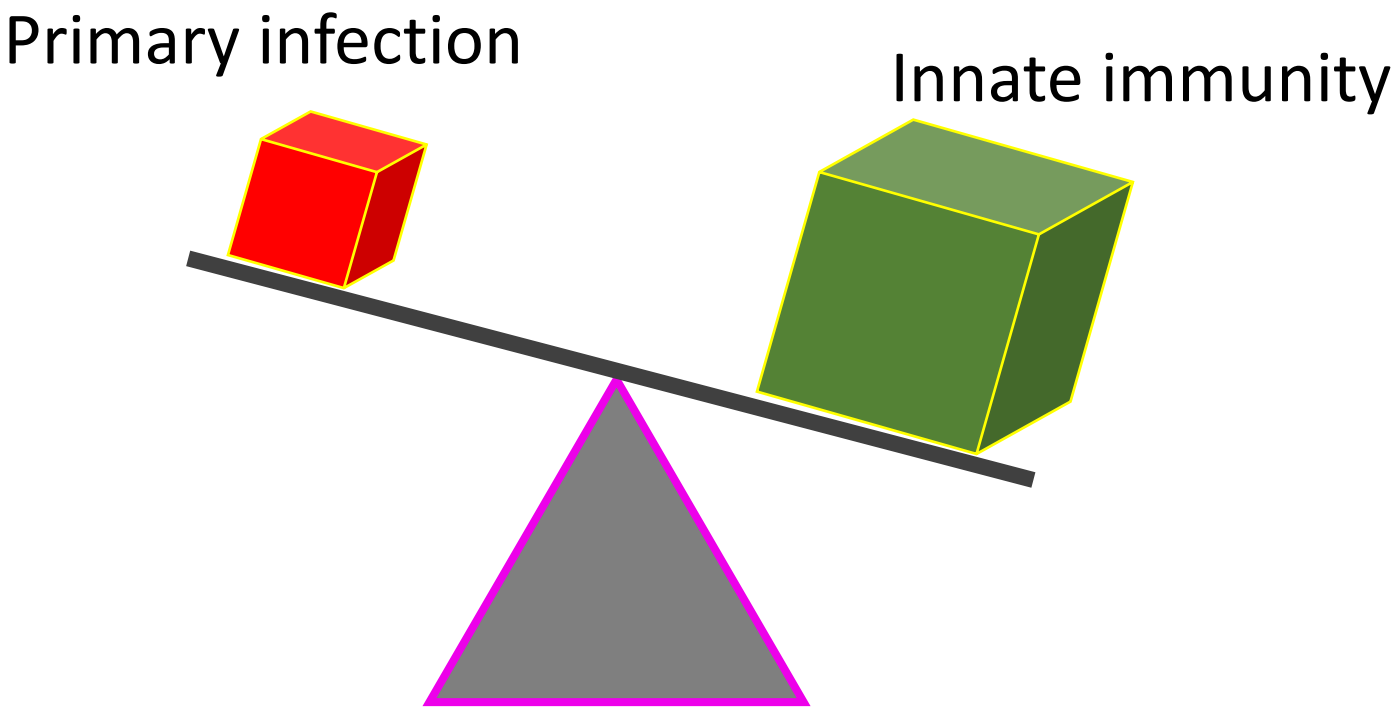
Infection: upper hand over innate immunity



Death or
chronic, debilitating disease

Nature (2009) 423:20

Infection overcome by innate immunity

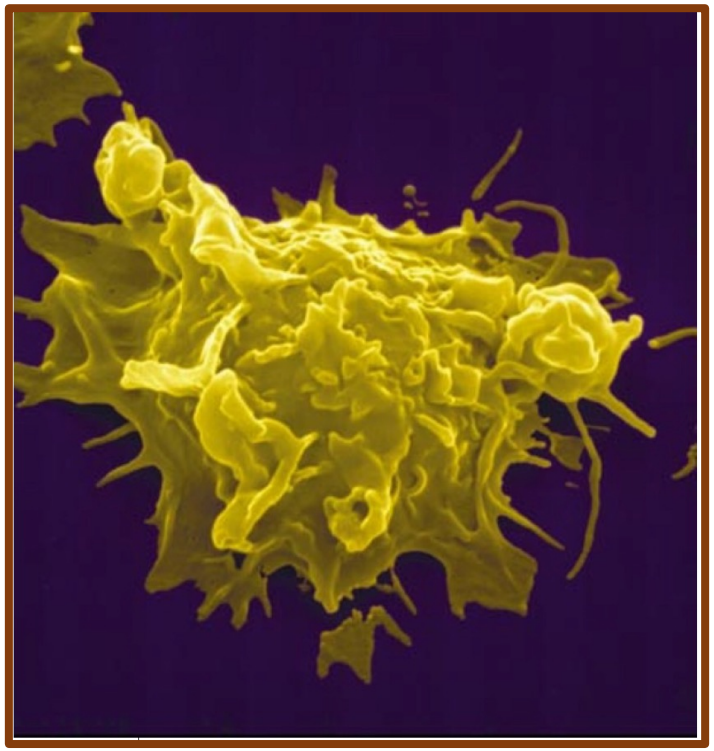


Possibility 1: innate immunity, by itself, terminates infection

Possibility 2: innate immunity reinforces defences by triggering adaptive immunity

Nature (2009) 423:20

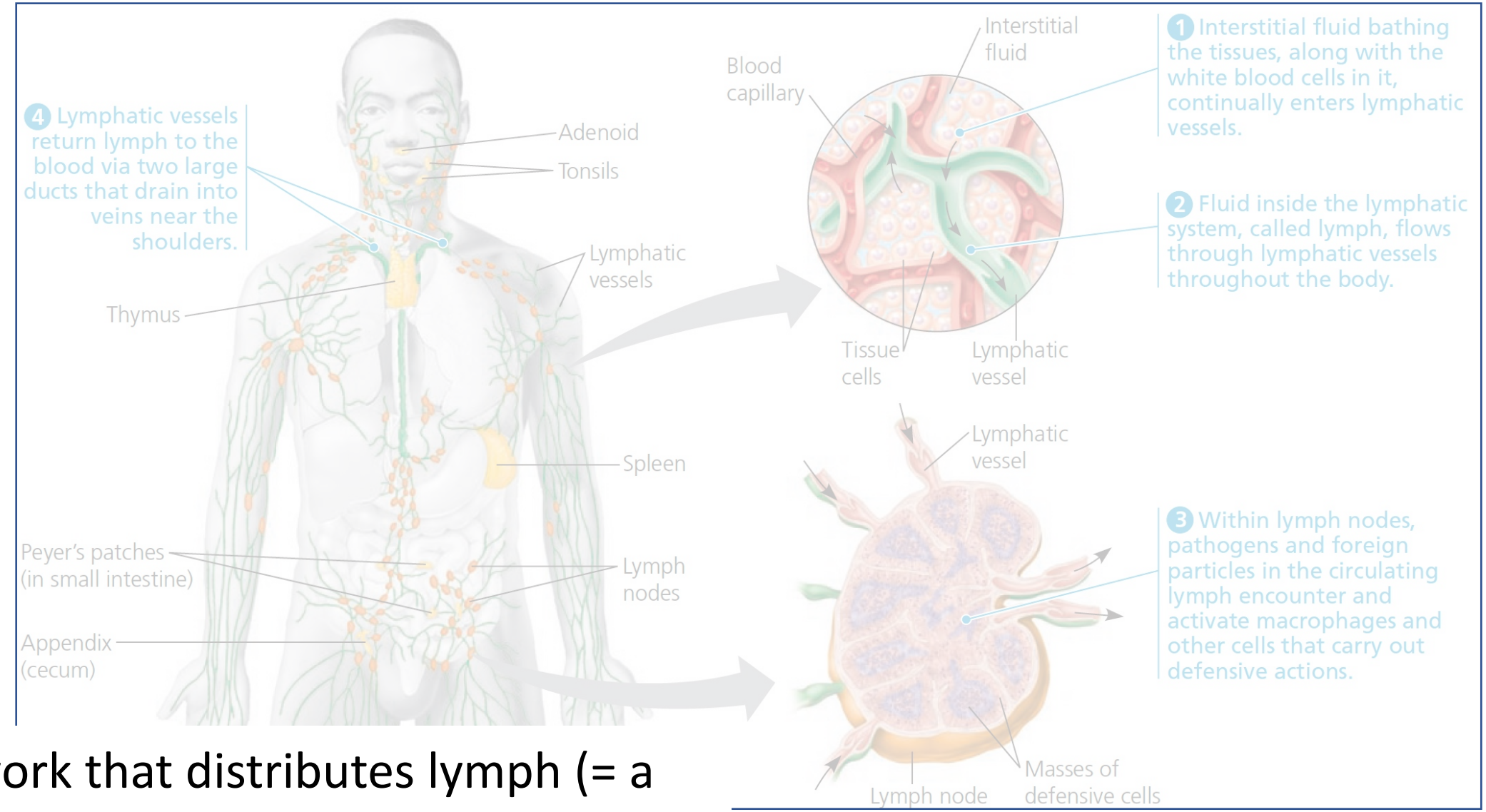
Natural killer cells



- Large, “well-armed”, and circulate in a state of readiness
- Kill infected cells; recruit other cells of innate immunity (e.g., macrophages)
- Decide if and when an adaptive immune response is needed

Nature (2009) 423:20

Lymphatic system in vertebrates



A network that distributes lymph (= a type of body fluid) throughout the body

Figure 43.7 in Campbell Biology (10th edition)

A local inflammatory response

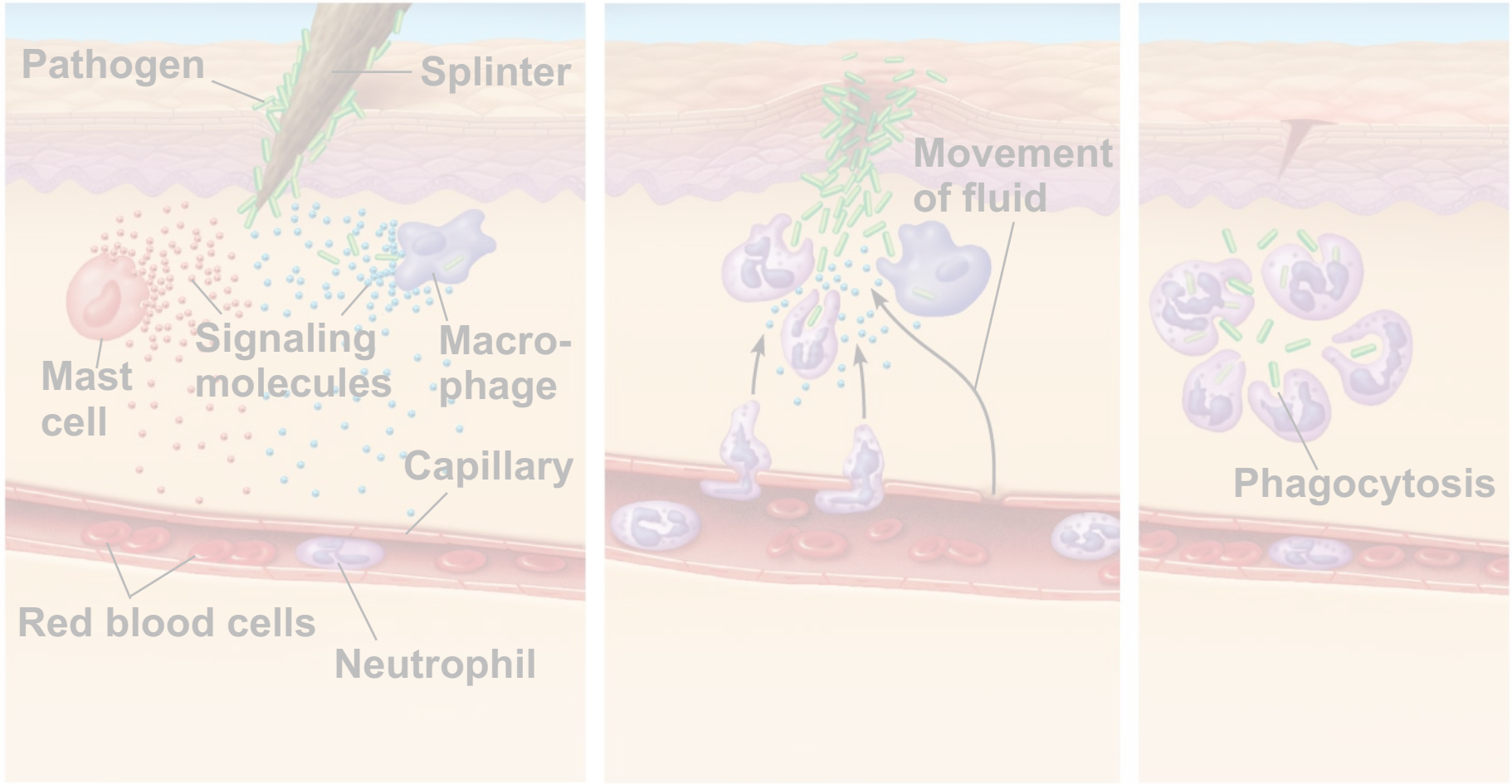
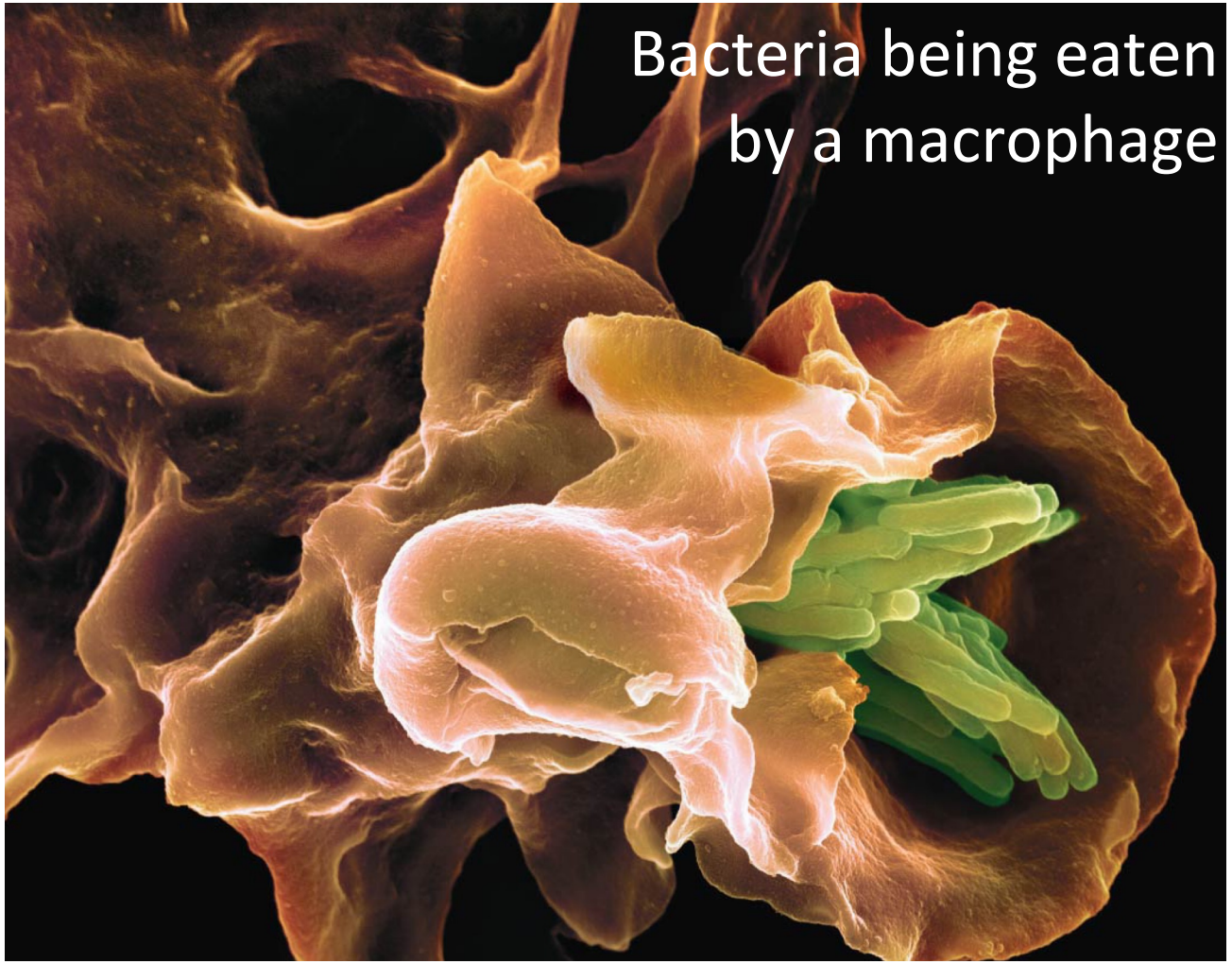


Figure 43.8 in Campbell Biology (10th edition)

Phagocytosis – illustration



Bacteria shown here are *Mycobacterium tuberculosis* which causes tuberculosis (p952)

https://www.idiva.com/news-relationships/14-crazy-things-most-mumbaikars-do-are-you-a-true-blue-mumbaikar/30913

Figure 43.1 and page 952 in Campbell Biology (10th edition)

Phagocytosis

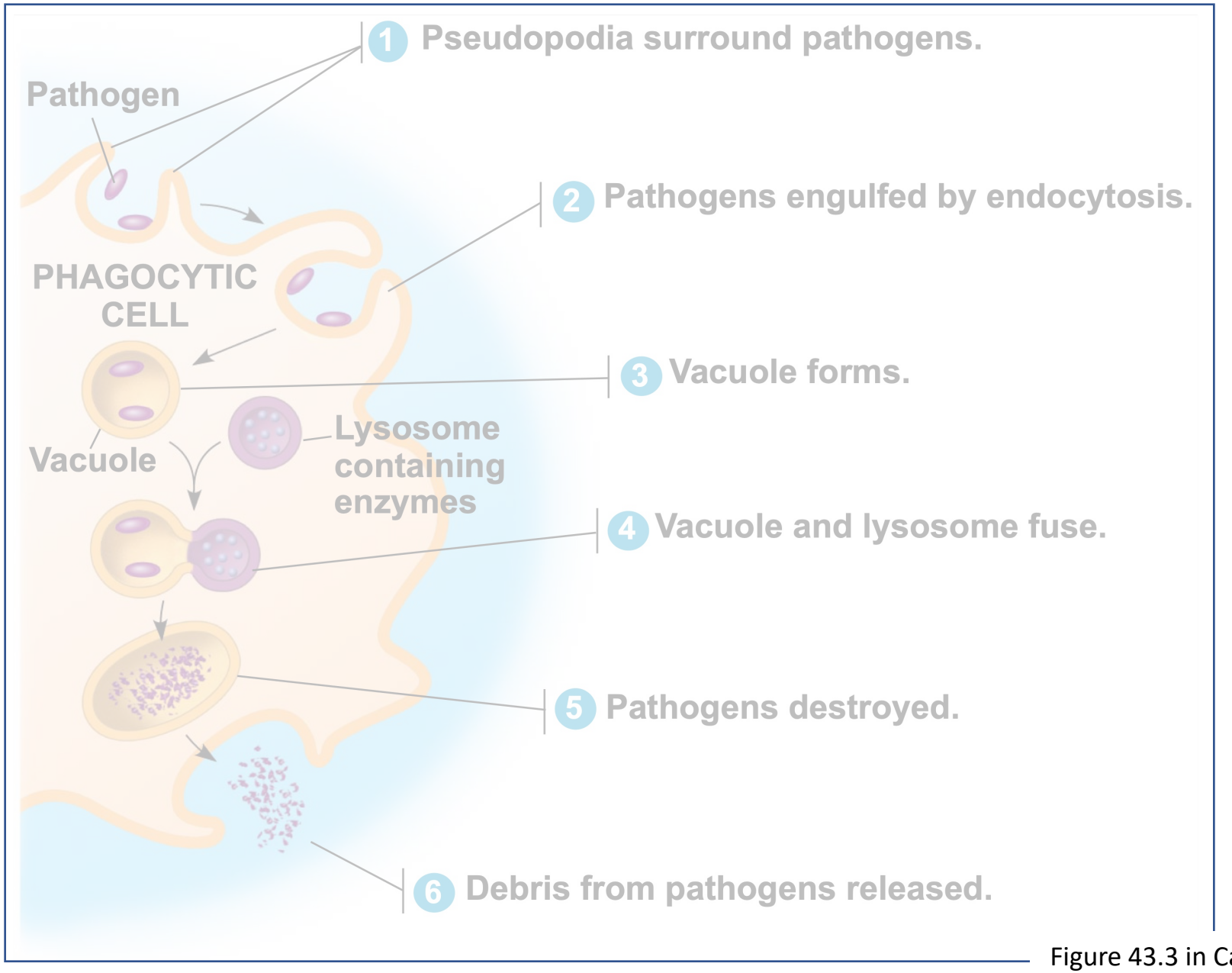
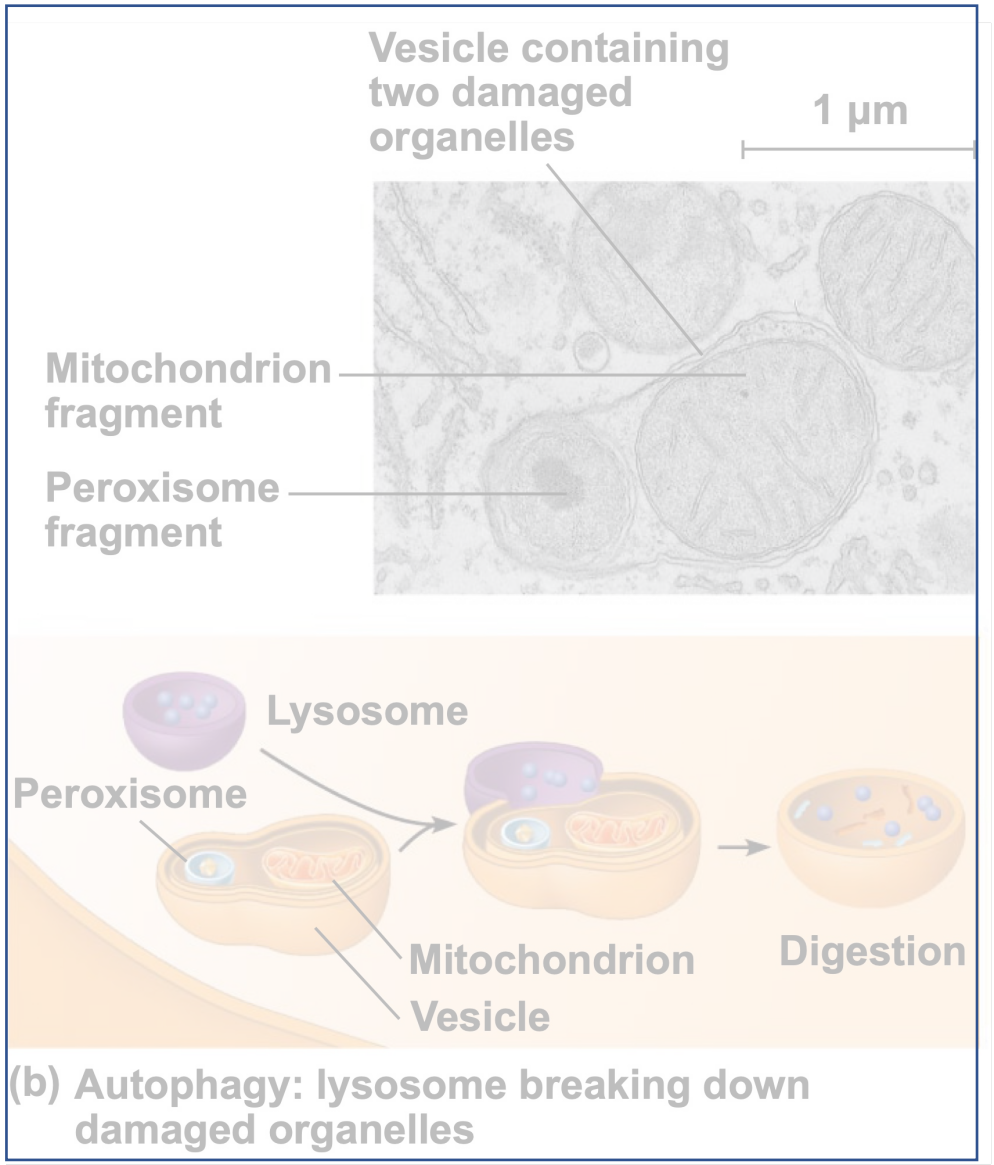


Figure 43.3 in Campbell Biology (10th edition)

Autophagy (= self-eating)

Yoshinori Ohsumi
2016 Nobel Prize in Physiology / Medicine
Discovery of autophagy



Lyso- = break down
-some = part of a cell

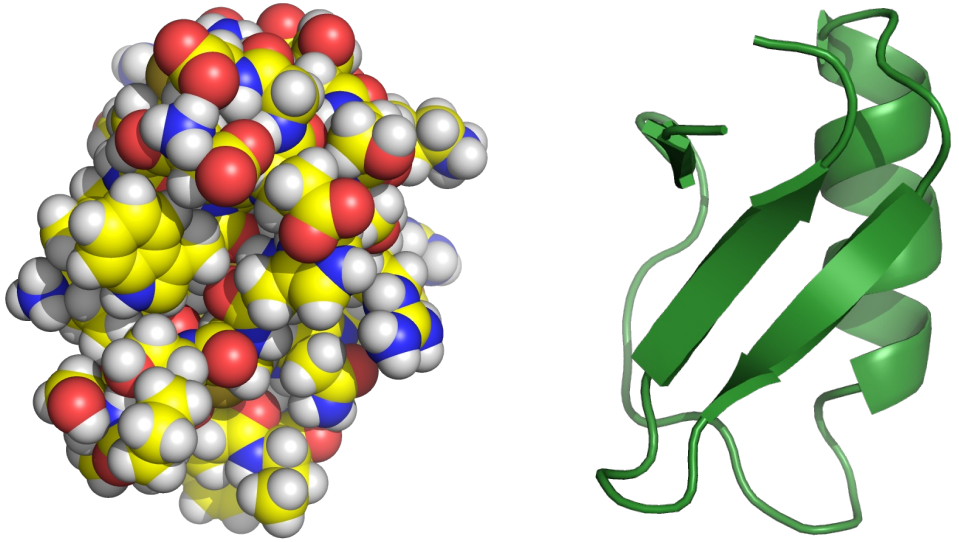
Figure 6.13b in Campbell Biology (10th edition)

Anti-microbial peptides

- Antimicrobial peptides and proteins are part of innate immunity
  - Attack pathogens and impede their reproduction

https://en.wikipedia.org/wiki/Drosophila_melanogaster

Two different forms of visual representation
Approximately, 24 Å height, 12 Å width
643 atoms



3D structure of drosomycin, an anti-microbial peptide from fruit fly

Amino acid sequence: DCLSGRYKGP CAVWDNETCR RVCKEEGRSS GHCSPSLKCW CEGC

Protein data bank accession id: 1MYN.pdb

Specificity of anti-microbial peptides

Fruit fly variant	Trait / description
Wild type	Fly commonly found in nature
Mutant	Production of anti-microbial peptides is blocked
Mutant + drosomycin	Mutant engineered to produce drosomycin
Mutant + defensin	Mutant engineered to produce defensin

Specificity of anti-microbial peptides Experiment 1 of 2

Fruit fly survival after infection by bacteria *Micrococcus luteus*

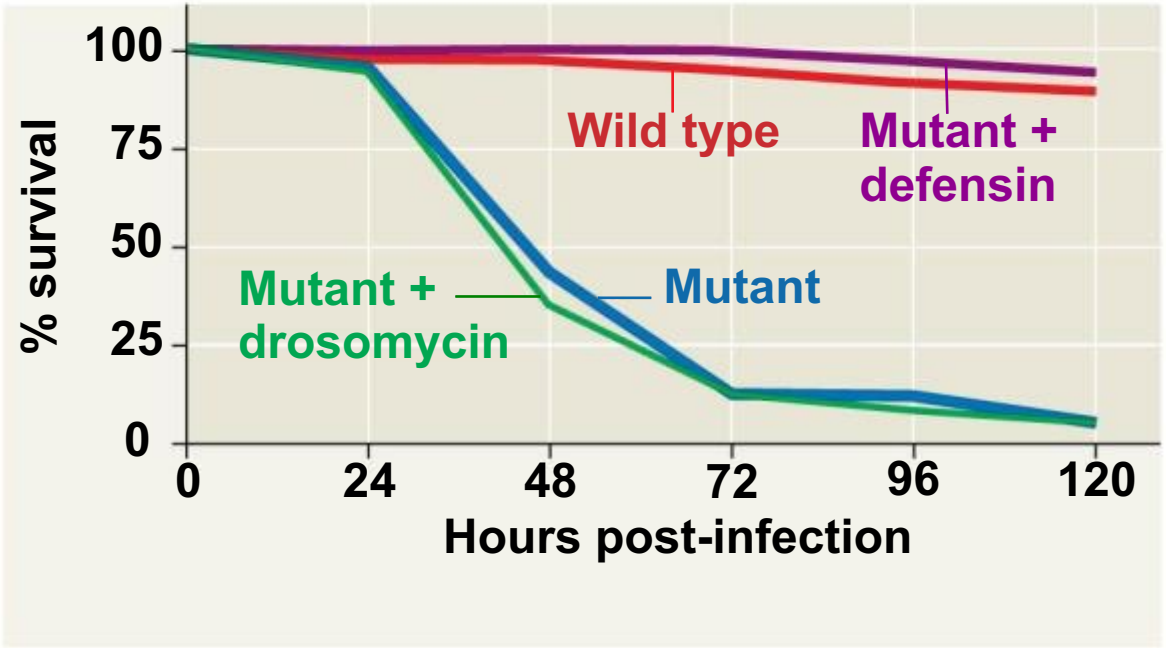


Figure 43.5 in Campbell Biology (10th edition)

Specificity of anti-microbial peptides Experiment 2 of 2

Fruit fly survival after infection by fungus *Neurospora crassa*

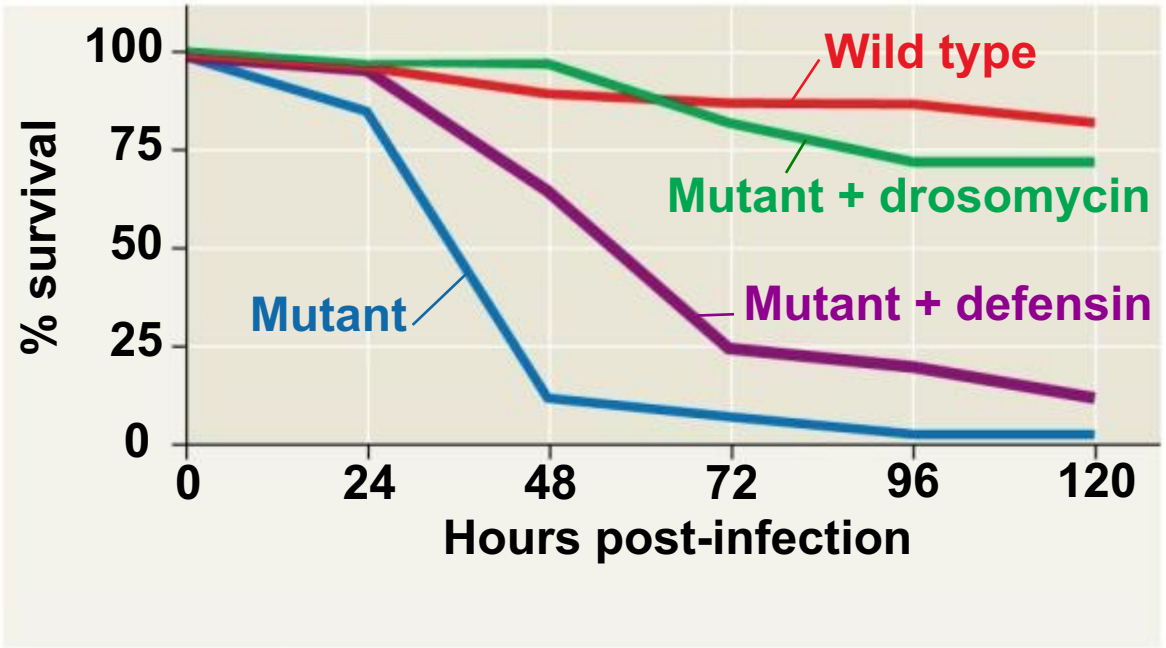


Figure 43.5 in Campbell Biology (10th edition)

Today's topics

- Innate immunity
- Adaptive immunity
- How do plants protect themselves?
- Bacterial defense mechanisms

Immune system

Innate immunity

Generic
First line of defence
Immediate response

Pretty ubiquitous i.e., found in animals, plants, and bacteria

Innate = inborn, natural

Acquired immunity

Specific to a pathogen

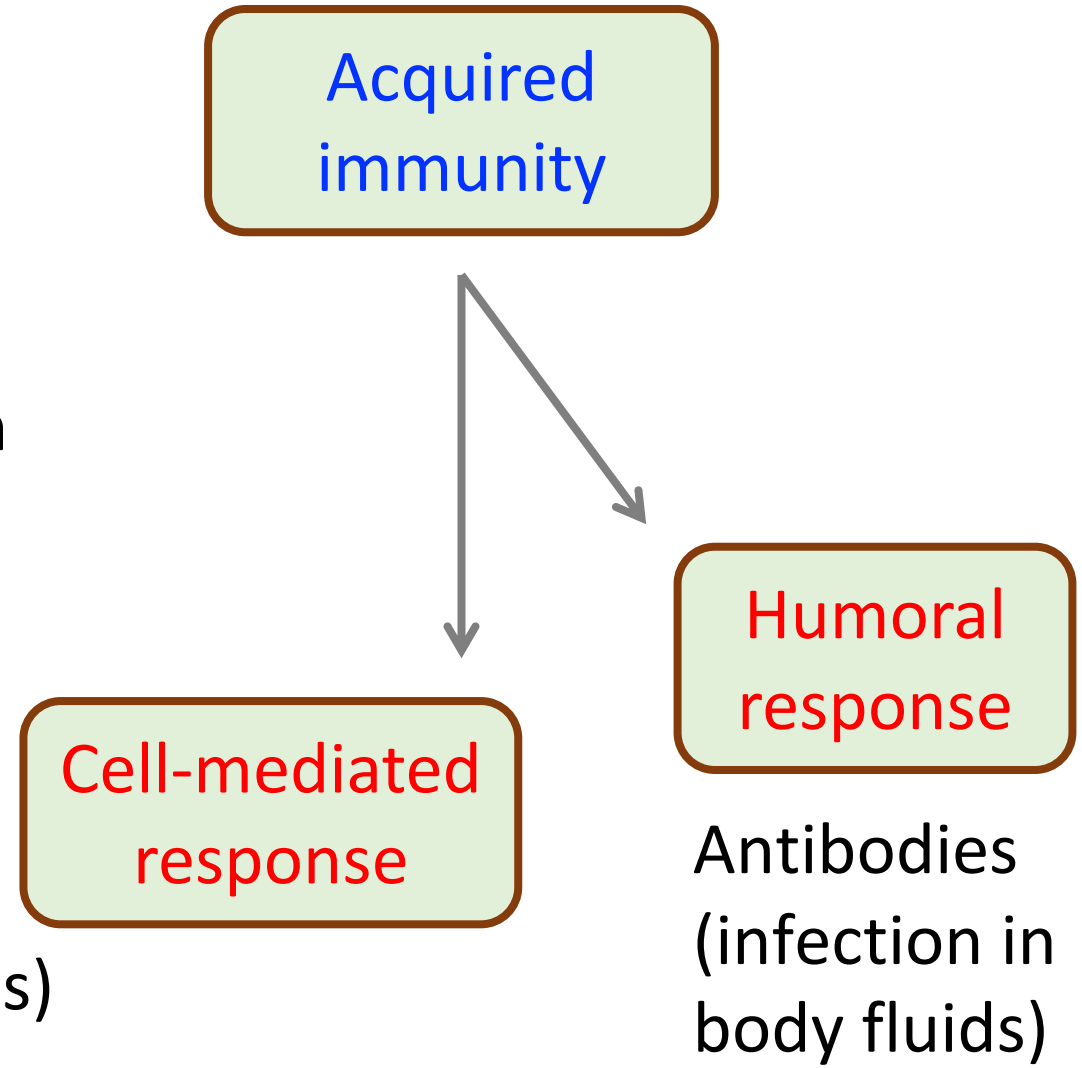
In vertebrates, plants, and bacteria; in addition to innate immunity

Acquired immunity is also called as adaptive immunity

Figure 43.2 in Campbell Biology (10th edition)

Immune system

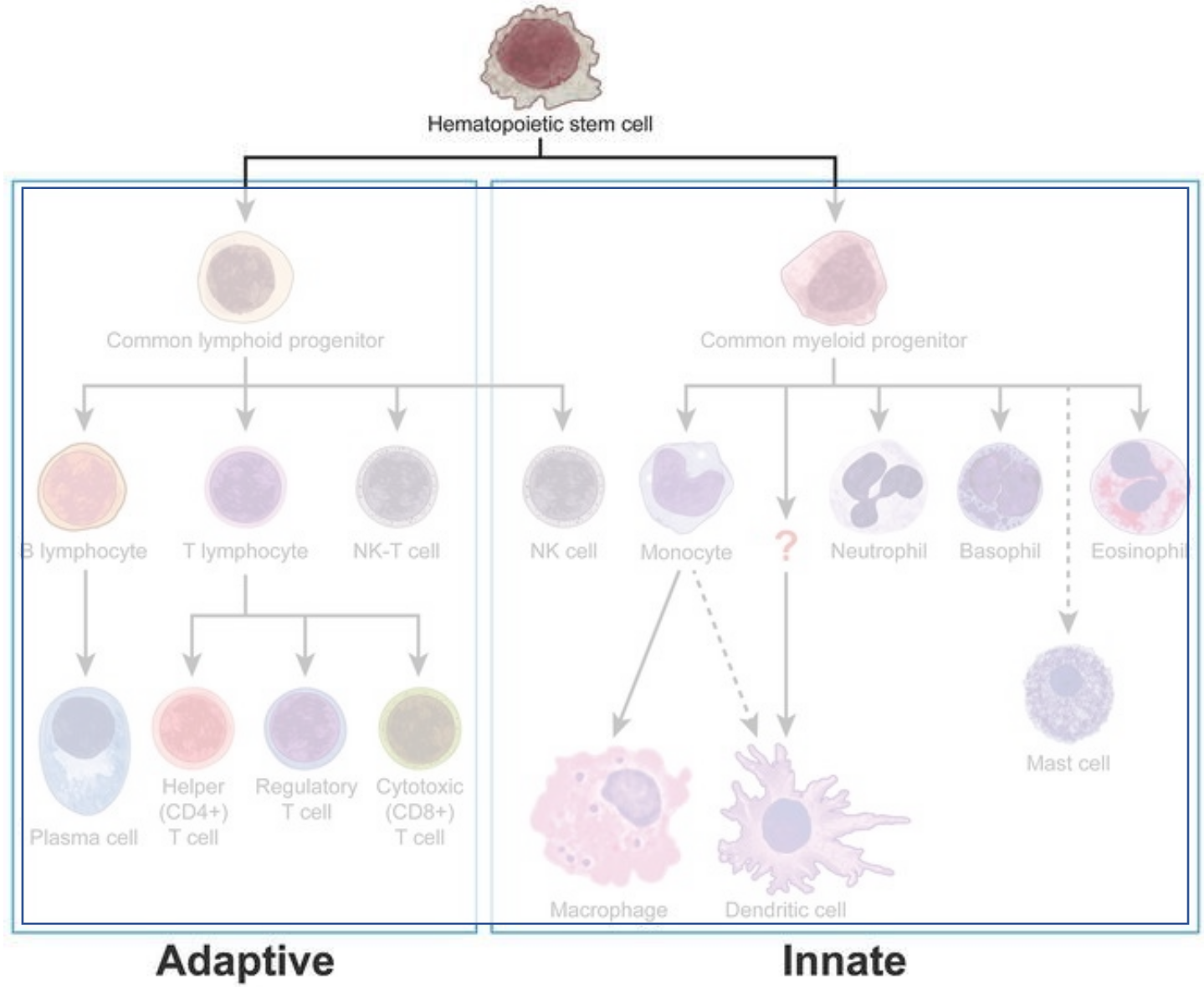
- Antigen is a “foreign” [= non-self] substance, particle, organism, etc.
- **Adaptive (acquired) immunity** develops AFTER EXPOSURE to antigen
- Involves a very specific response to pathogens



Humoral = relating to body fluids, especially in the context of immune response
Strictly speaking, an antigen is a substance that elicits B cell and/or T cell response

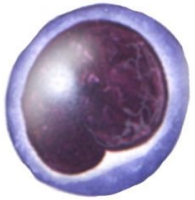
Figure 43.2 in Campbell Biology (10th edition)

Hematopoietic stem cells



https://link.springer.com/referenceworkentry/10.1007/978-3-642-54596-2_925

Maturation of lymphocytes



Lymphocyte (a type of white blood cell)

T cells
Mature in the thymus (an organ; above the heart)

B cells
Mature in the bone marrow itself

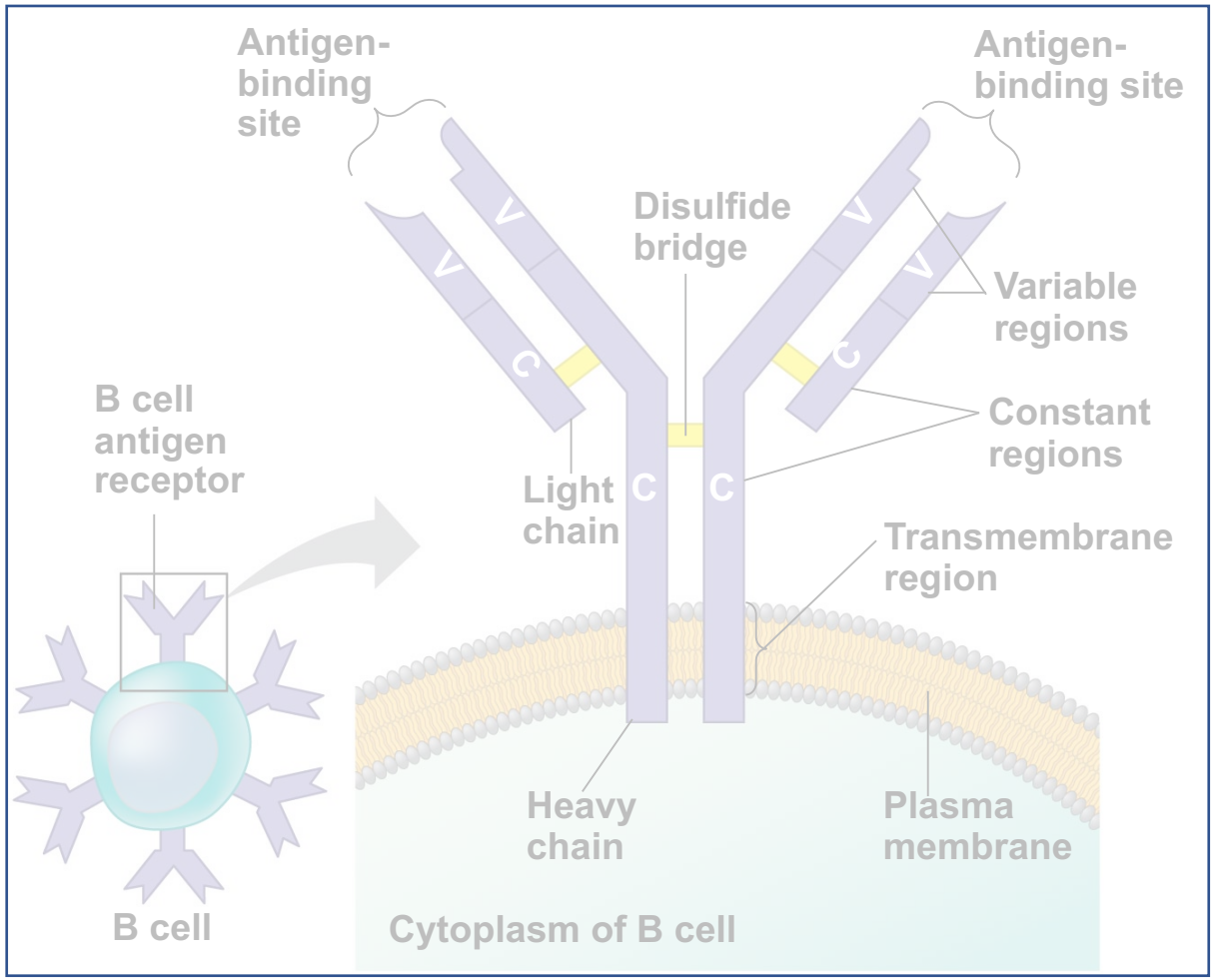
NK cells
Mature in the blood (NK = natural killer)

Adaptive immune response

Innate immune response

https://www.cancer.gov/publications/dictionaries/cancer-terms/def/lymphocyte

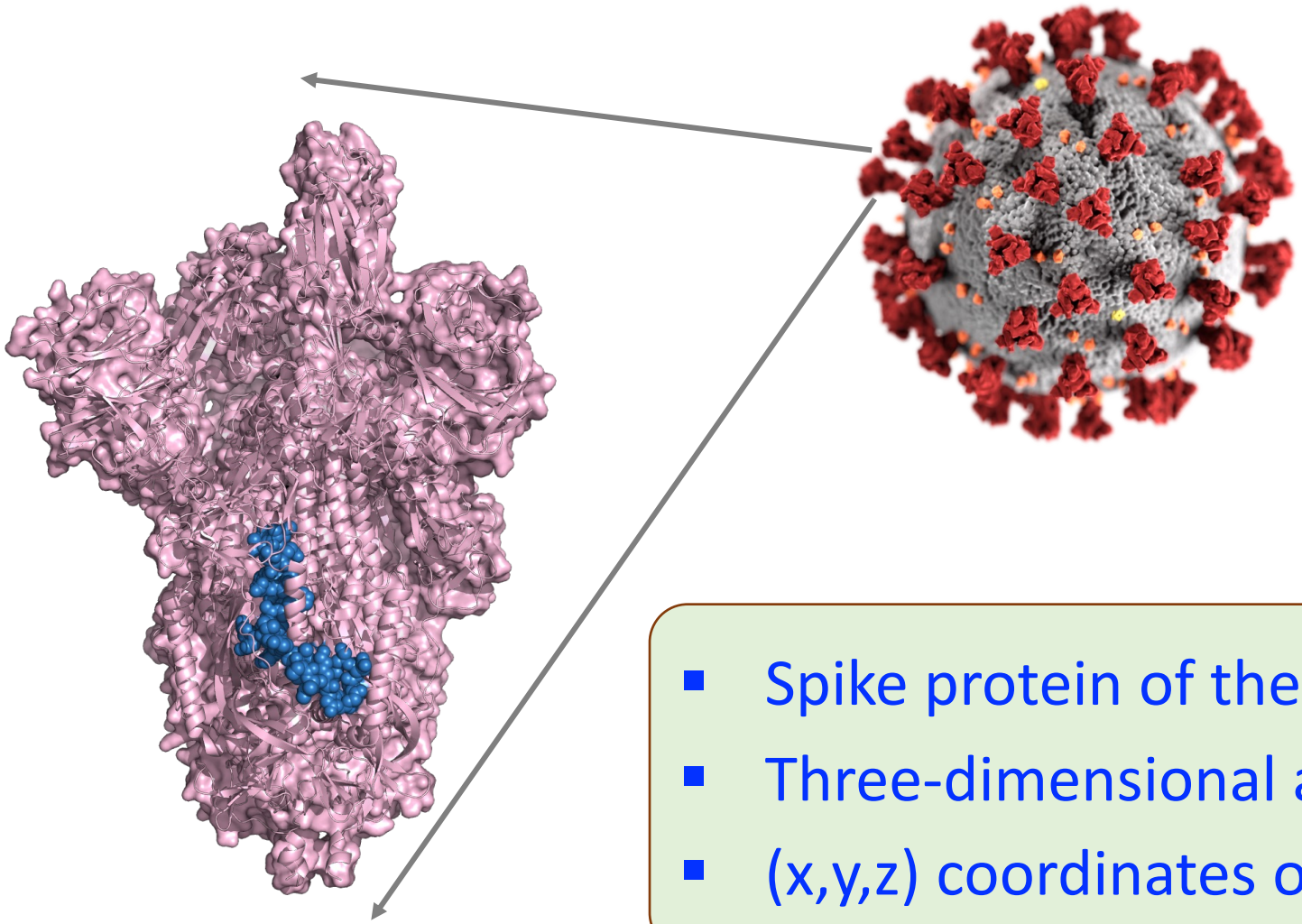
B cells



- B-cells carry receptors for antigens (more specifically, epitopes) on their surface
  - **Each cell surface receptor is specific to an epitope**
- Millions of antigen receptors with specificities for different antigens are (can be) present

Figure 43.9 in Campbell Biology (10th edition)

SARS-CoV-2 spike protein

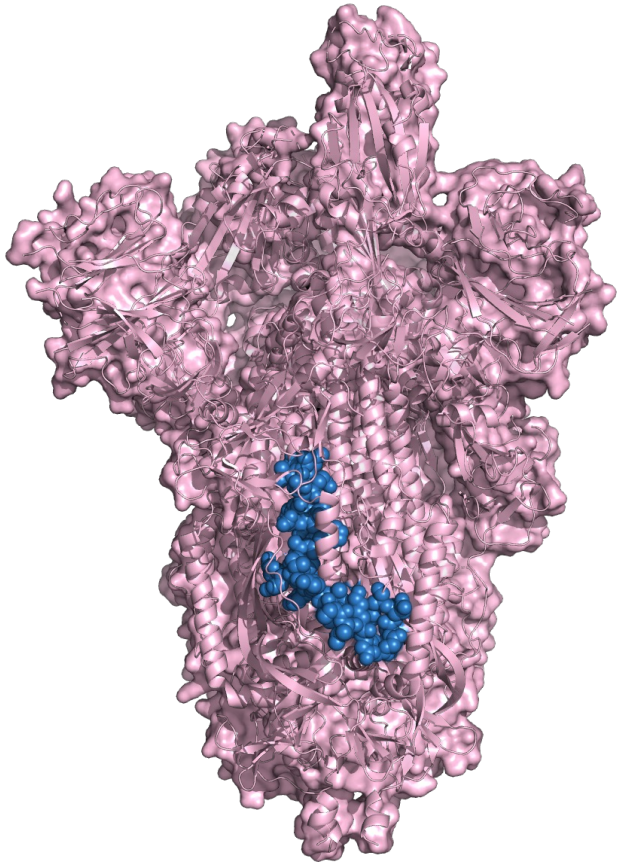


- Spike protein of the SARS-CoV-2
- Three-dimensional atomic structure of the protein
- (x,y,z) coordinates of each and every atom is known

Protein data bank accession id: 6VSB
Three overlapping epitopes S20P2+S20P3+S20P4
^{769}GIAVEQDKNTQEVFAQVKQIYKTPPIKDFGGFNF^{802}
Part of this region of the protein is buried
eBioMedicine (2020) 58:102911

https://commons.wikimedia.org/wiki/File:SARS-CoV-2_without_background.png

Antigen and epitopes



- Epitope is a small region of the antigen that is accessible to the antigen receptor
- Typically, each epitope on an antigen is unique

- One of the epitopes is marked in blue

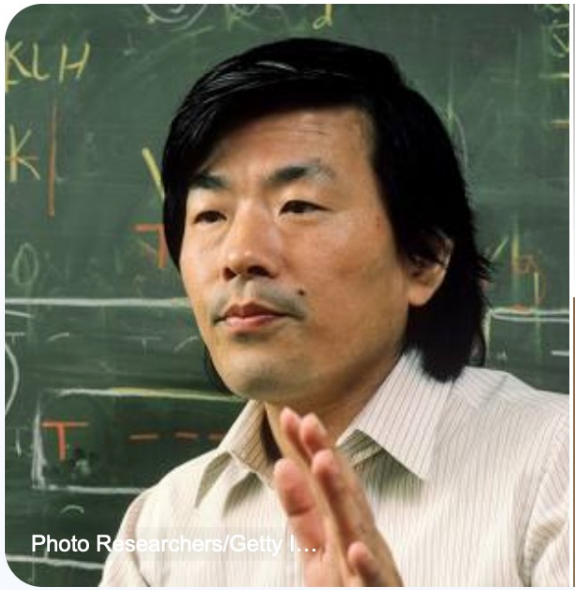
Protein data bank accession id: 6VSB
Three overlapping epitopes S20P2+S20P3+S20P4
^{769}GIAVEQDKNTQEVFAQVKQIYKTPPIKDFGGFNF^{802}
Part of this region of the protein is buried
eBioMedicine (2020) 58:102911

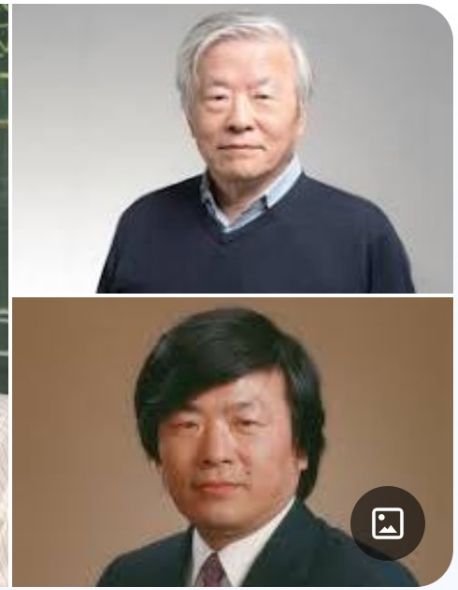
BB10
Marc
Lectu

susumu tonegawa

31

Susumu Tonegawa
Nobel prize in Physiology or Medicine in 1987 (sole recipient)
For the discovery of antibody diversity





Massachusetts Institute of Technol...

Dr. Susumu Tonegawa

Tonegawa is currently the Picower Professor of Biology and Neuroscience at the Massachusetts Institute of Technology (MIT) and the Director of the RIKEN-MIT ...

Age

83 years

Children

Satto Tonegawa

Nobel Prize

Susumu Tonegawa – Biographical - NobelPrize.org

Wikipedia
https://en.wikipedia.org › wiki › Susumu_Tonegawa

Susumu Tonegawa

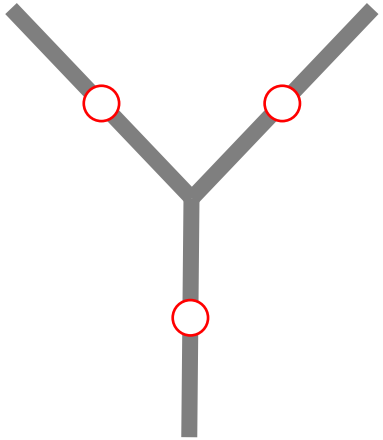
Susumu Tonegawa is a Japanese scientist who was the sole recipient of the Nobel Prize for Physiology or Medicine in 1987 for his discovery of V(D)J ...

Influenced: Adrian Hayday (postdoc) Alci... Awards: Louisa Gross Horwitz Prize (1...

About

Susumu Tonegawa is a Japanese scientist who was the sole recipient of the Nobel Prize for Physiology or Medicine in 1987 for his discovery of VJ recombination, the genetic mechanism which produces antibody diversity. Wikipedia

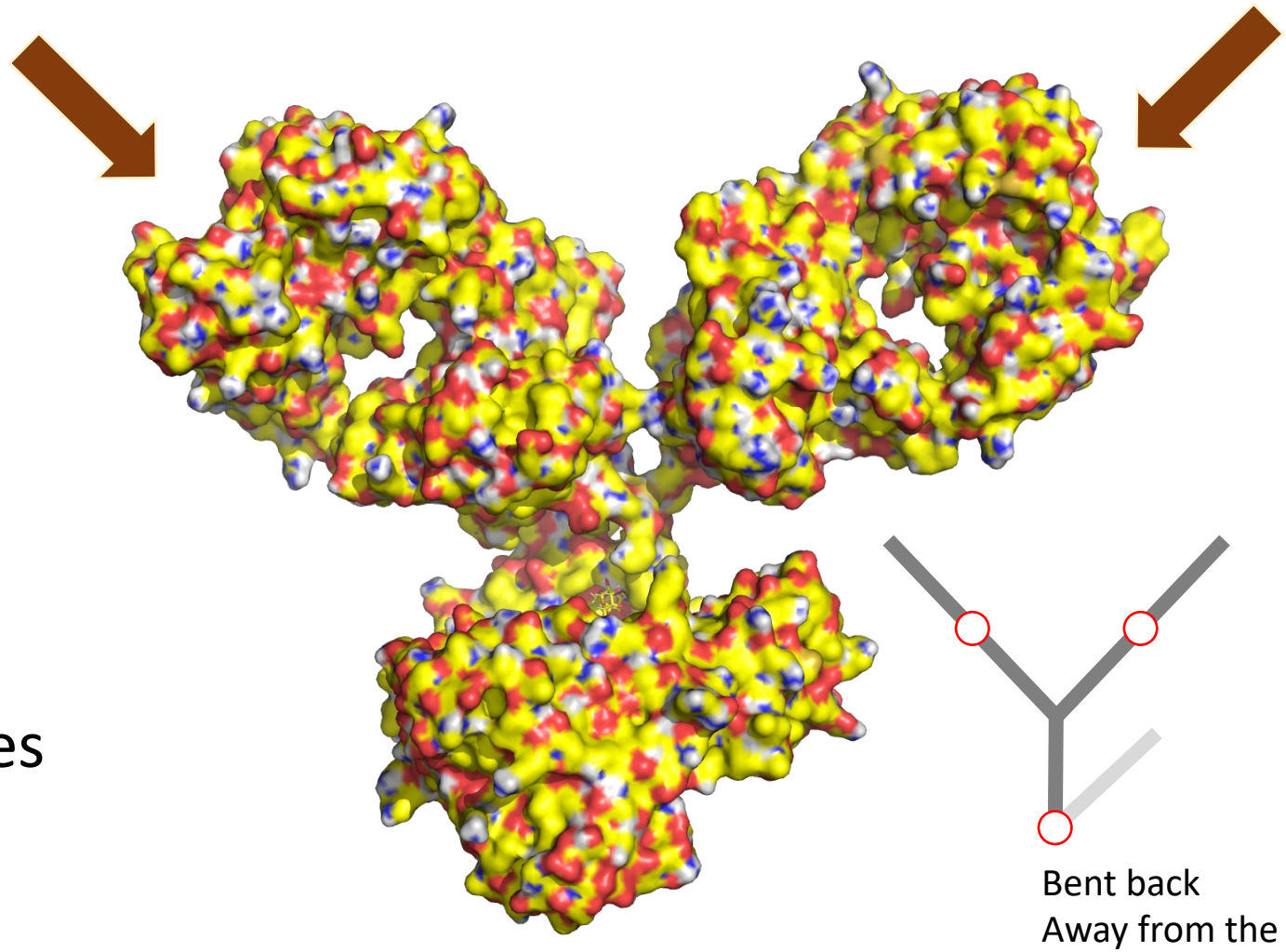
Antibody (or, immunoglobulin, Ig)



Y-shaped

Circles may be viewed as hinges

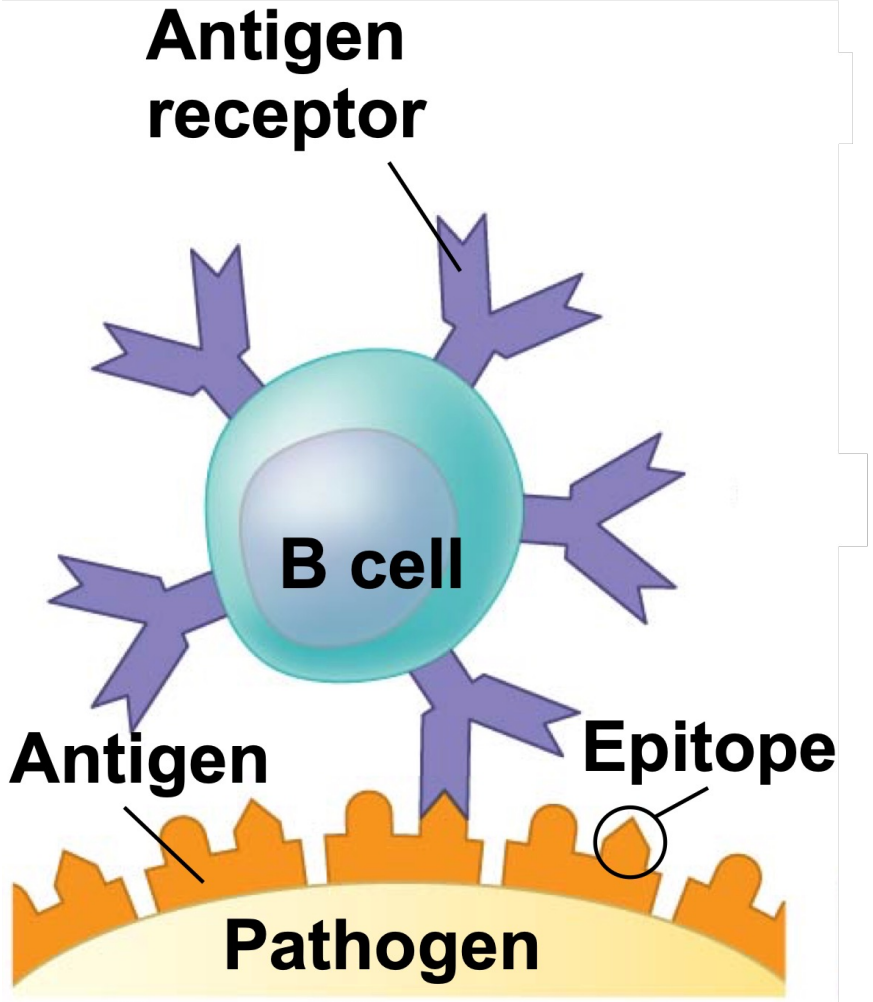
Antigen binding site (1 of 2)



Bent back
Away from the eye

Protein data bank accession code: 1IGY
Approximately 12,300 atoms

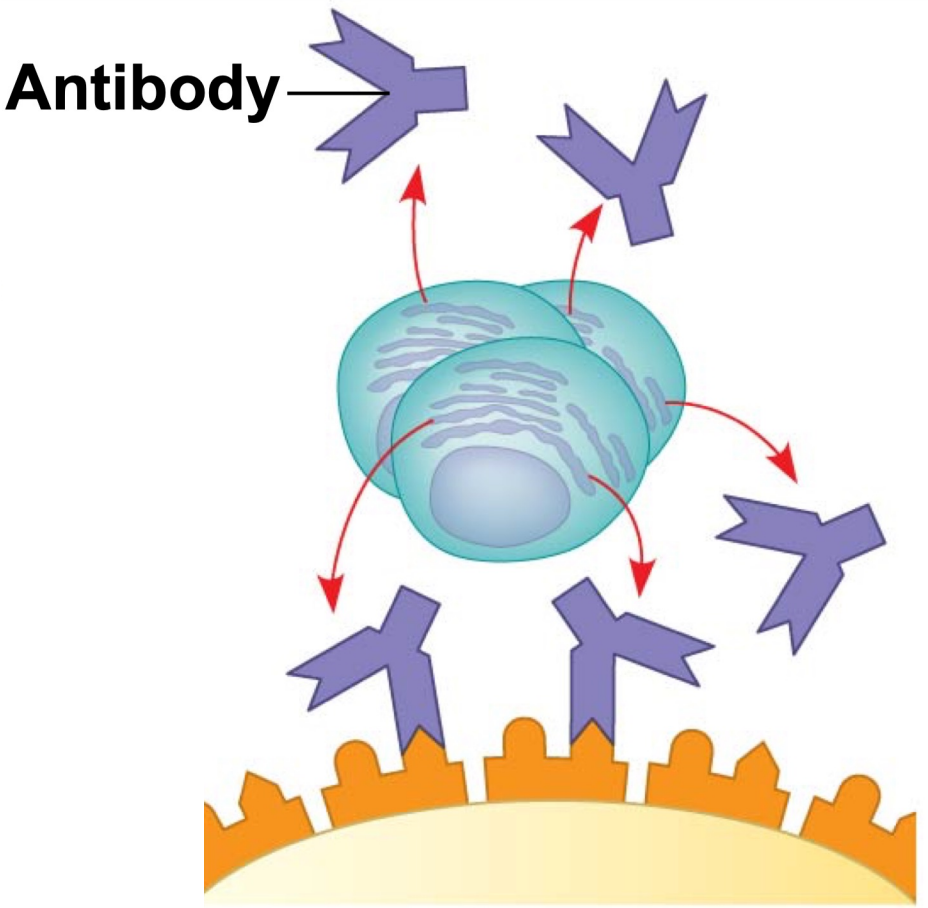
Where are antibodies found?



Some antibodies are anchored on the surface of B cells

Figure 43.10a in Campbell Biology (10th edition)

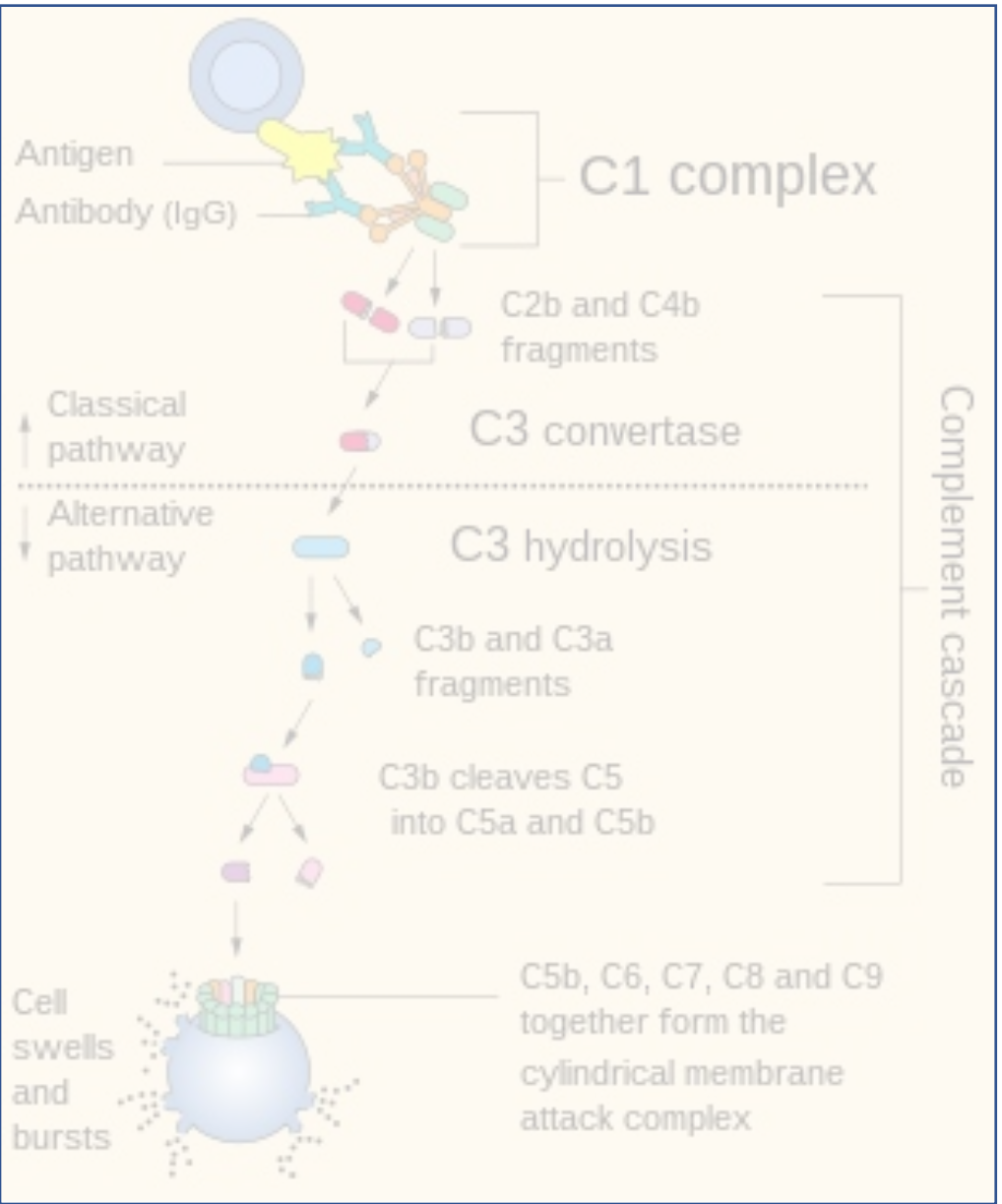
Where are antibodies found?



Some antibodies are released into blood by B cells

Figure 43.10a in Campbell Biology (10th edition)

How do antibodies "take care of" pathogens?



Antibody binds to antigen

↓

Trigger a signaling pathway that leads to the bursting of the pathogen

https://en.wikipedia.org/wiki/Complement_system

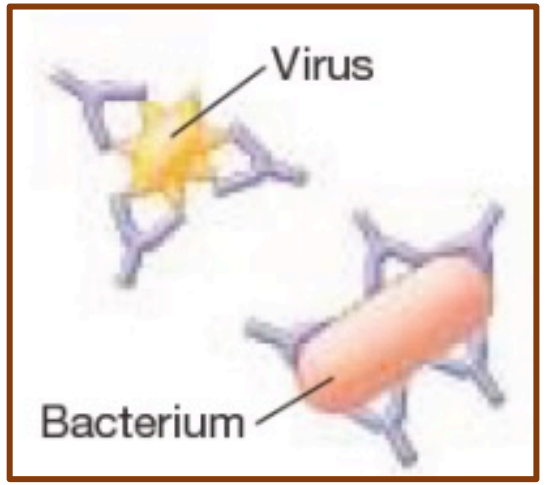
How do antibodies "take care of" pathogens?

Antibody binds to antigen

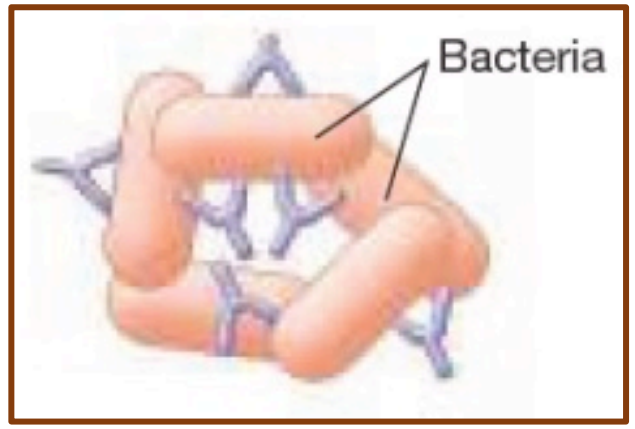
Neutralization by

1. Blocking viral binding sites
2. Coating bacteria

Inactivates antigens

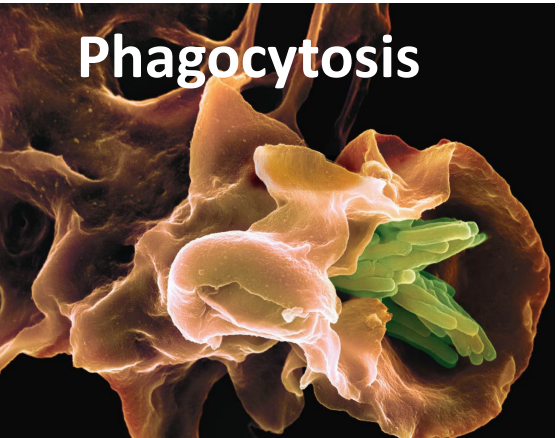


Agglutination



Phagocytosis

Figure 43.1 in Campbell Biology (10th edition)



Where did these images come from? (Swati)

Immunological memory

Individuals who had recovered from the plague could safely care for those who were sick or dying,

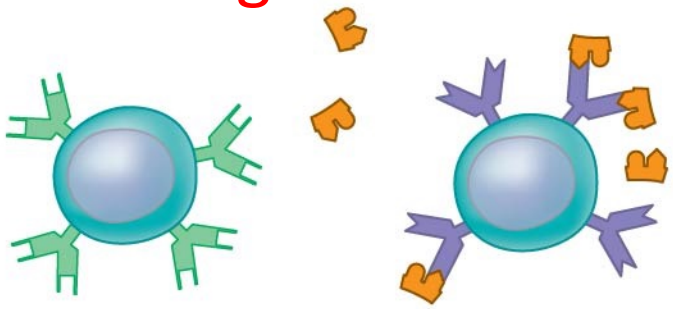
"for the same man was never attacked twice – never at least fatally"

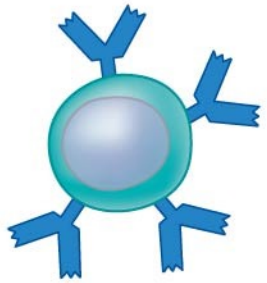
Greek historian Thucydides
~2,400 years ago

Concept 43.2, pp56, in Campbell Biology (10th edition)

Formation of immunological memory: Step 1 of 3

Antigen

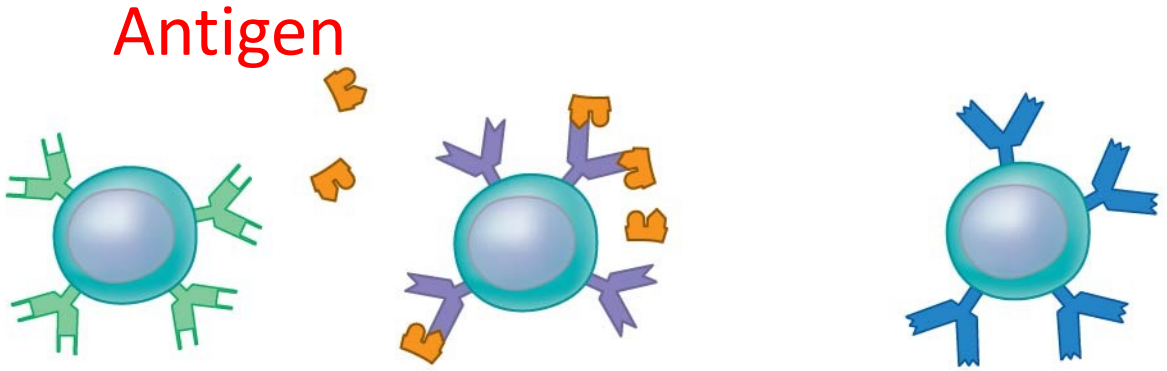




Population of B-cells

Different shapes of antibodies reflect differences in the antigen specificities

Formation of immunological memory: Step 1 of 3

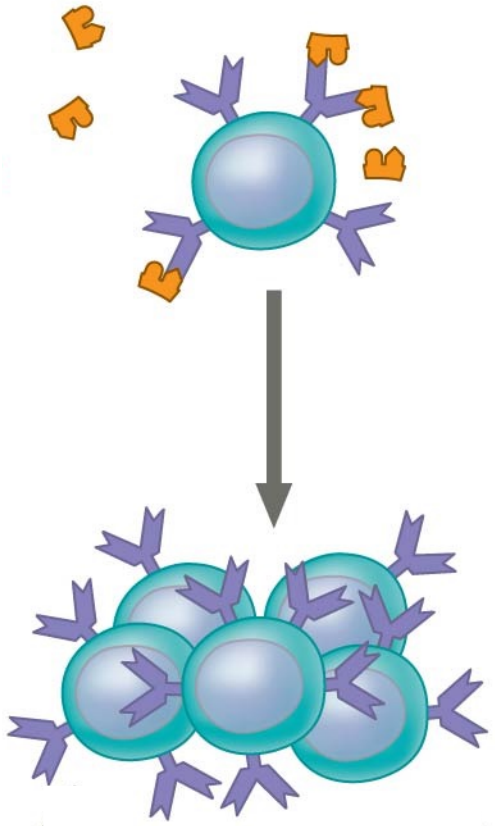


Different shapes of antibodies reflect differences in the antigen specificities

- A population of B-cells containing receptors (= antibodies) of different specificity exist
- Antigens bind to antigen receptors of only one of these B-cells dictated by the specificity of the antibody
- This is clonal selection

Concept 43.14, pp56, in Campbell Biology (10th edition)

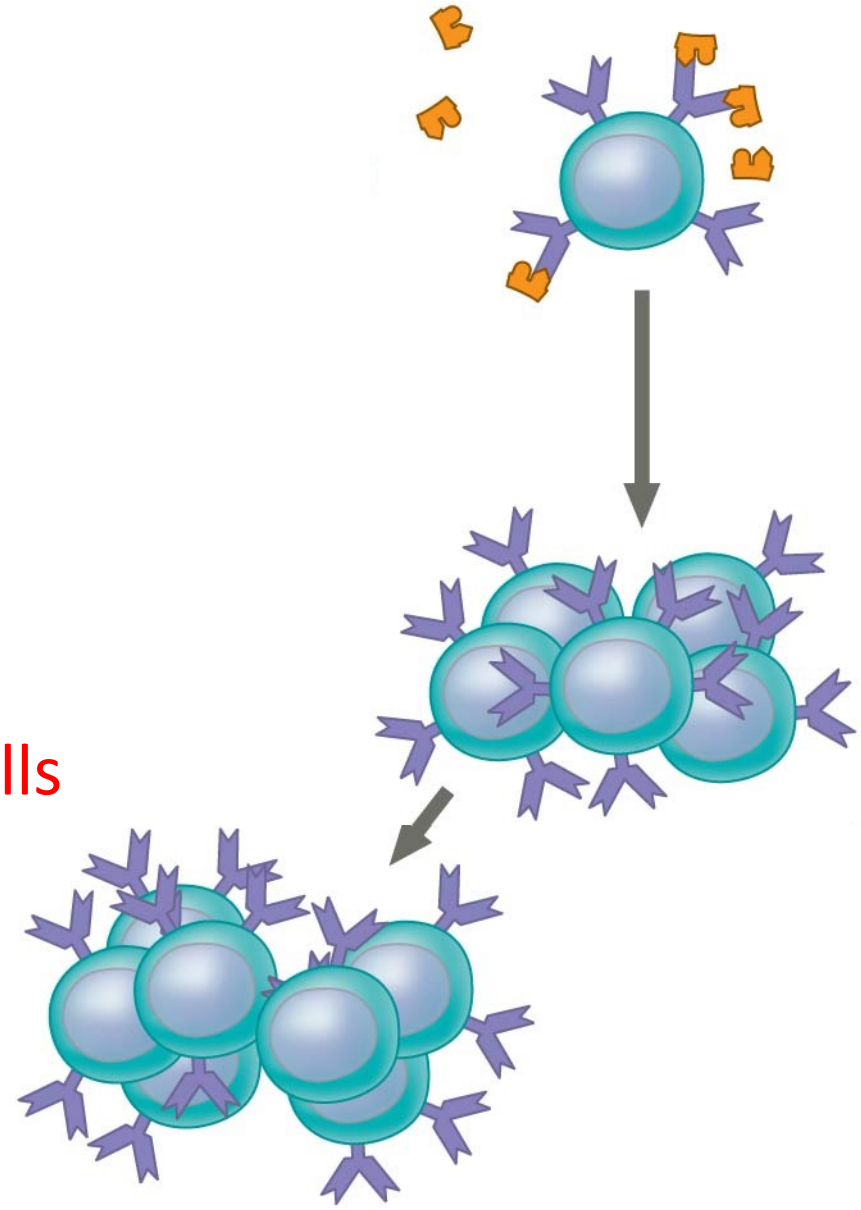
Proliferation of the selected B-cell: Step 2 of 3



- Selected B-cell proliferates
- Clones of B-cells bearing antibodies of same antigen-specificity

Concept 43.14, pp56, in Campbell Biology (10th edition)

Formation of memory cells: Step 3 of 3



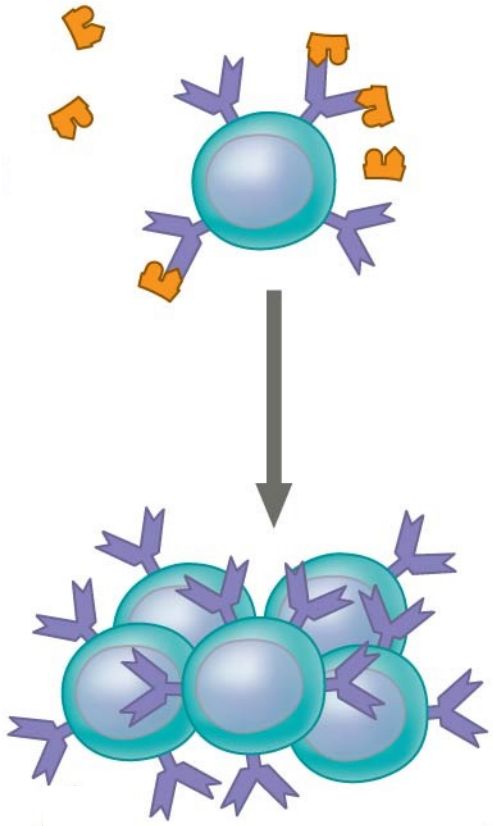
Memory cells

Some daughter cells develop into long-lived memory cells

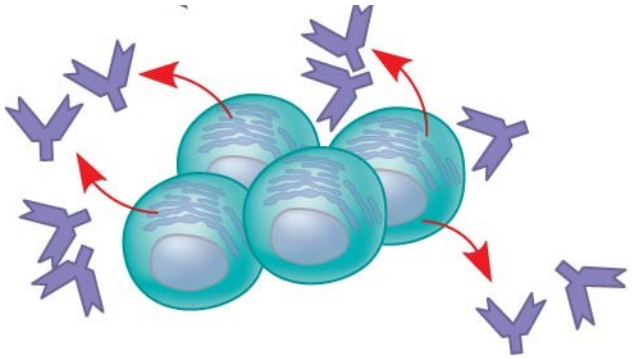
Respond rapidly upon subsequent exposure to the same antigen…

Concept 43.14, pp56, in Campbell Biology (10th edition)

Formation of secretory antibodies



Secreted antibody



Some daughter cells develop into short-lived plasma cells that secrete antibodies specific for the antigen

Concept 43.14, pp56, in Campbell Biology (10th edition)

Formation of immunological memory

- Immunological memory is responsible for long-term protection
- Primary immune response
  - Triggered by the first exposure to a specific antigen
  - Selected B cells give rise to “memory cells”
- Secondary immune response
  - Memory cells facilitate a faster, more efficient response
  - T cells (not discussed) also play a role in immunological memory

The concept of vaccines

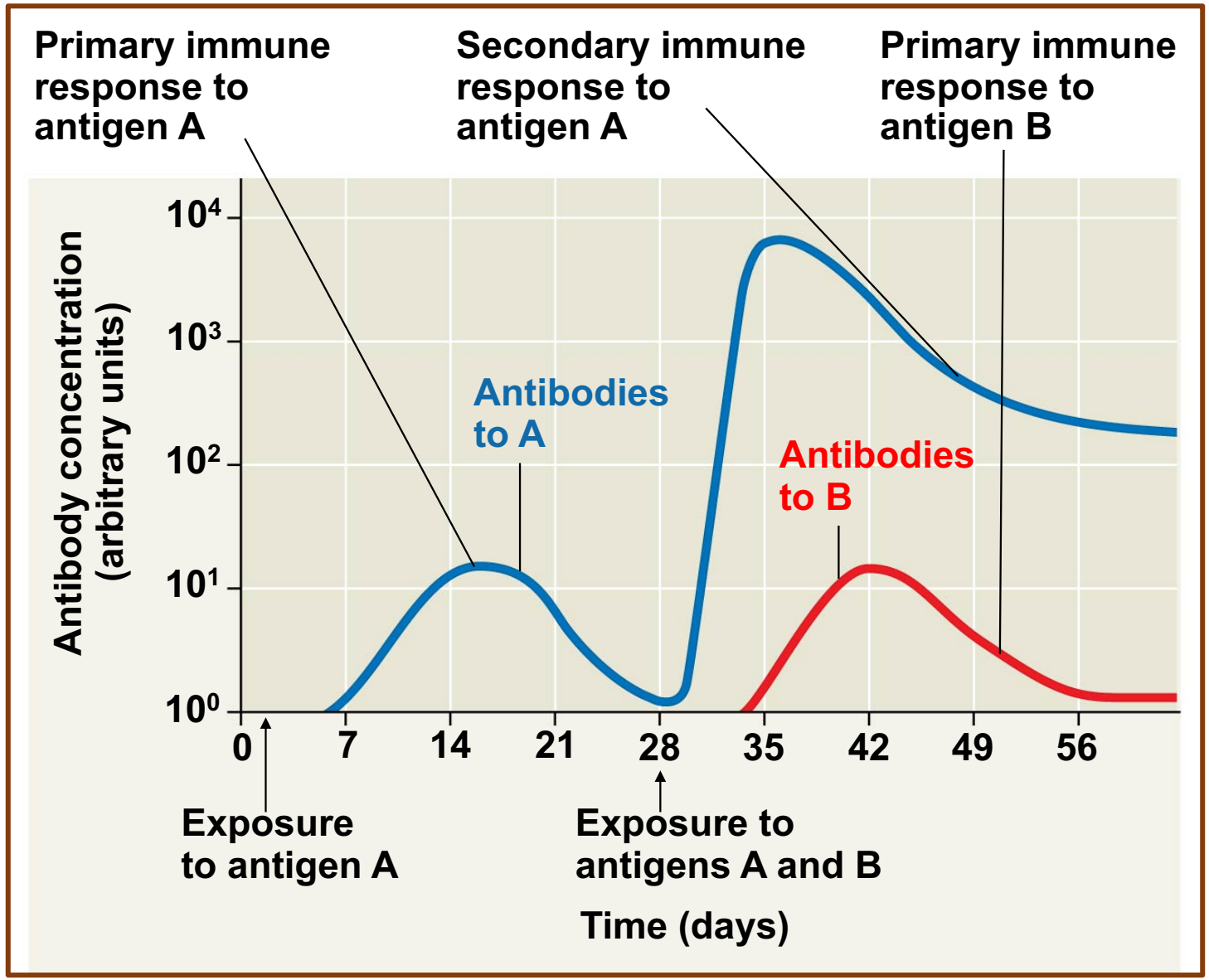


Figure 43.15, pp56, in Campbell Biology (10th edition)

Small pox: eradicated…
Polio: eradicated (?)
Corona virus: controlled…

https://www.unicef.org/sites/default/files/styles/standard_banner/public/UN0735381.jpg?itok=1CQ4o0Fm

Today's topics

- Innate immunity
- Adaptive immunity
- How do plants protect themselves?
- Bacterial defense mechanisms

Plant disease outbreaks that affected human lives

1845-1849 great famine of Ireland

Sculptures, Dublin City

Major cause: Late blight disease of potato

Human lives lost: ~1 million

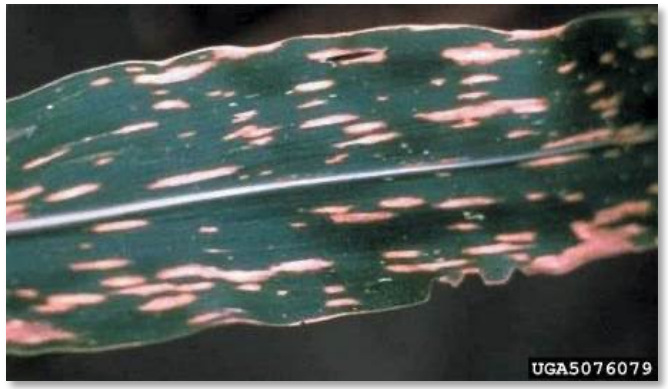
Socio-economic impact

Major human migrations

Histological model of a potato leaf cross-section, Botanical Museum Greifswald

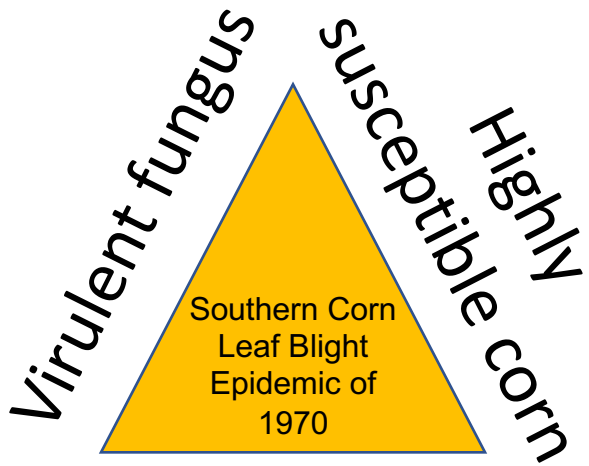
https://www.britannica.com/event/Great-Famine-Irish-history

1970 southern corn leaf blight epidemic



Corn leaf

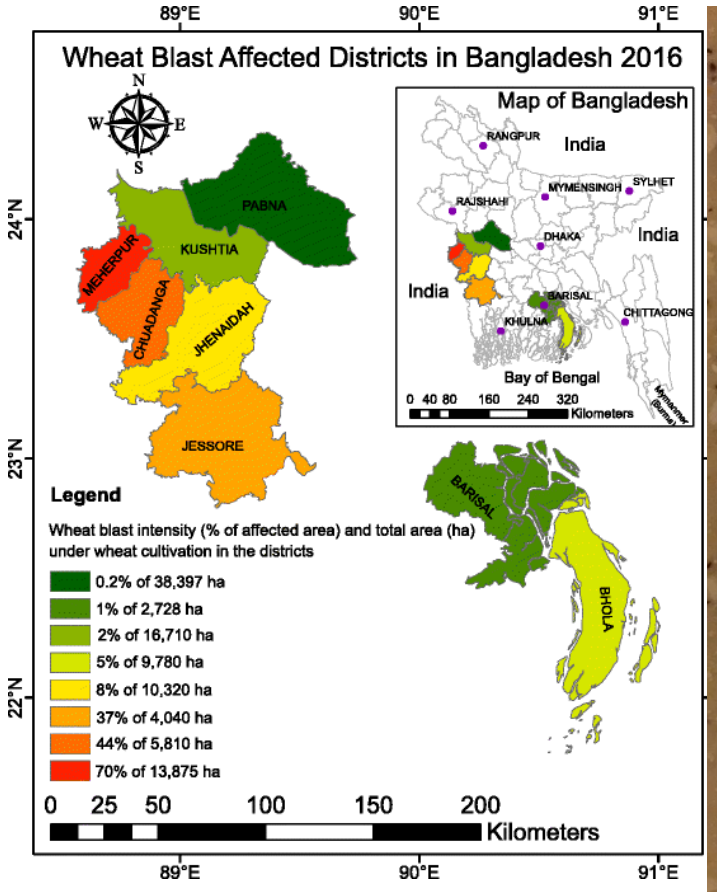
Fungal Pathogen



In 1970, *Cochliobolus heterostrophus* was responsible for the worst epidemic in US agricultural history

https://www.ars.usda.gov/ARSUserFiles/60663500/Publications/Bruns/2017/Bruns_2017_Corn%20Leaf%20Blight.pdf

2016-17 Wheat blast in Bangladesh



2016

DT 6

FRIDAY, NOVEMBER 25, 2016

Farmers of five districts asked to stop wheat cultivation

Tribune Desk

The Department of Agricultural Extension has advised the farmers of five southwestern districts not to cultivate wheat, as these districts saw the breakout of 'wheat blast' disease last year.

According to DAE officials, wheat blast was spotted in Kushtia, Meherpur, Chuadanga, Jhenidah and Jessore last year where many wheat farmers were adversely affected due to the alien disease.

"Farmers are discouraged to cultivate wheat in seven districts of the country, including the five southwester districts, to check any wheat blast outbreak further," said DAE Deputy Director of Jossore office Emdad Hossain Sheikh.

He claimed that the DAE had already taken various programmes to make the farmers aware of the wheat blast disease.

He said: "There is no alternative to suspension of wheat cultivation to check it."

"Even though wheat seeds do not carry the virus of the disease, it may remain in weeds of the arable land. The disease can break out next year as well. So, farmers are asked to stop wheat cultivation in these districts this year," he said.

Caused by a fungus, wheat blast is one of the most fearsome and intractable wheat diseases first discovered in Brazil in 1985, reports UNB.

According to official estimates, the blast disease last year affected 15,000 hectares of wheat fields in Jessore, Kushtia, Chuadanga, Meherpur, Jhenidah, Magura, Barisal, and Bhola causing up to 40% of crop damage.

বাংলাদেশ ব্যাংক

2017

THE FINANCIAL EXPRESS

TOP NEWS: Who will be new Uttarakhand chief minister? Former RSS man Trivendra Raw

Home / India news / 'Wheat blast' disease enters India from Bangladesh, ICAR official says damage contained

'Wheat blast' disease enters India from Bangladesh, ICAR official says damage contained

'Wheat blast', a fungal disease that attacks the standing crop, has been reported in a few pockets in Nadia and Murshidabad districts of Bengal.

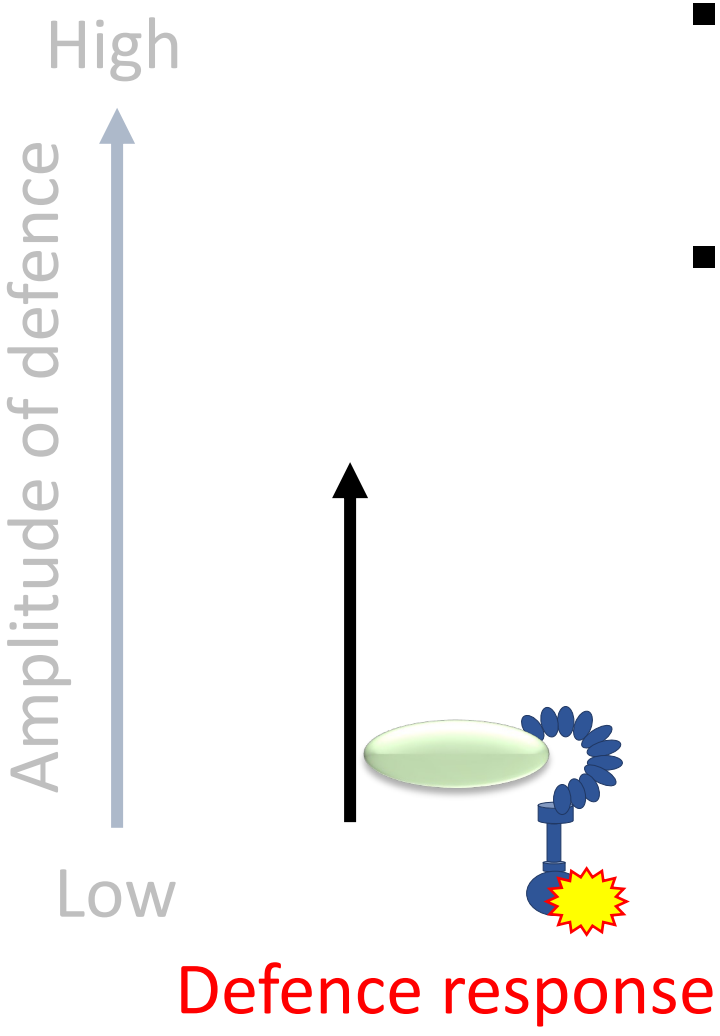
By: Sandip Das | New Delhi | Updated: March 6, 2017 5:29 AM

How do plants protect themselves from pathogen attack?

Plants resist pathogens through active processes that include **recognition** of the pathogen and **defence responses** to fight it

https://www.youtube.com/watch?v=AKY_pelBZek

Zig-zag model of plant-pathogen interactions



Phase 1

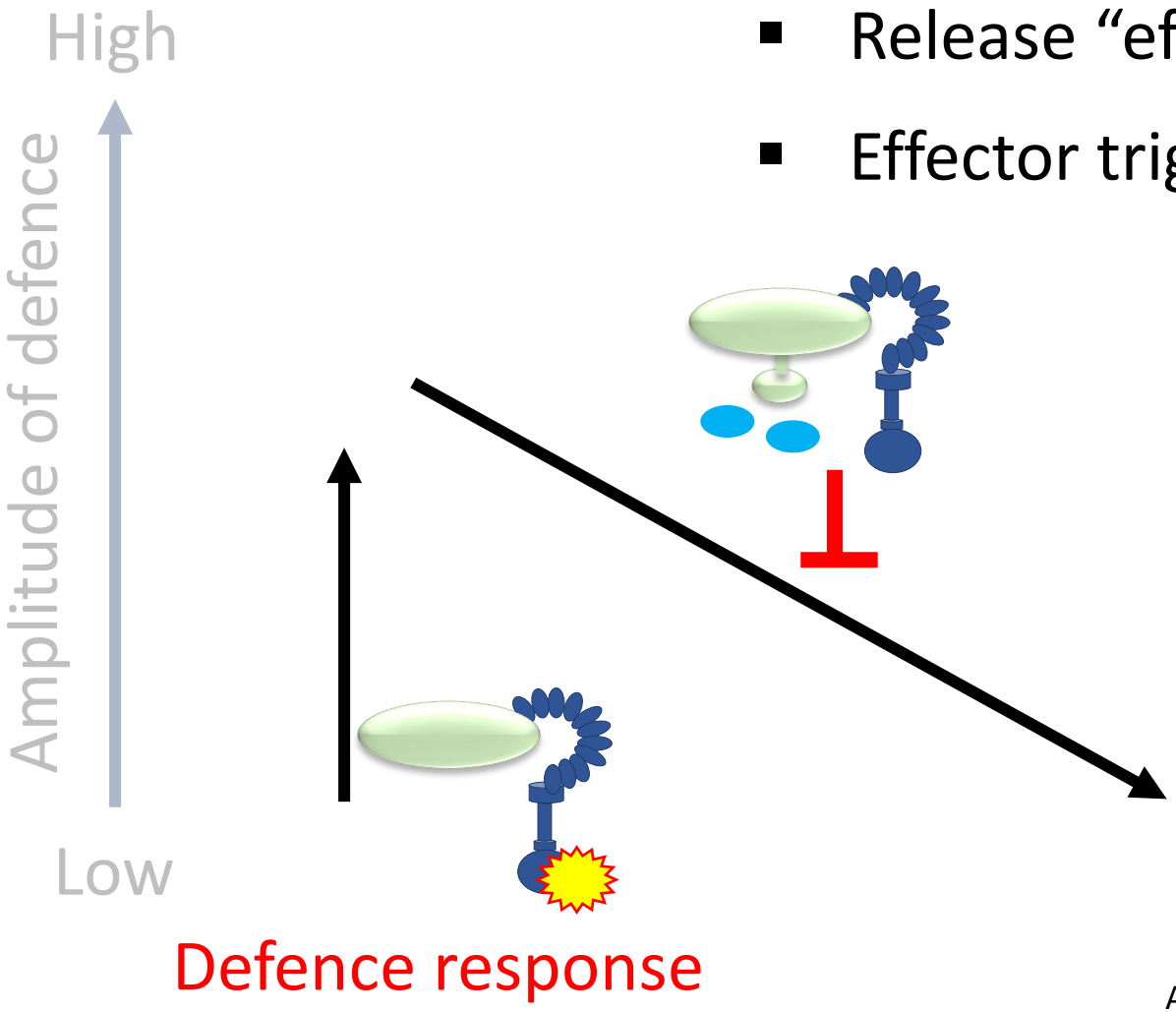
- Cell surface receptors recognize **patterns**
  - Molecular structures common to some pathogens
- Trigger a response
  - Pattern triggered immunity or immune response

Adapted from Jones and Dangl (2006) The plant immune system. Nature. 444: 323-329.

Zig-zag model of plant-pathogen interactions

Phase 2

- Some pathogens manage to survive
- Release “effectors” that suppress defence response
- Effector triggered susceptibility



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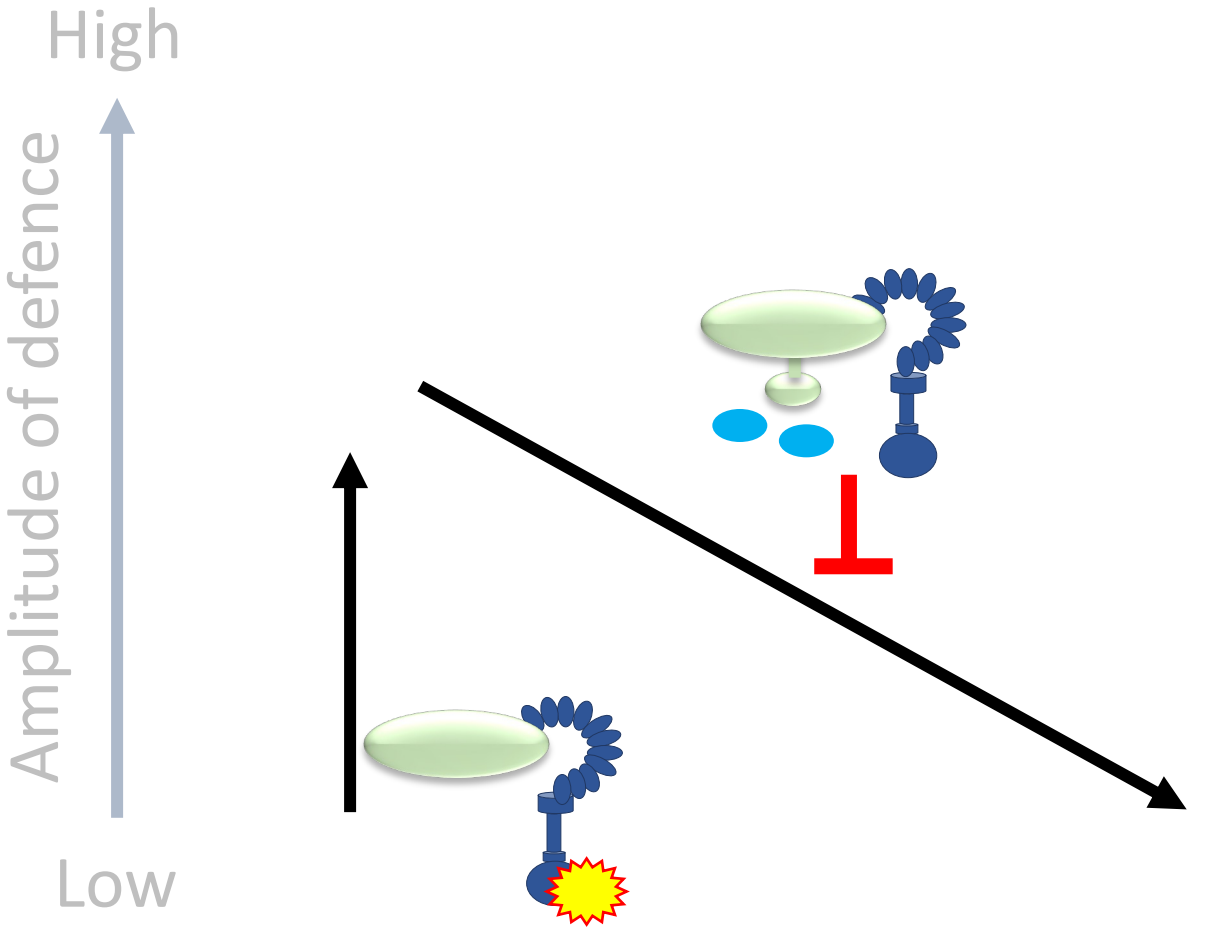
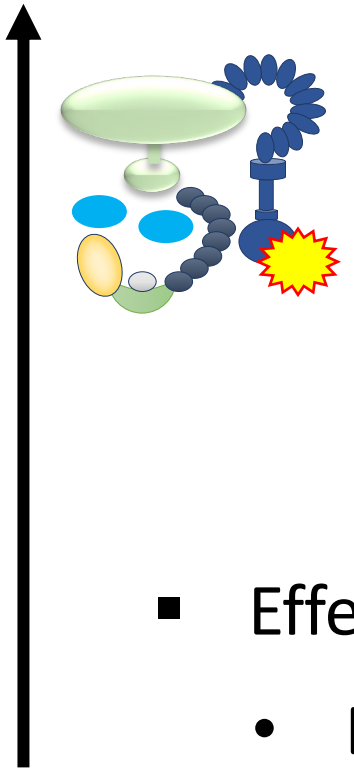
Zig-zag model of plant-pathogen interactions





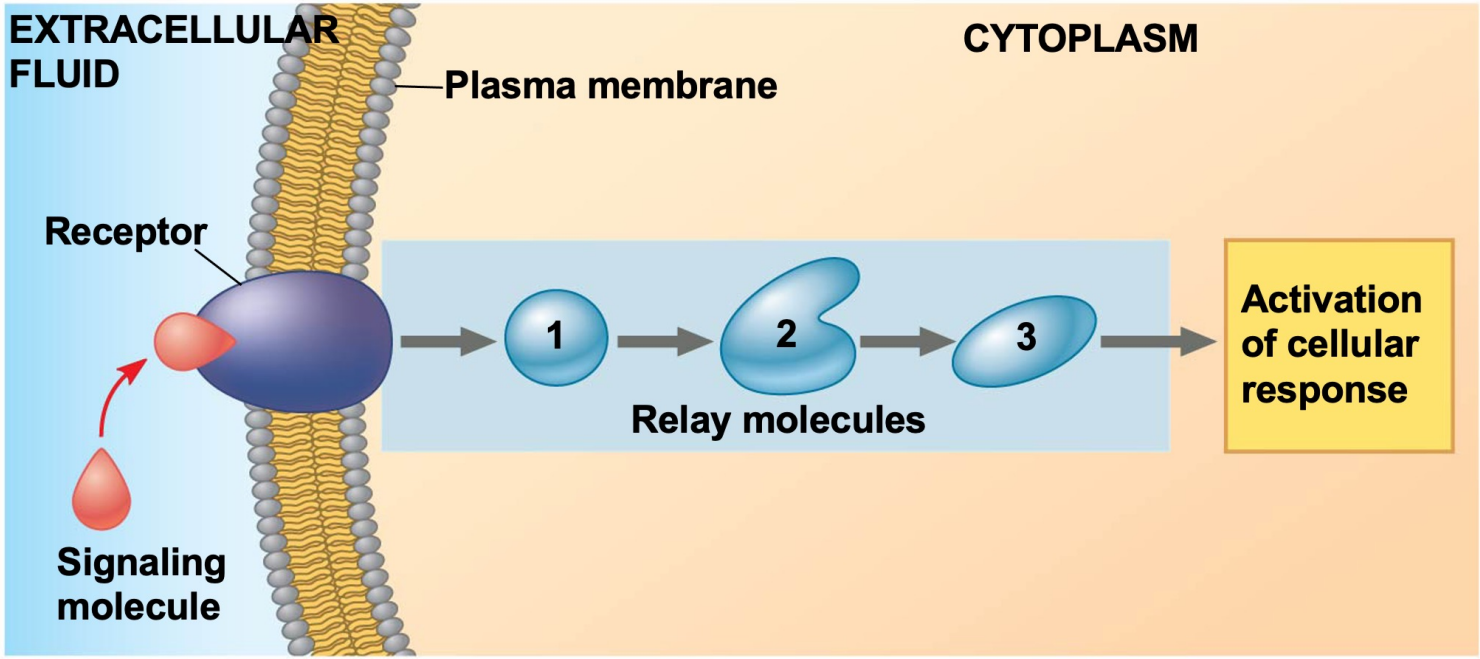
Robust Defence response

- Phase 3
- Effector is “recognized”
  - **Effector Triggered Immunity**

Adapted from Jones and Dangl (2006) The plant immune system. Nature. 444: 323-329.

Slide from Lecture 8

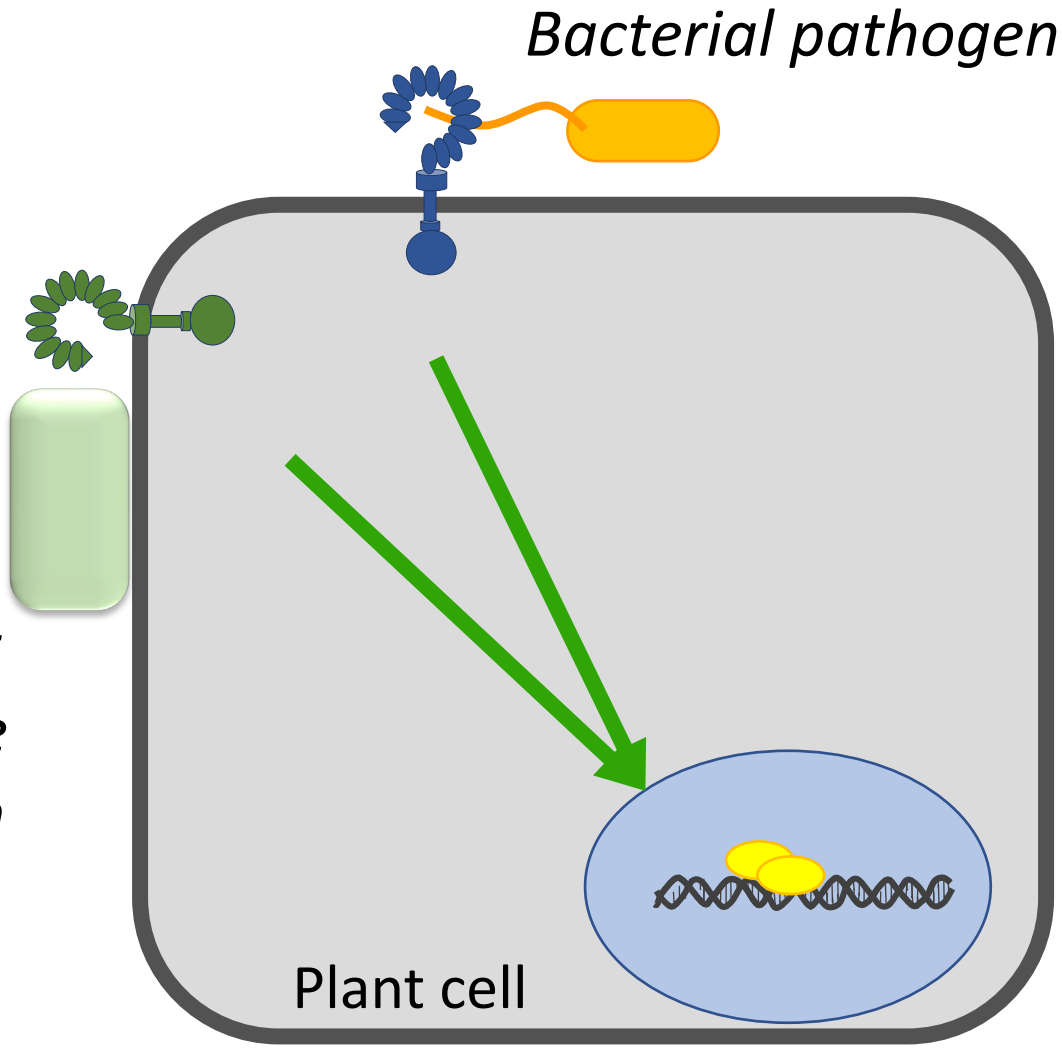
Signal transduction: 3. Response



- Response can be of different types:
  1. Catalysis of a reaction by an enzyme
  2. Activation of specific genes (gene expression)
  3. Rearrangement of the cytoskeleton

Figure 11.6 of Campbell Biology by Reece and others (10th edition)

Pattern recognition receptors



Extracellular recognition domain

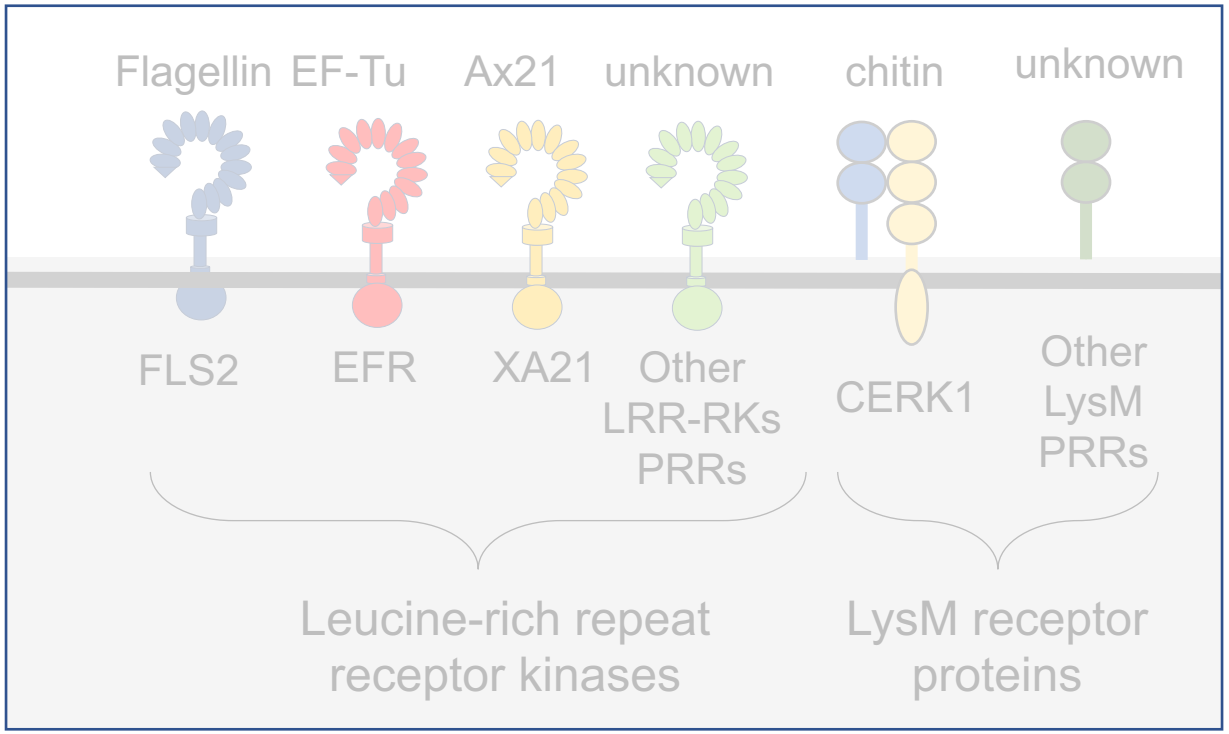
Intracellular response-triggering domain

Oomycete is a fungus-like pathogen

Modified from Dodds, P.N. and Rathjen, J.P. (2010). Nat Rev Genet. 11: 539-548.

Pattern recognition receptors

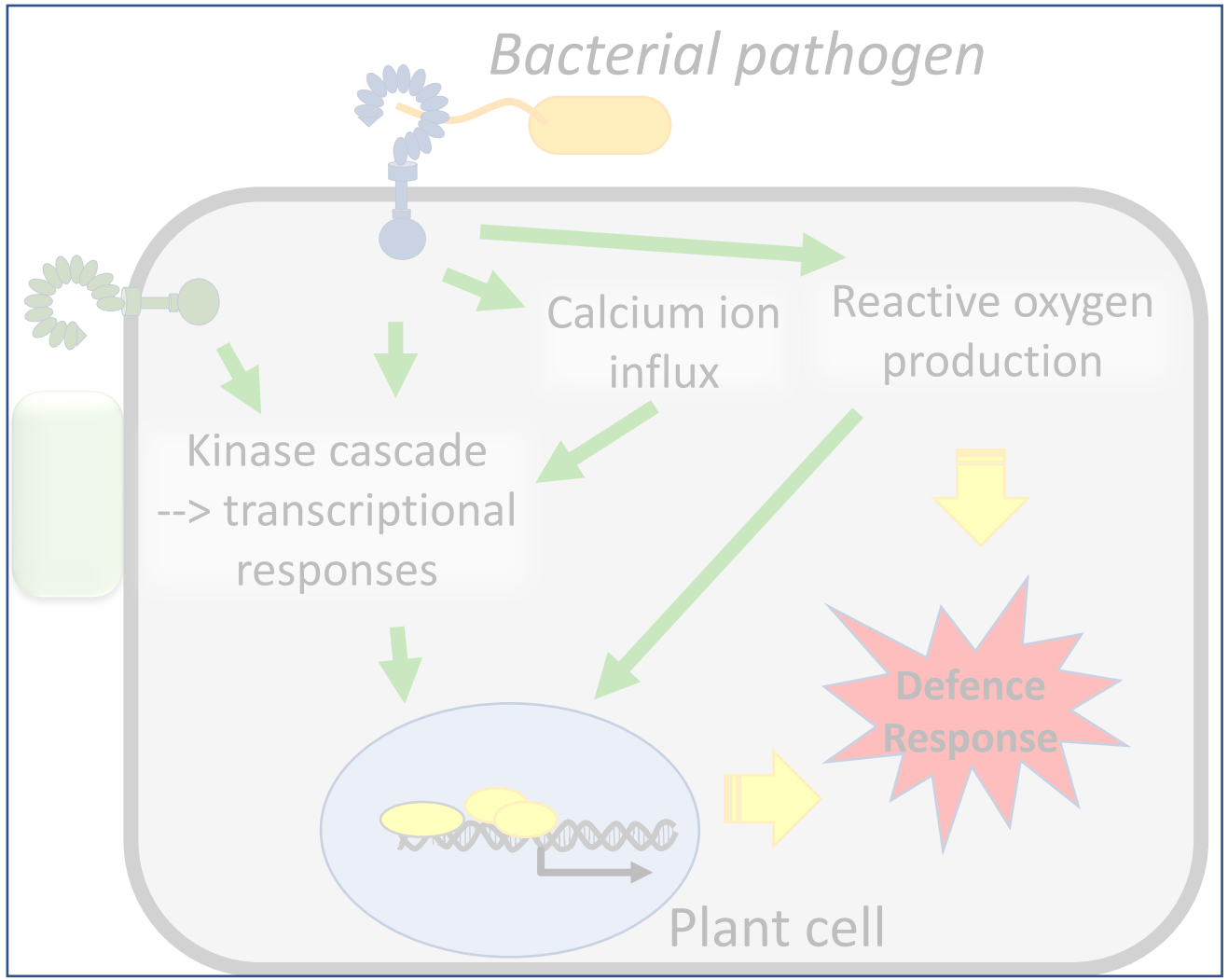
- **Patterns** are molecular structures shared by some pathogens
  - Several Pathogen-Associated Molecular Patterns are known
  - Several pattern recognition receptors have been identified



Adapted from Segonzac, C. and Zipfel, C. (2011). Curr. Opin. Microbiol. 14: 54-61.

Pattern-triggered immunity (immune response)

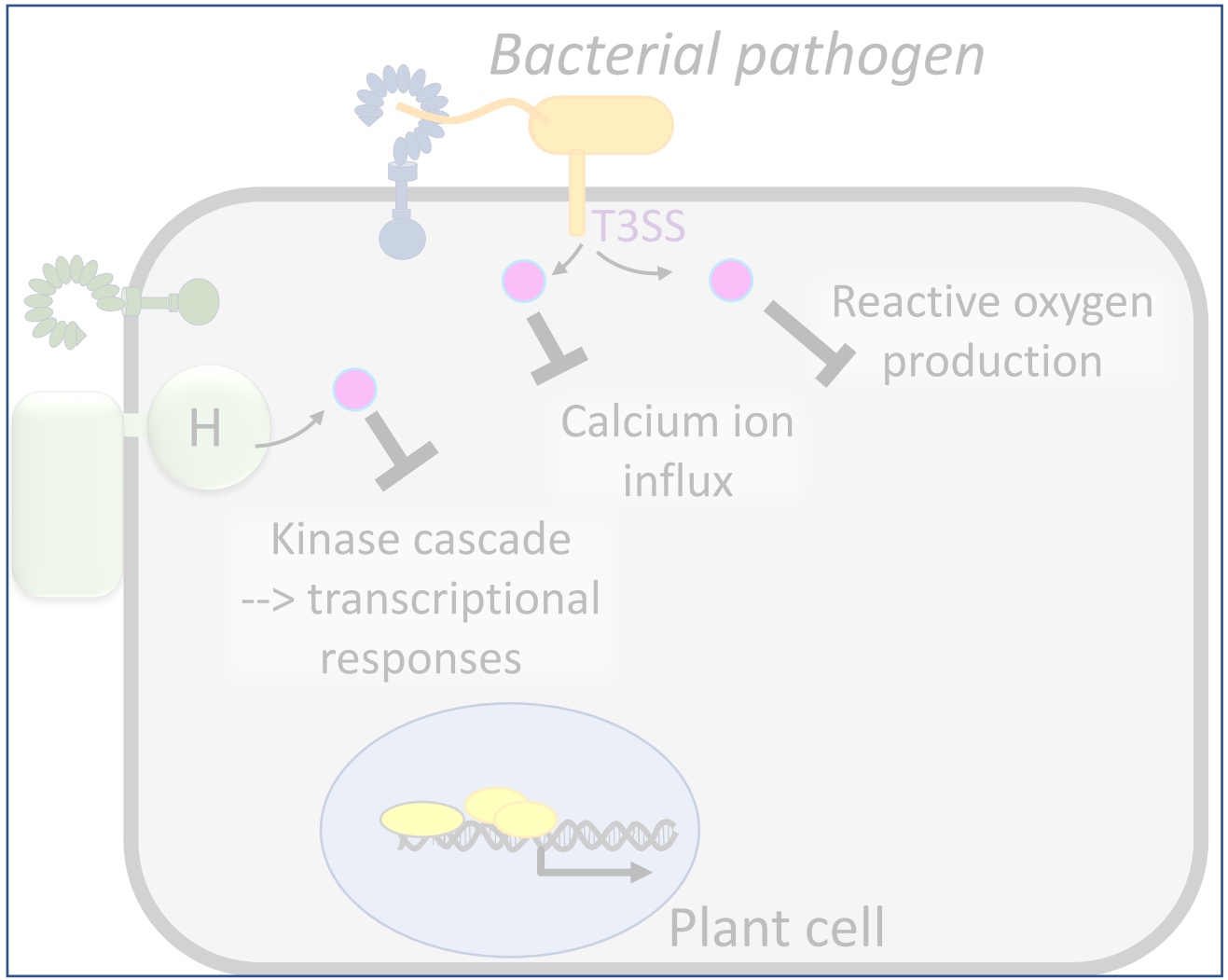
Fungal or oomycete pathogen



Response: secretion of phytochemicals

Modified from Dodds, P.N. and Rathjen, J.P. (2010). Nat Rev Genet. 11: 539-548.

Pathogens secrete effectors to suppress host response

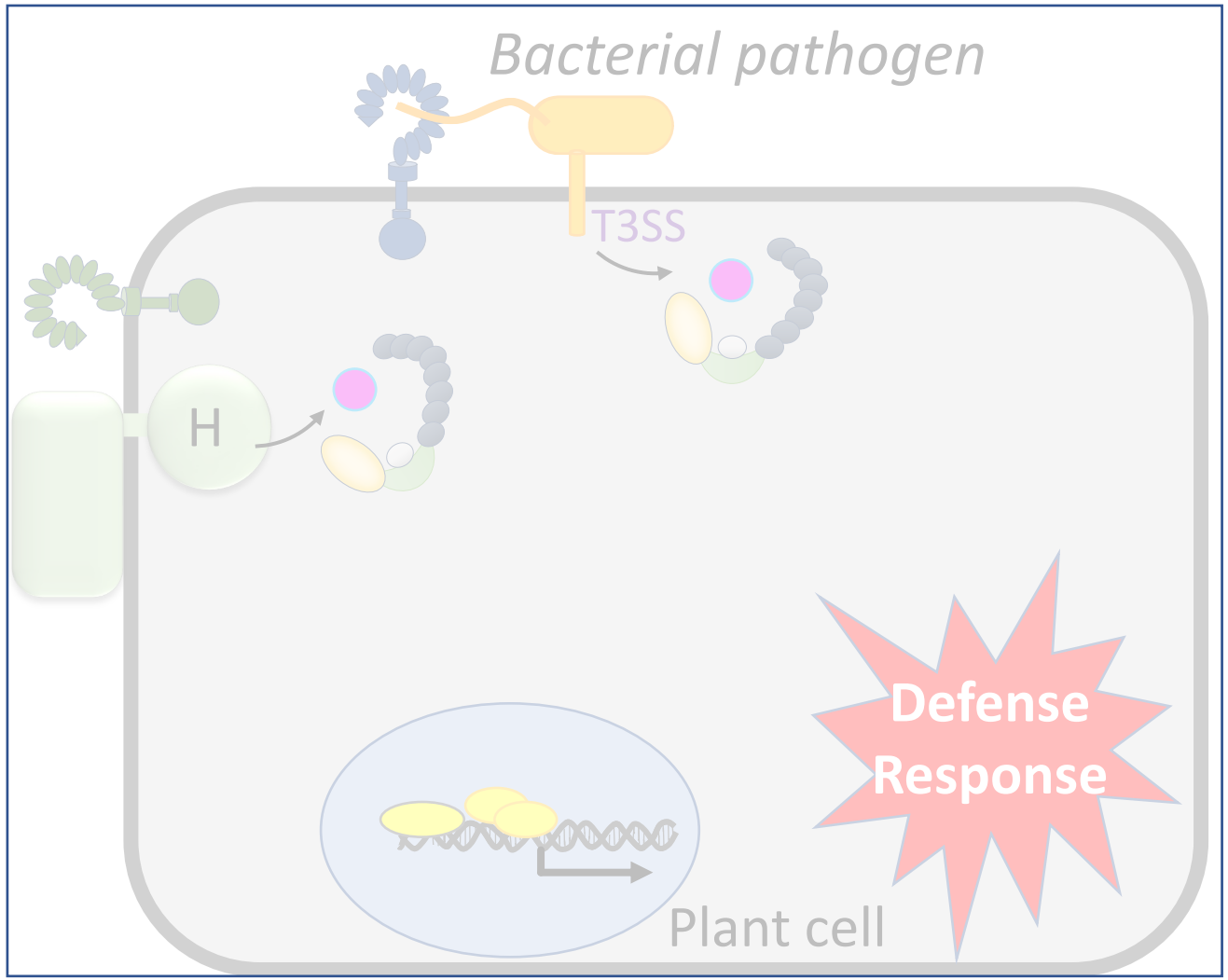


Fungal or oomycete pathogen

Oomycete is a fungus-like pathogen

Modified from Dodds, P.N. and Rathjen, J.P. (2010). Nat Rev Genet. 11: 539-548.

R (resistance) proteins neutralize effectors

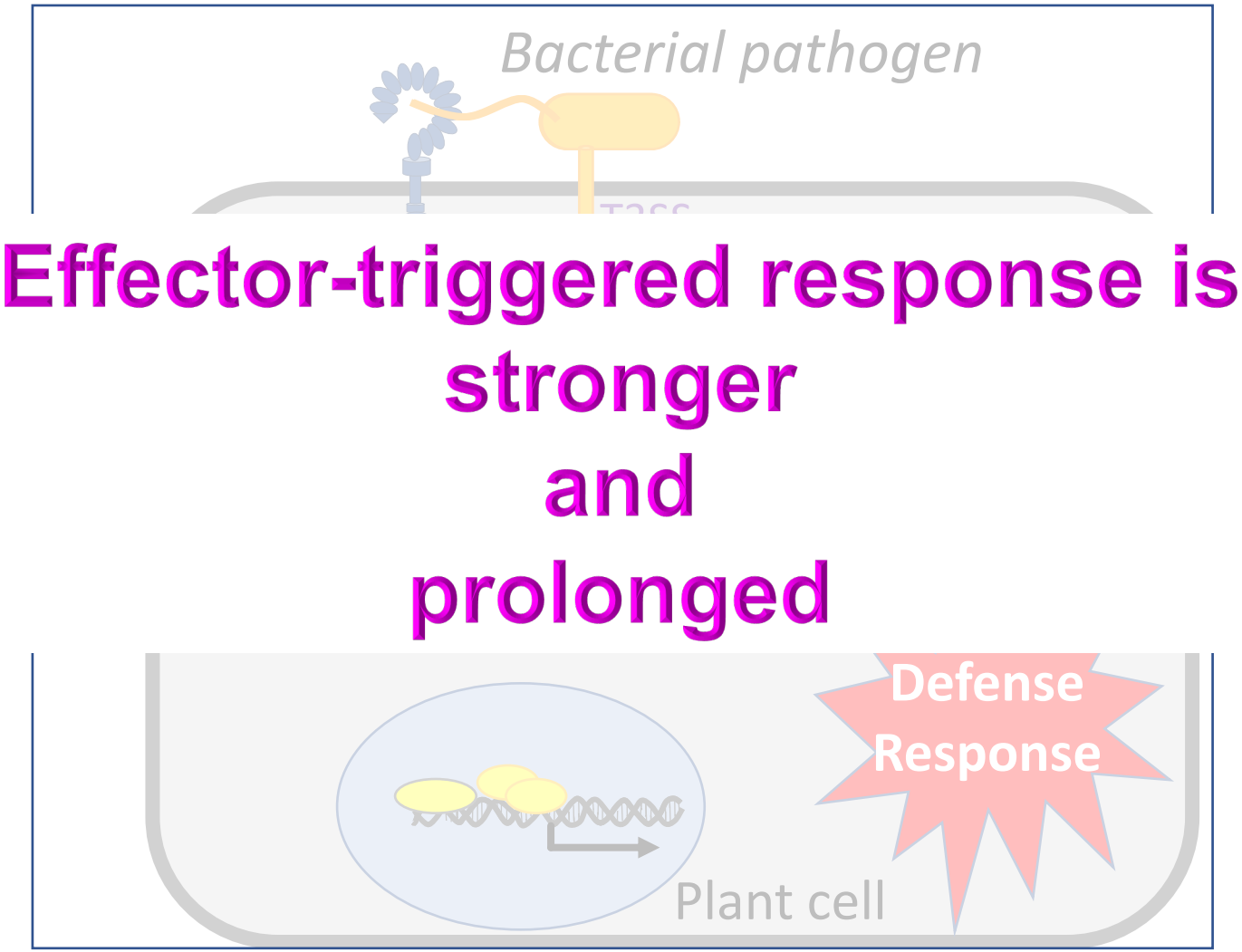


Response: death of invaded cell

Oomycete is a fungus-like pathogen

Modified from Dodds, P.N. and Rathjen, J.P. (2010). Nat Rev Genet. 11: 539-548.

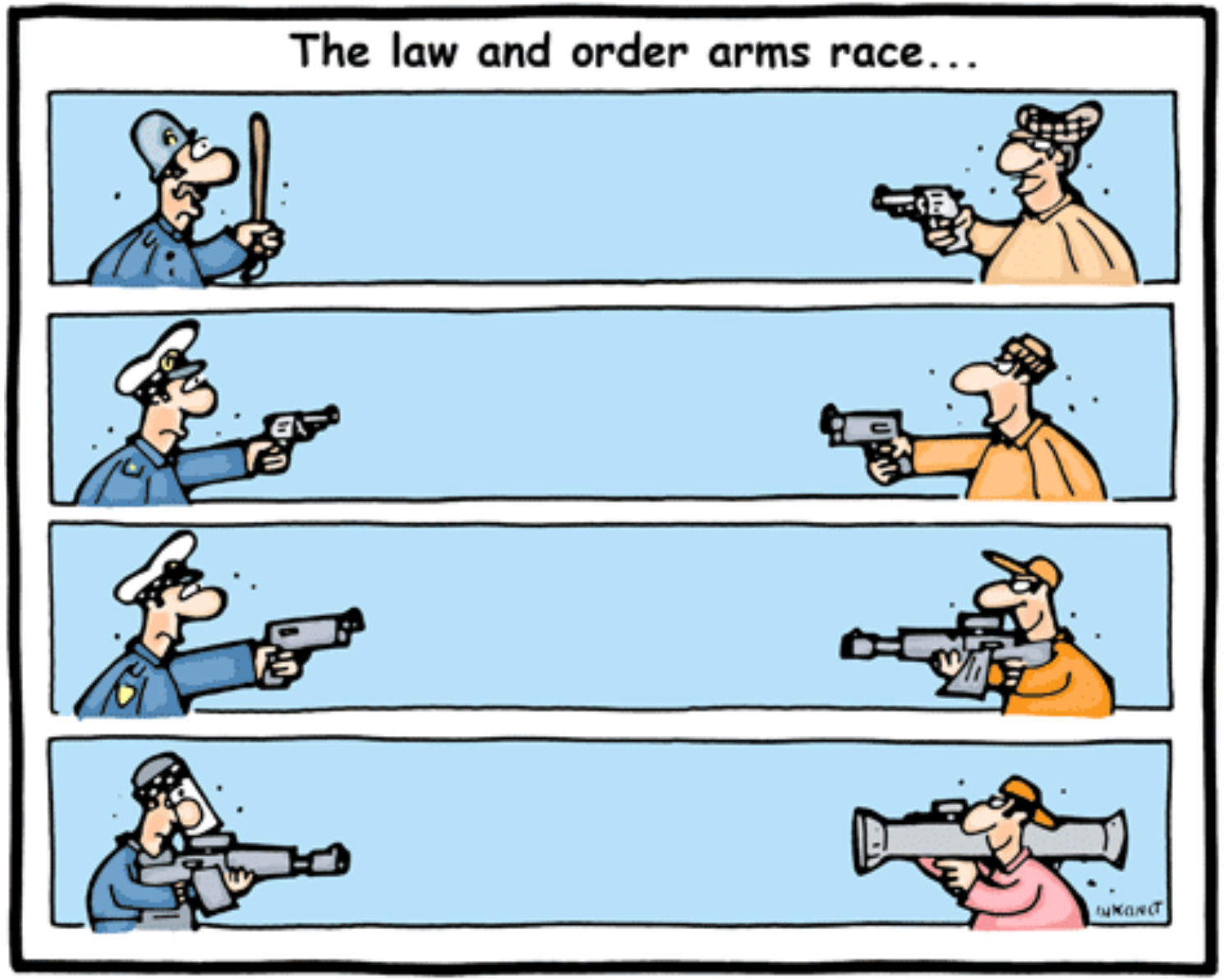
Effector-triggered immune response



Oomycete is a fungus-like pathogen

Modified from Dodds, P.N. and Rathjen, J.P. (2010). Nat Rev Genet. 11: 539-548.

Host-pathogen interactions “arms race”



Today's topics

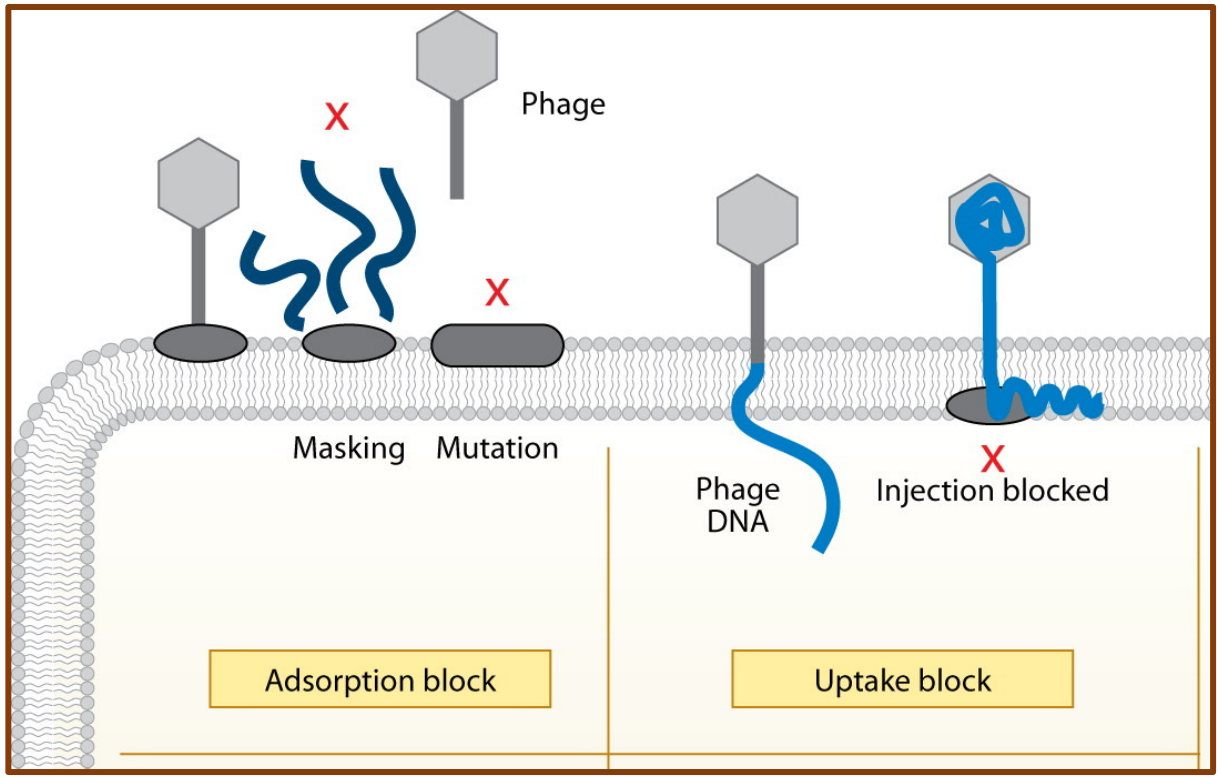
- Innate immunity
- Adaptive immunity
- How do plants protect themselves?
- Bacterial defense mechanisms

Defense mechanisms in bacteria

- What do bacteria need to protect themselves from?
  - Viruses (phages)!
  - Bacteria are constantly under attack by viruses
- From basic research to applications
  - CRISPR-Cas is a defense mechanism
  - CRISPR-Cas has been used for “gene editing”

CRISPR is pronounced as crisper.
It is an acronym. An abbreviation that is pronounced as a word is an acronym
CRISPR = Clustered Regularly Interspaced Short Palindromic Repeats
Cas = CRISPR-Associated System

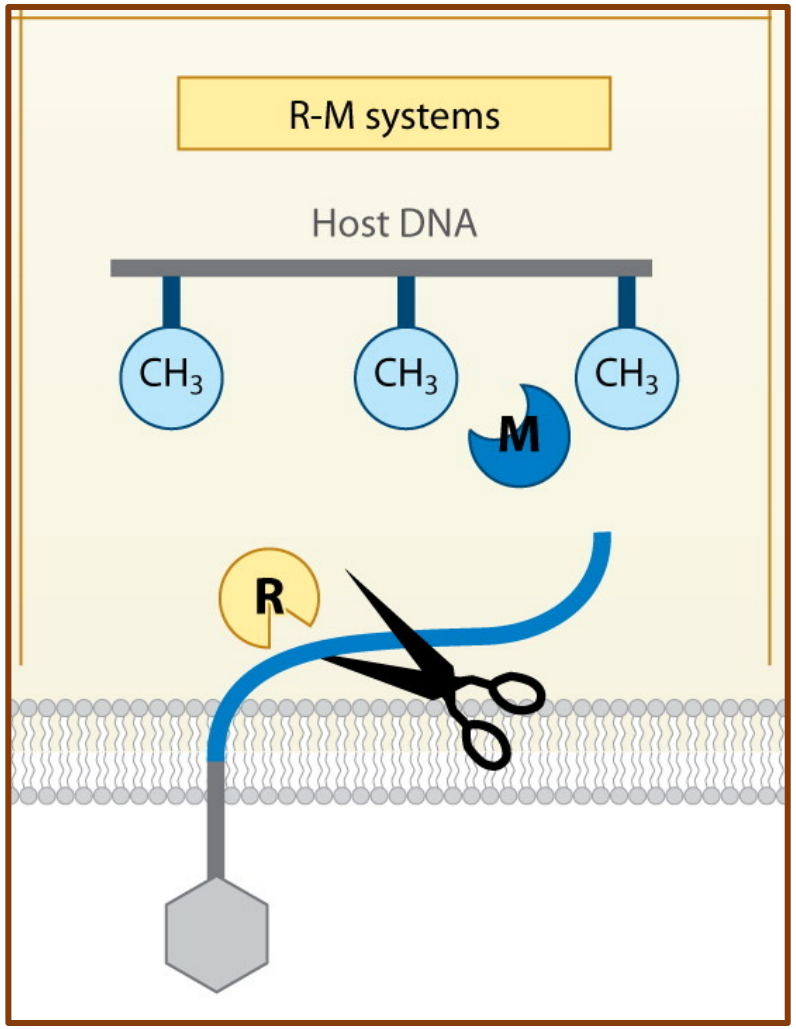
Bacterial defense mechanisms: masking and blocking



1. Mask the entry by coating with polysaccharides
2. Reduce the level of expression of the gene that codes for the receptor
3. Use a protein that blocks the entry of viral DNA

Annu. Rev. Genet. (2012) 46:311

Bacterial defense mechanisms: R-M systems

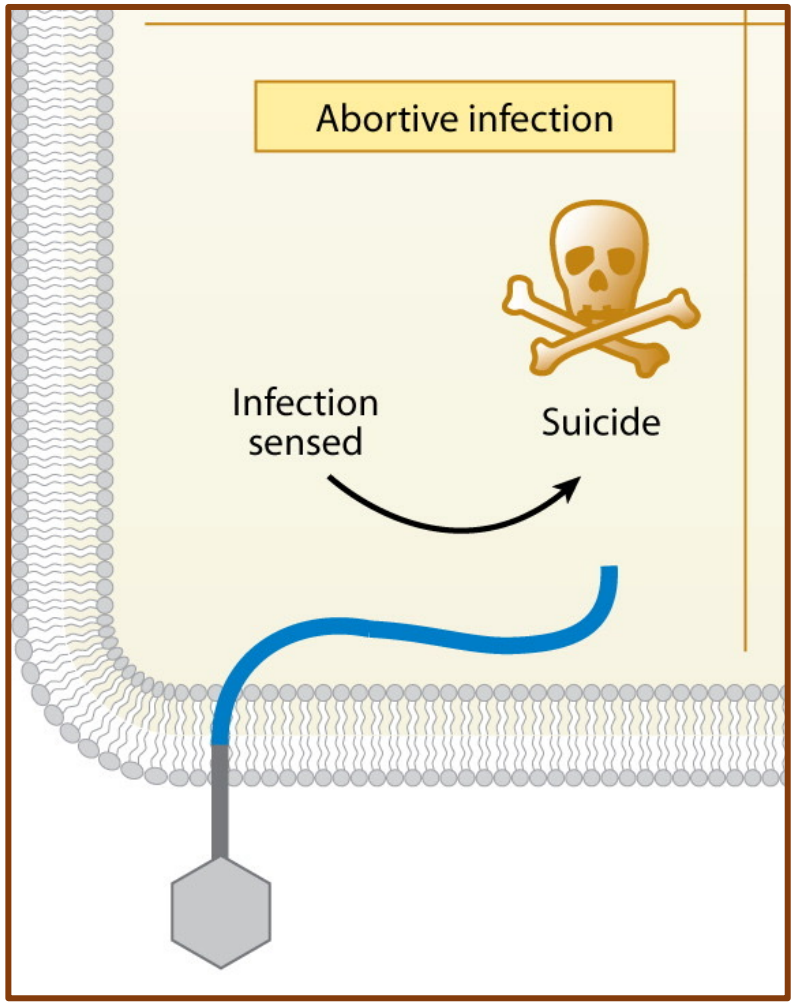


4. Use of Restriction – Modification (R-M) systems

- Add a "protective tag" (= methylation) to host DNA
- This is the modification step
- Release an enzyme that hydrolyzes any DNA which is not "tagged"
- These enzymes are called "restriction" enzymes
- The word restriction is related to how the site for hydrolysis is chosen

Annu. Rev. Genet. (2012) 46:311

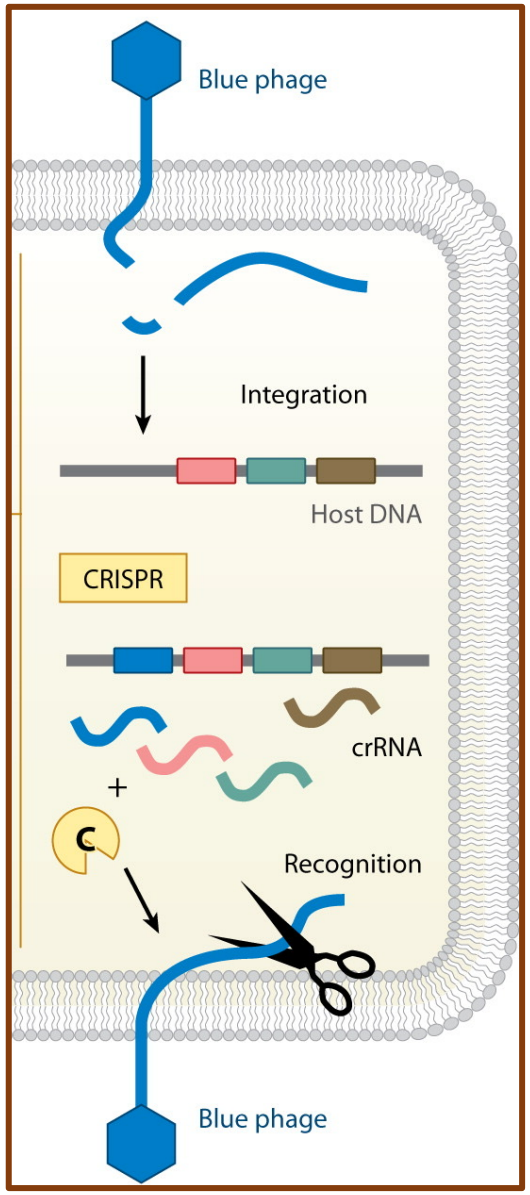
Bacterial defense mechanisms: self-death



5. Trigger "self-death" program
    - Similar to apoptosis
    - This is a sacrifice – protect other bacteria

Annu. Rev. Genet. (2012) 46:311

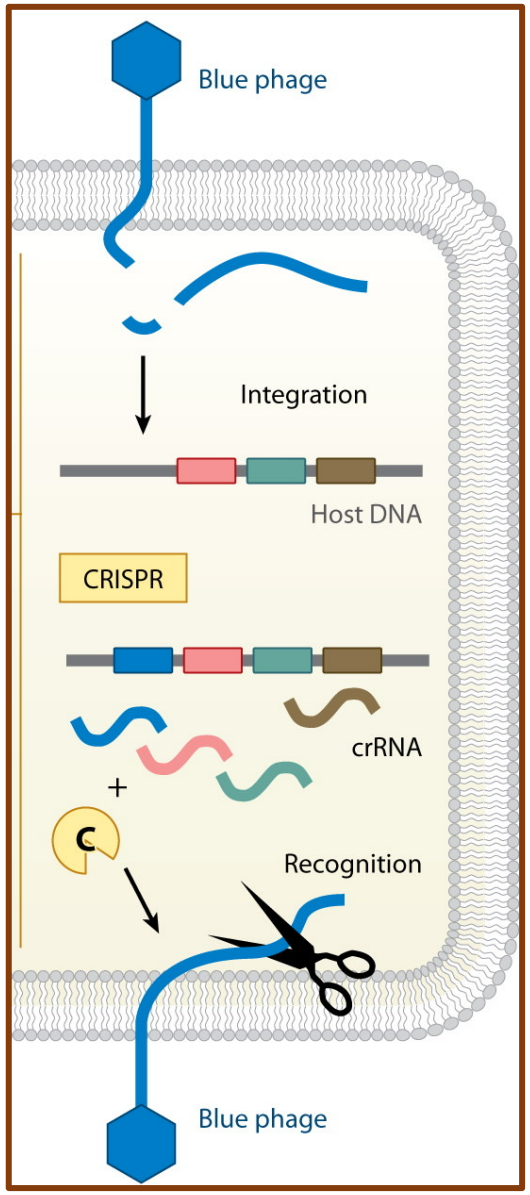
Bacterial defense mechanisms: adaptive immunity



6. Host-derived repeat sequence
   - Pathogen-derived spacer sequence
   - This is a sacrifice – protect other bacteria

Annu. Rev. Genet. (2012) 46:311

Bacterial defense mechanisms: adaptive immunity



6. Three components

   i. Adaptation – integrate a new spacer (from a pathogen) into the CRISPR array

   ii. Expression – express the entire CRISPR array and process to generate individual spacers

   iii. Resistance – individual spacers guide CRISPR-associated systems to the pathogen and mark it for degradation

Annu. Rev. Genet. (2012) 46:311

https://www.nobelprize.org/prizes/chemistry/2020/summary/ 80%

Chemistry | The Nobel Prize in Chemistry 2020 | Summary

The Nobel Prize in Chemistry 2020

Emmanuelle Charpentier
Jennifer A. Doudna

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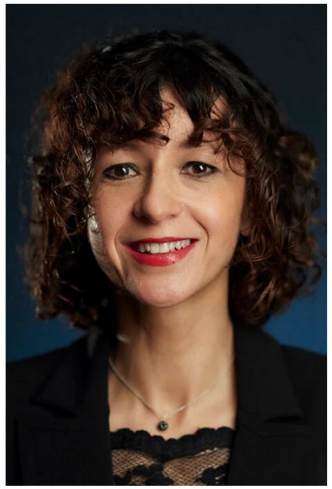
The Nobel Prize in Chemistry 2020



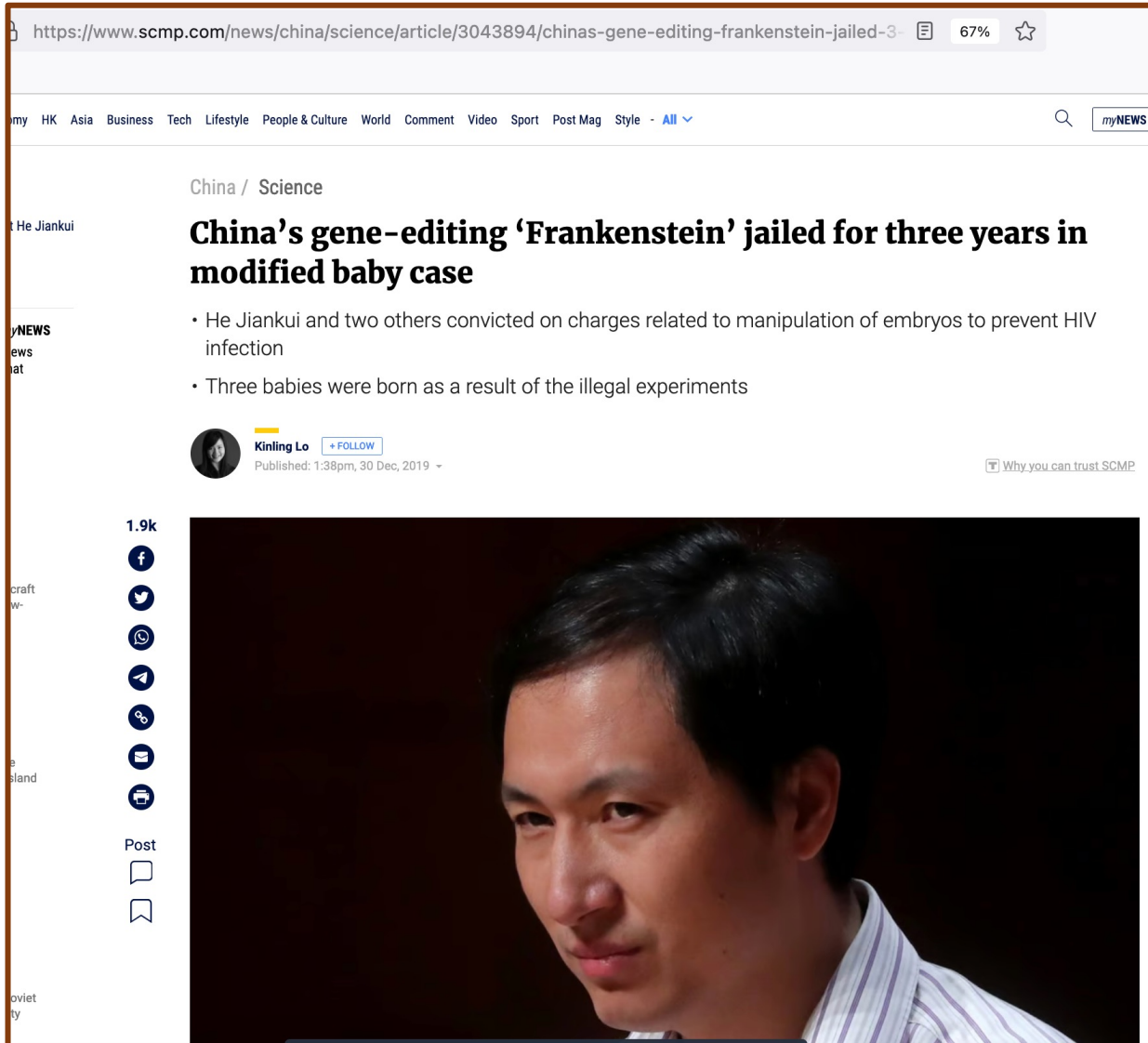
© Nobel Prize Outreach. Photo: Bernhard Ludewig
Emmanuelle Charpentier
Prize share: 1/2

© Nobel Prize Outreach. Photo: Brittany Hosea-Small
Jennifer A. Doudna
Prize share: 1/2

The Nobel Prize in Chemistry 2020 was awarded jointly to Emmanuelle Charpentier and Jennifer A. Doudna "for the development of a method for genome editing"

Applications of CRISPR-Cas system

- Gene editing in diseases (cancer)
- Diagnostic kits (Covid)
- Replacing mosquitoes in the wild with genetically modified mosquitoes that are resistant to diseases
- Genetic manipulation of crop species
- Many, many others….



Lectures 11 to 21

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