Preparing for the Battle

Antibiotic Resistance

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News

ANTIBIOTIC RESISTANCE – A CAL GLOBAL ACTION

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6 April 2011 Last updated at 22:57 ET

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Europe 'losing' superbugs battle

ections have reached
and now outstrip our
th existing drugs,
ts are warning.

r 25,000 people die of
are able to outsmart

Analysis: Humans Losing War Against Antibiotic-Resistant 'Superbugs'

A prominent researcher says humans have "fallen way behind" in the war against superbugs.

ting superbugs

orial Board, Published: October 7, 2012

the most urgent global public health problems is the
g capability of bacteria to resist antibiotic drugs. The crisis
icrobial resistance is particularly acute in hospitals, where
s able to resist multiple drugs have spawned. More than 70
f the bacteria that cause hospital-related infections are
esistant to at least one type of antibacterial drug.

Battle Plan

1. Understand the enemy
2. Attack and counterattack
3. Intelligence from the frontlines
4. Join the fight

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Battle Plan

1. **Understand the enemy**
   - Meet your microbes
2. Attack and counterattack
3. Intelligence from the frontlines
4. Join the fight

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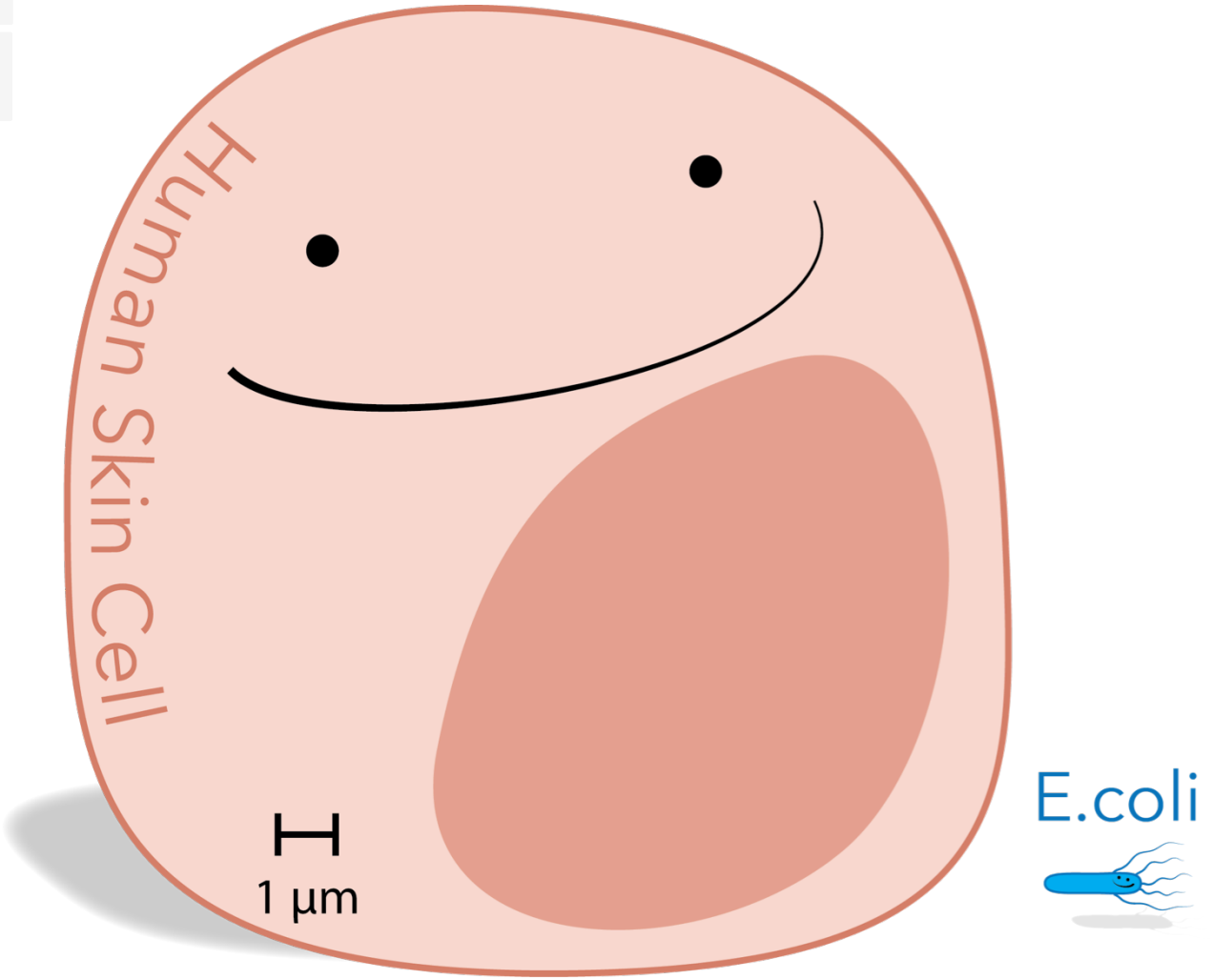
Bacteria are very small



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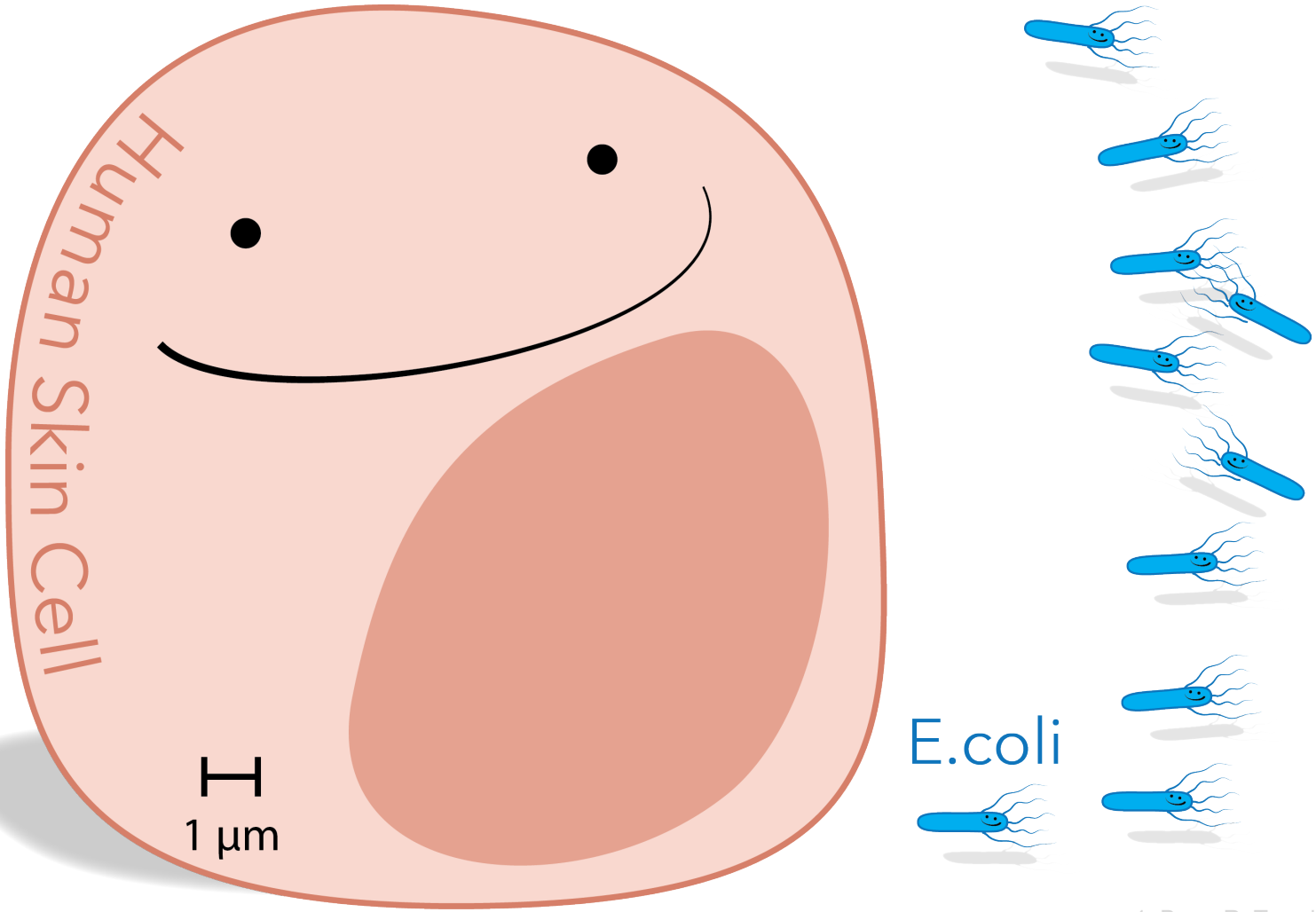
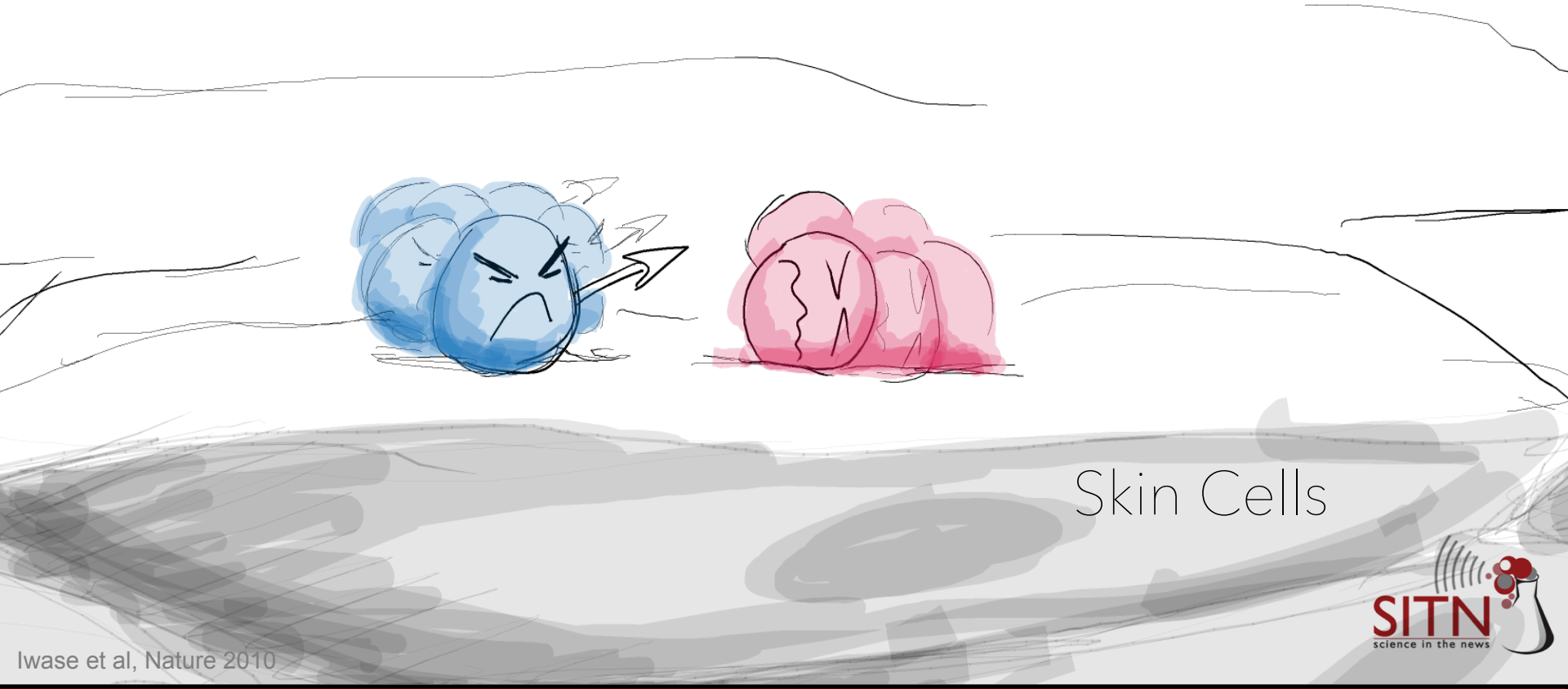
They outnumber us
>10:1 on our bodies



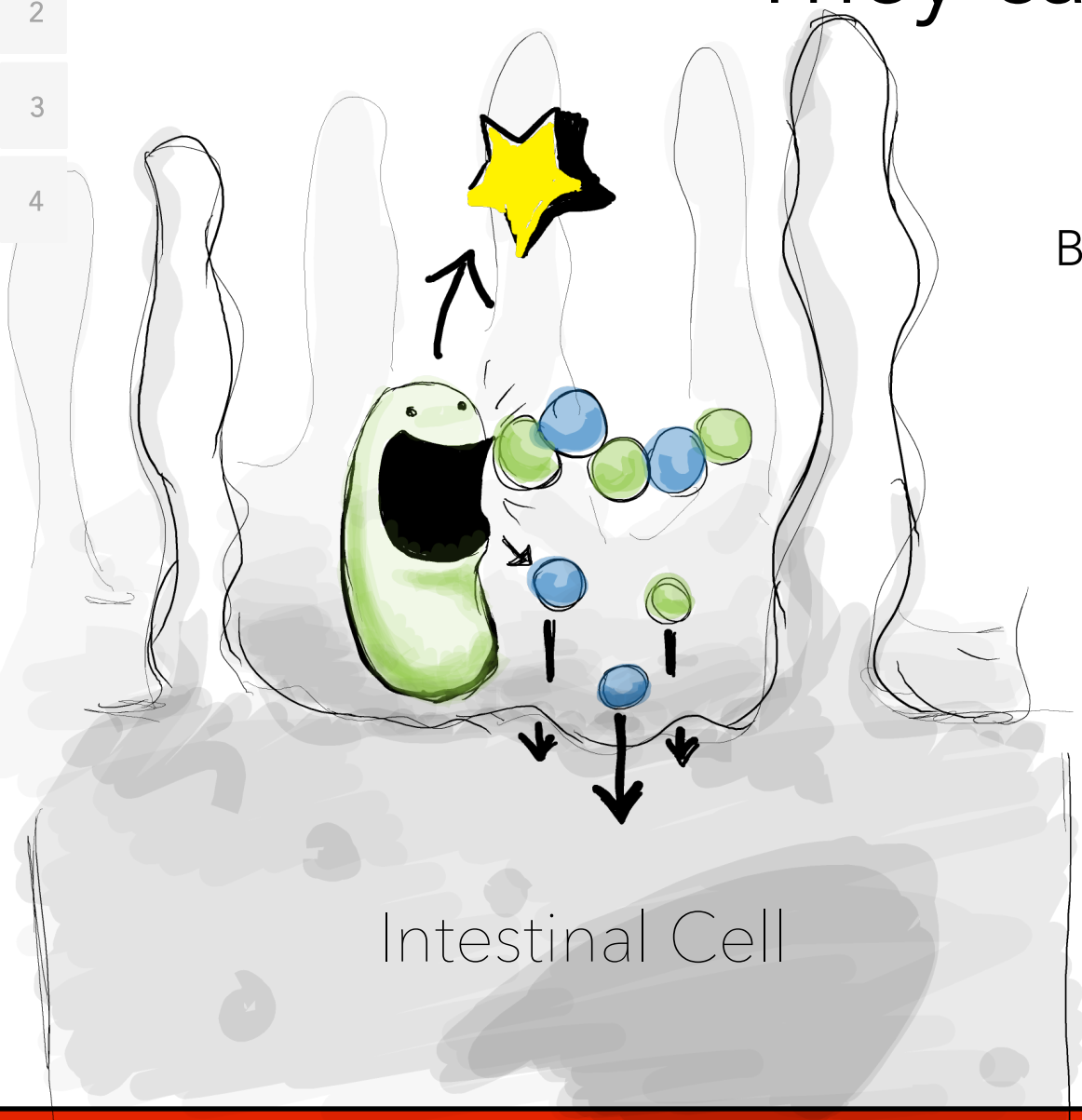
1. Berg, R. Trends in Microbiology, 1996

They can be **helpful**

S. epidermidis inhibits *S. aureus*[1] colonization



They can be **helpful**



Bacteria in the large intestine help us digest food, and produce useful compounds such as vitamins

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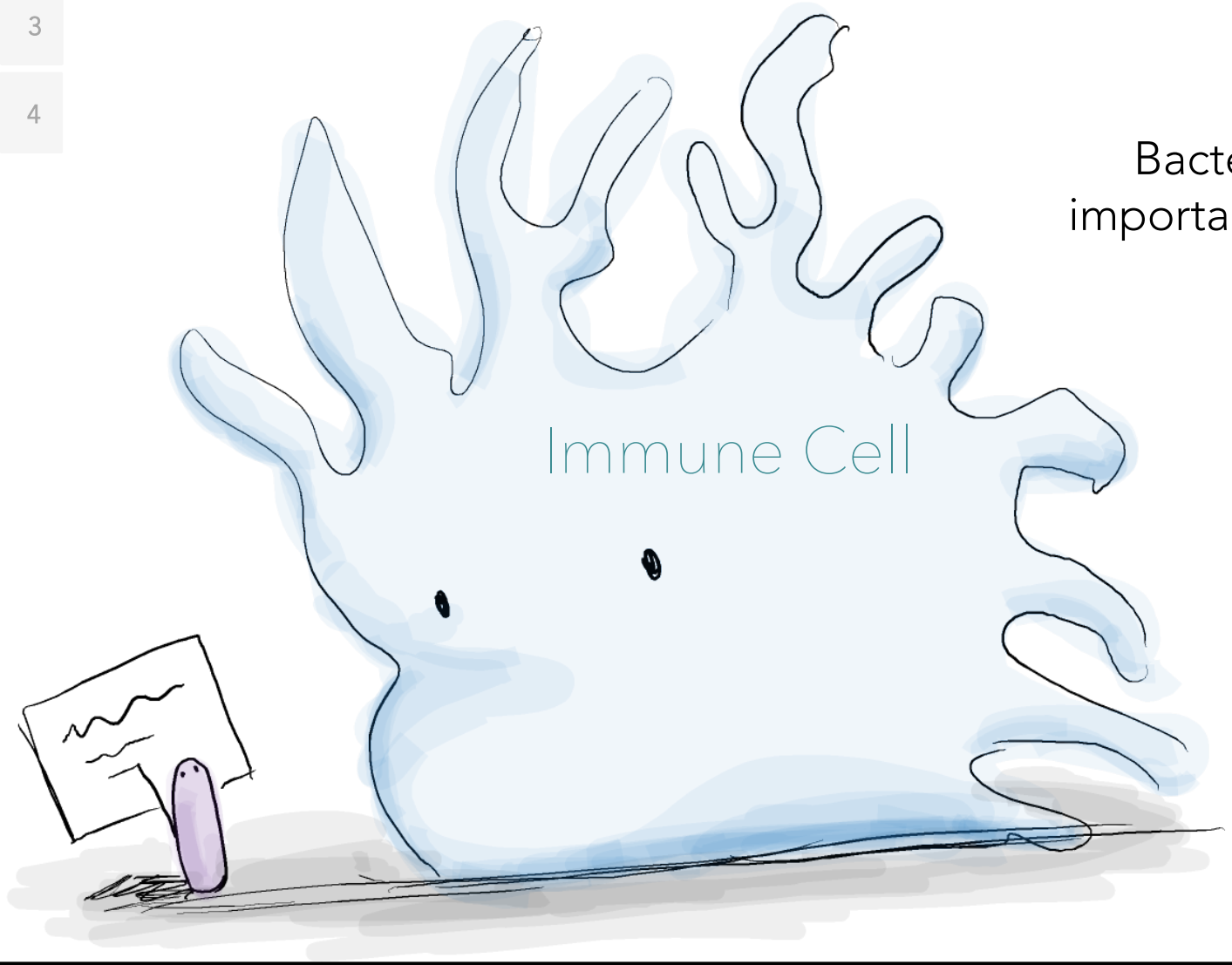
They can be **helpful**



Bacteria in the gut are important for training the immune system

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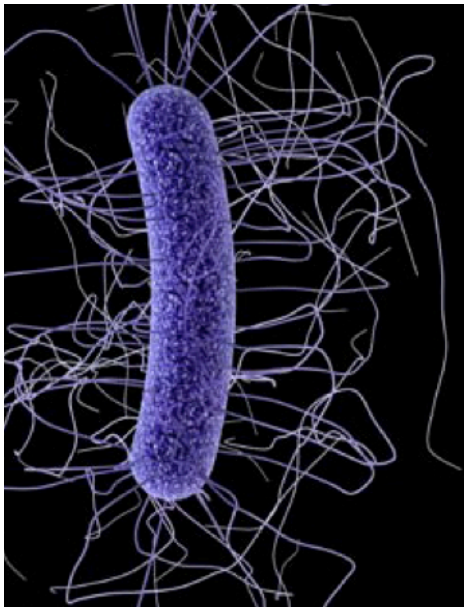
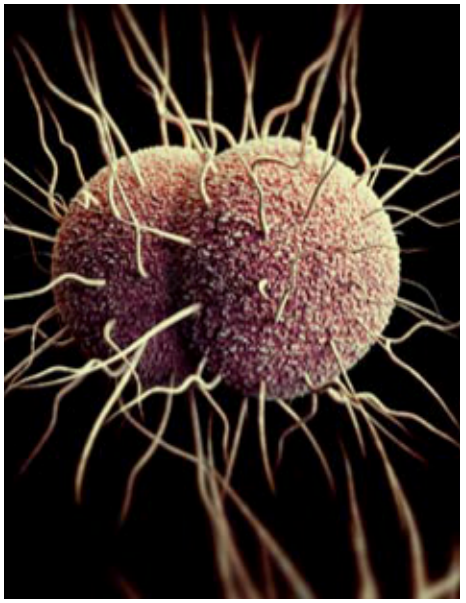
Not all bacteria are good



CLOSTRIDIUM DIFFICILE
250,000 Infections/ year

ENTEROBACTERIACEAE
9,000 Infections/year



NEISSERIA GONORRHOEAE
246,000 Infections/year

THREAT LEVEL
URGENT

This bacteria is an immediate public health threat that requires urgent and aggressive action.

Graphics and data adapted from CDC Report on Antibiotic Resistance, 2013

Not all bacteria are good

Each year, antibiotic resistant microbes cause at least

2,049,442 illnesses

23,000 deaths

Graphics and data adapted from CDC Report on Antibiotic Resistance, 2013

Battle Plan

1. Understanding the enemy
2. **Attack and counterattack**
   - History of antibiotics
   - How antibiotics work
   - What causes antibiotic resistance?
3. Intelligence from the frontlines
4. Join the fight

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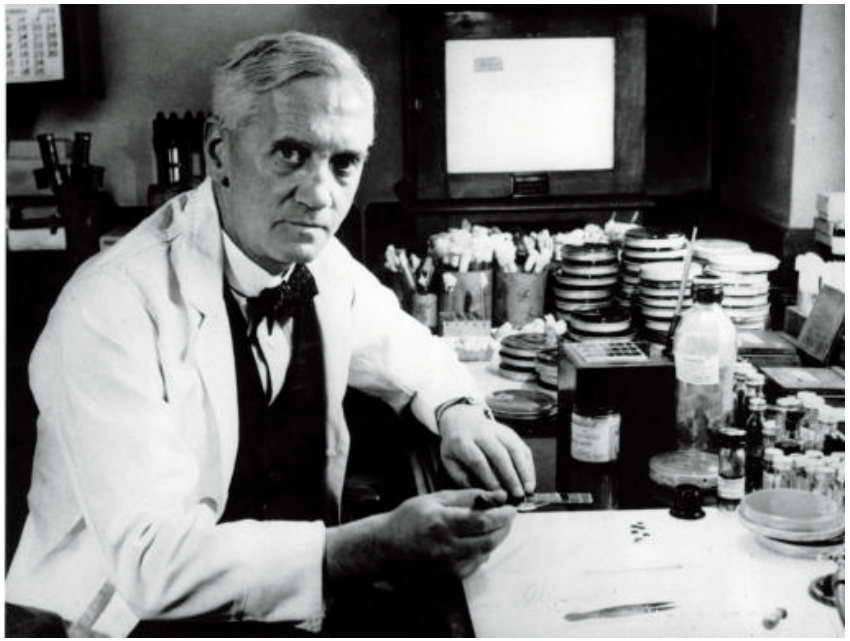
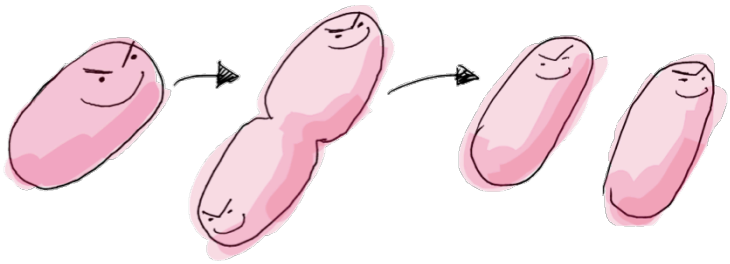
Antibiotics revolutionized medicine



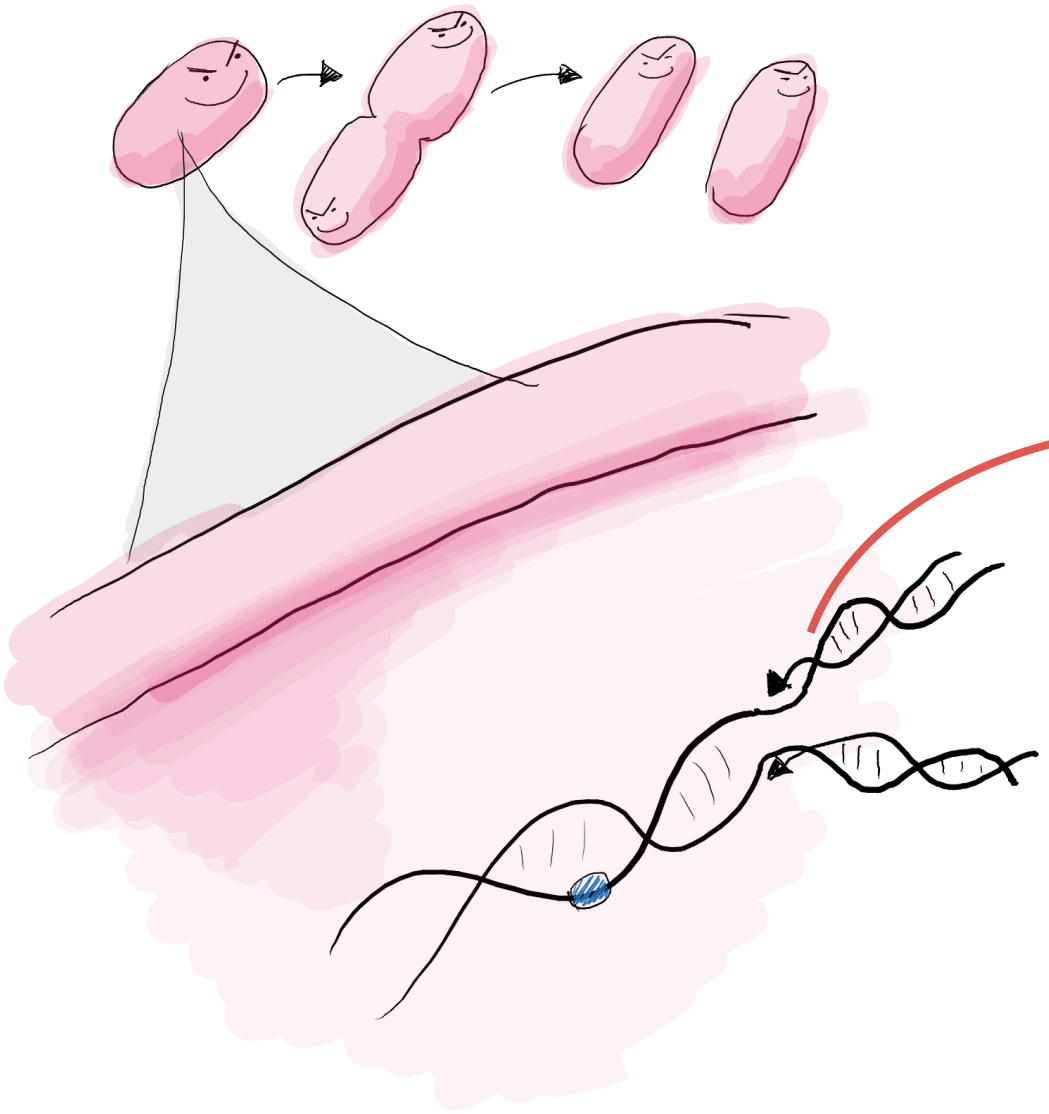
Alexander Flemming discovered Penicillin in 1928

Photo: http://en.wikipedia.org/wiki/Penicillin
Plate image adapted from: http://www.smccd.edu/accounts/case/graphics/staph.jpeg

Antibiotics target critical processes in the cell

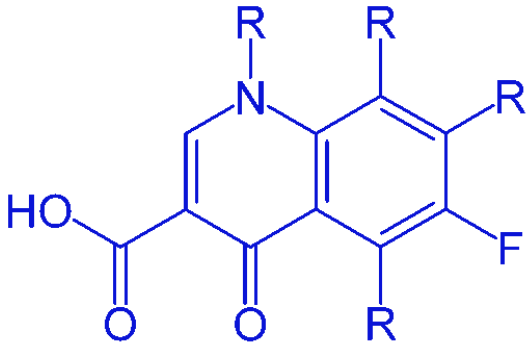


Antibiotics target critical processes in the cell



DNA Replication

Fluoroquinolones



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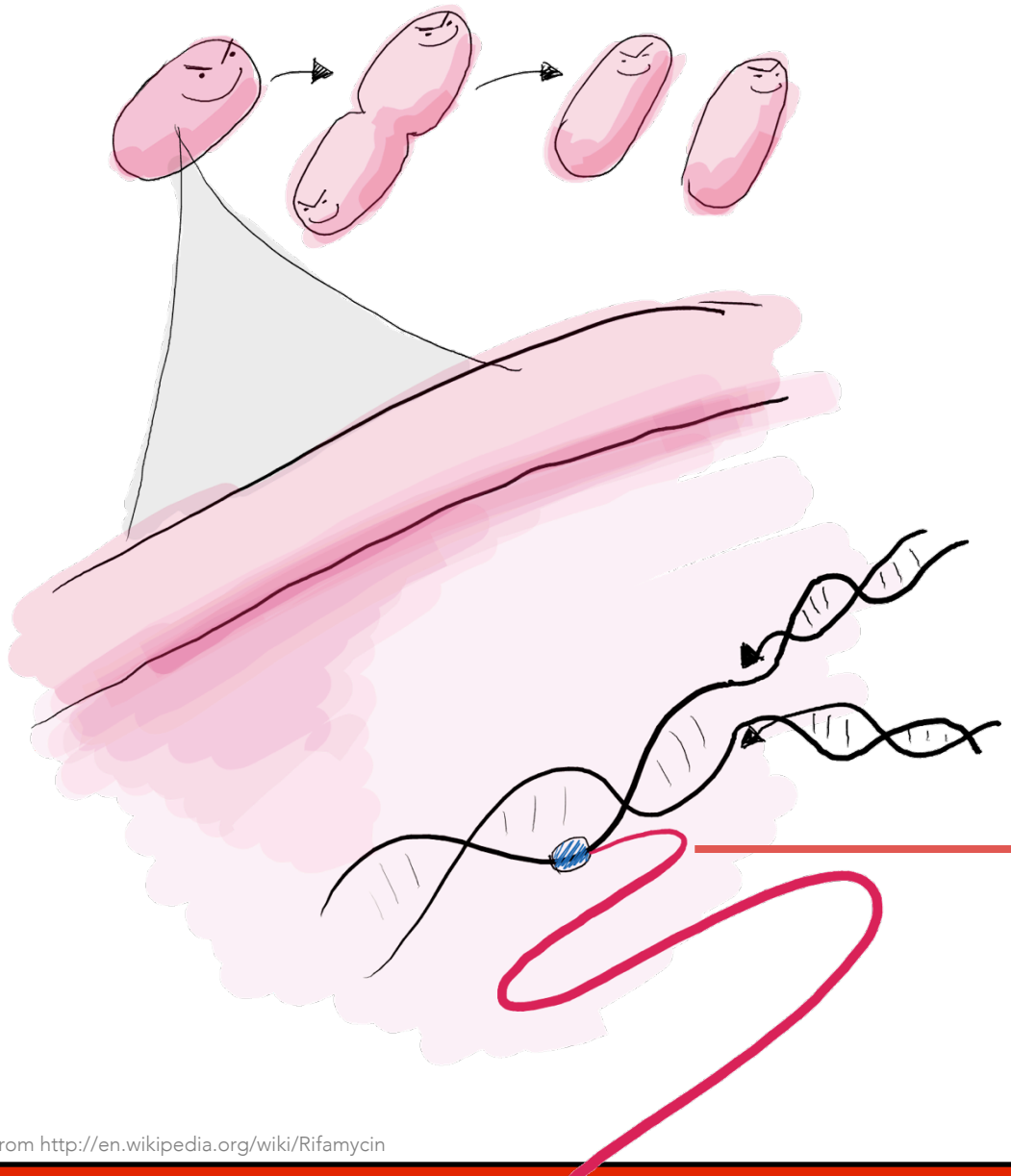
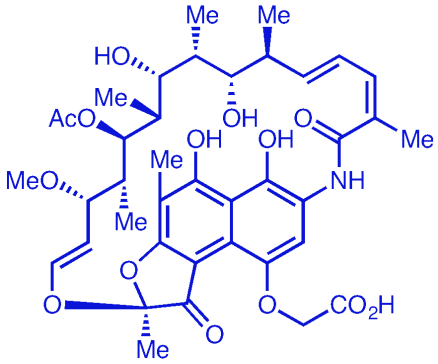
Adapted from http://en.wikipedia.org/wiki/Quinolone

Antibiotics target critical processes in the cell



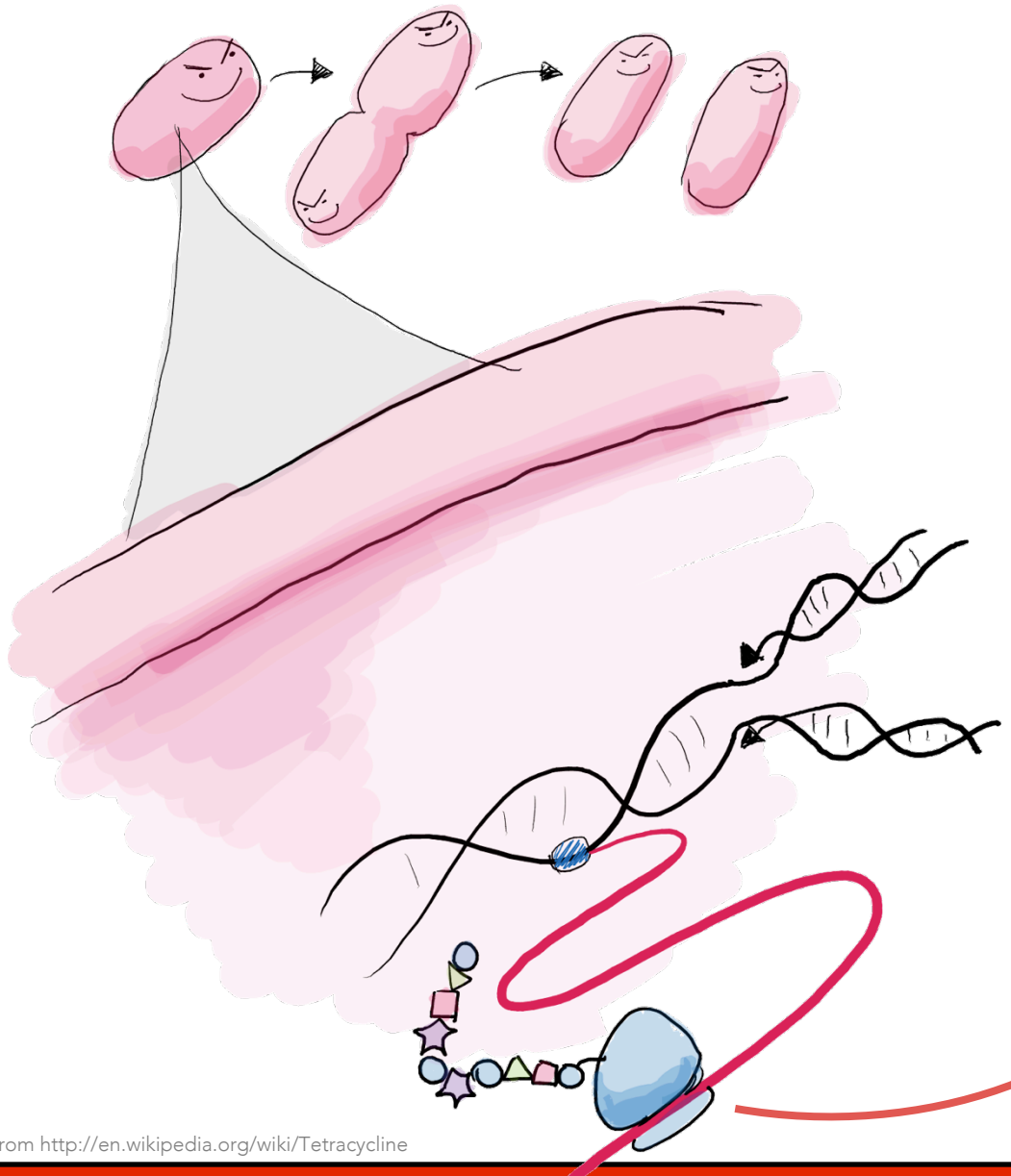


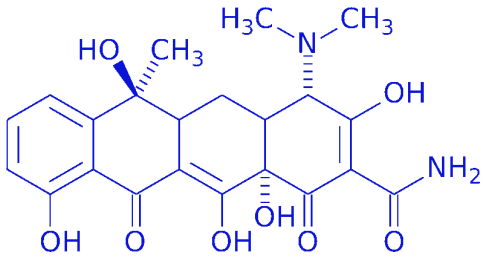
Rifamycin

RNA Transcription

Adapted from http://en.wikipedia.org/wiki/Rifamycin

Antibiotics target critical processes in the cell





Tetracycline

Protein Synthesis

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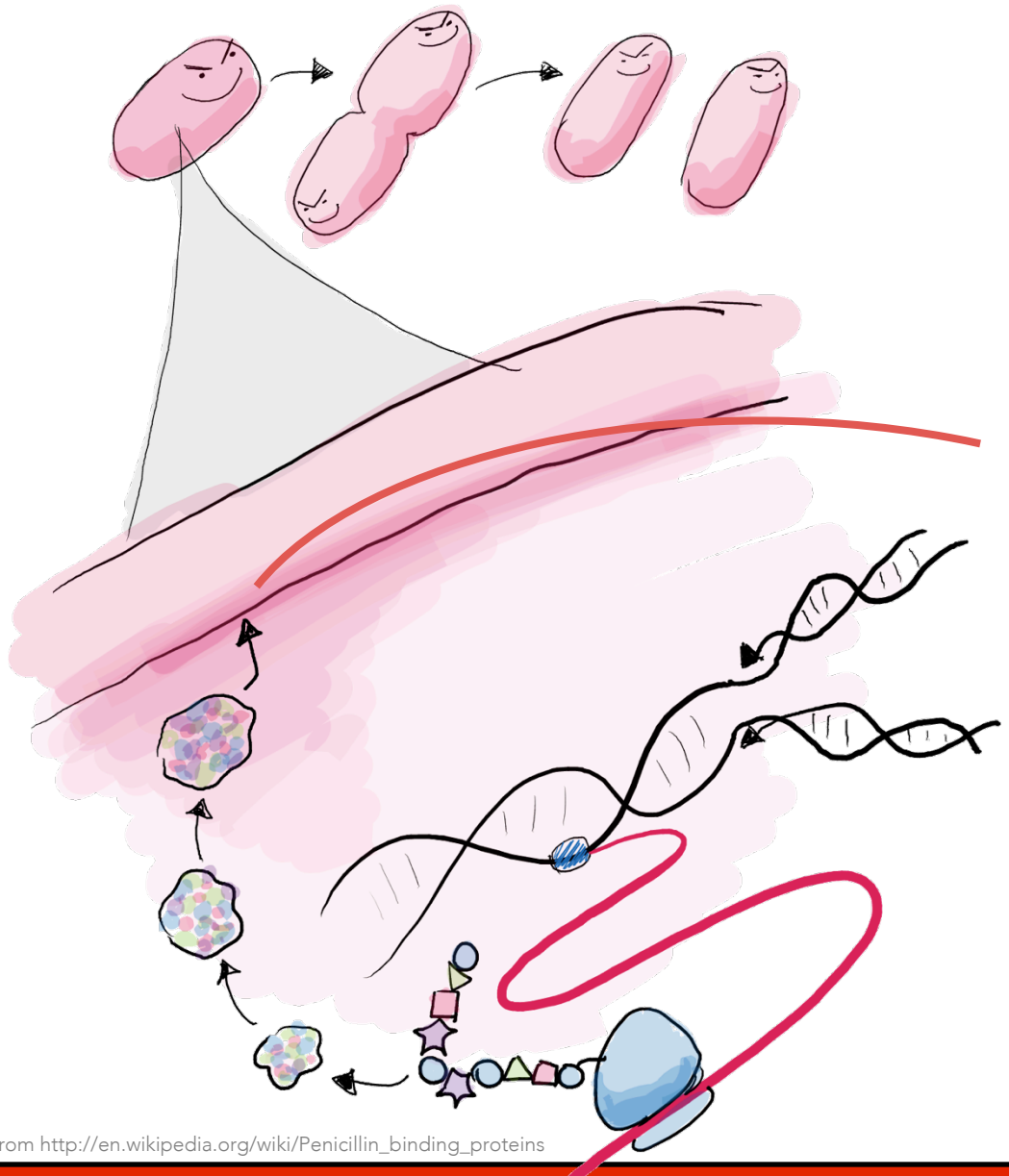
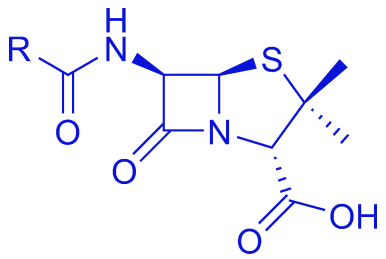
Adapted from http://en.wikipedia.org/wiki/Tetracycline

Antibiotics target critical processes in the cell





Penicillin

Cell Wall Synthesis

Adapted from http://en.wikipedia.org/wiki/Penicillin_binding_proteins

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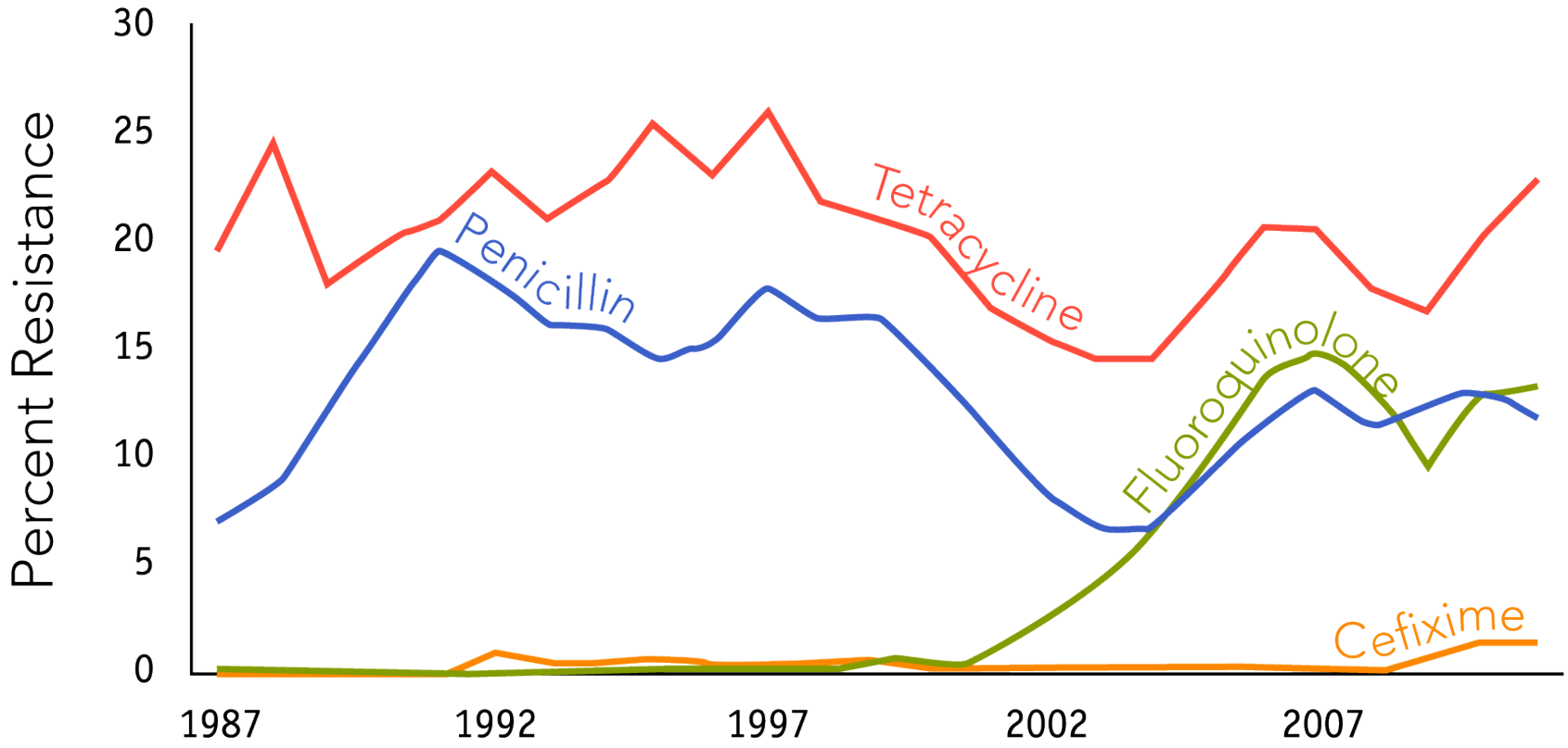
http://en.wikipedia.org/wiki/Antibiotic_resistance_in_gonorrhea

Our antibiotics are losing effectiveness against *Neisseria Gonorrhoeae*



CDC Report on antibiotic resistance, 2013

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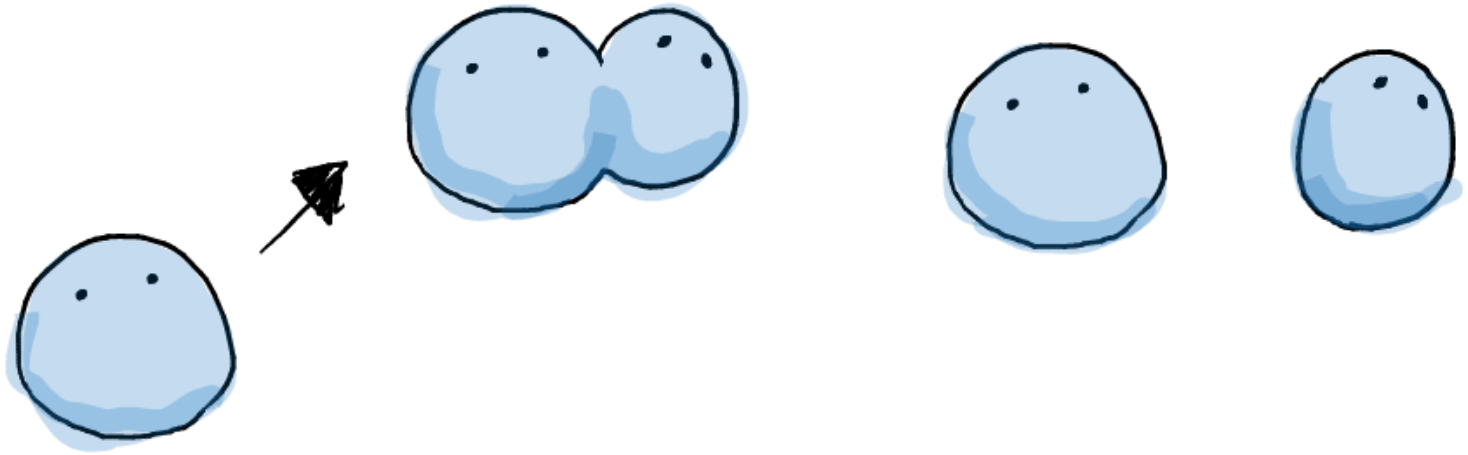
How did this happen?

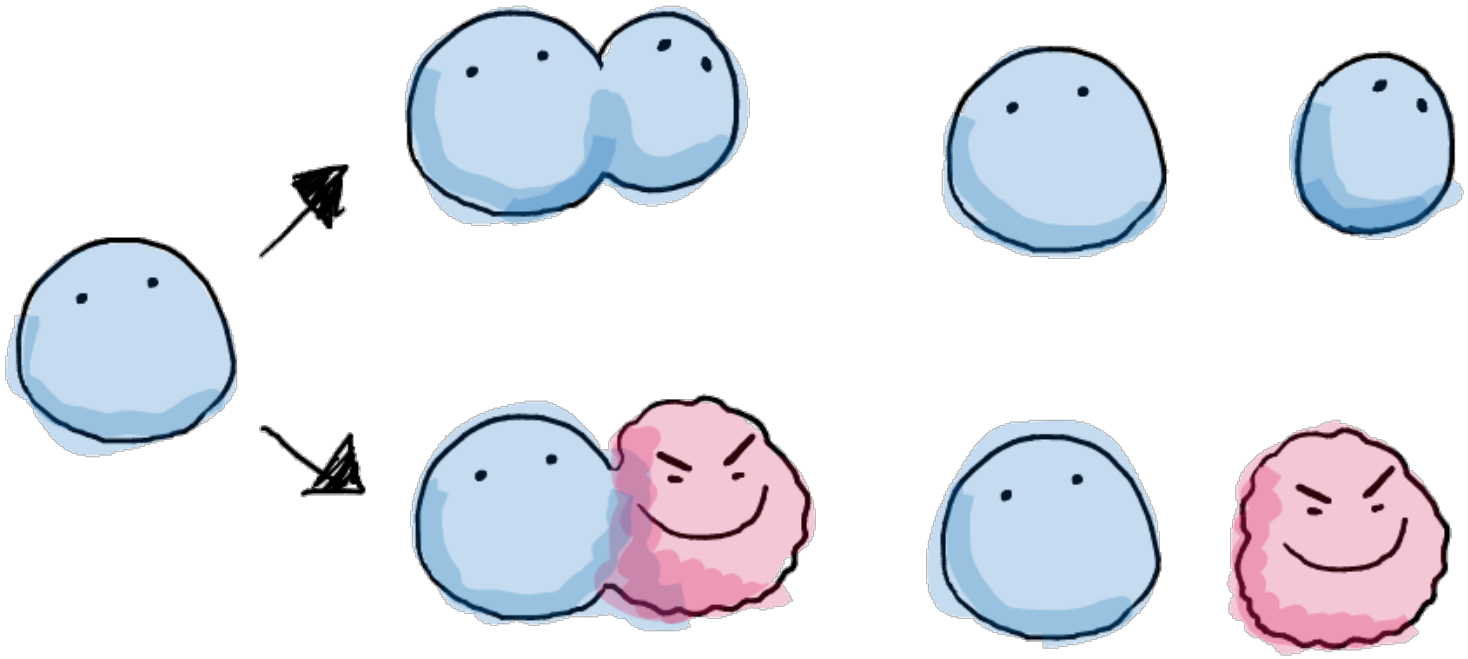
How did this happen?

EVOLUTION

Replication errors create diversity within a population

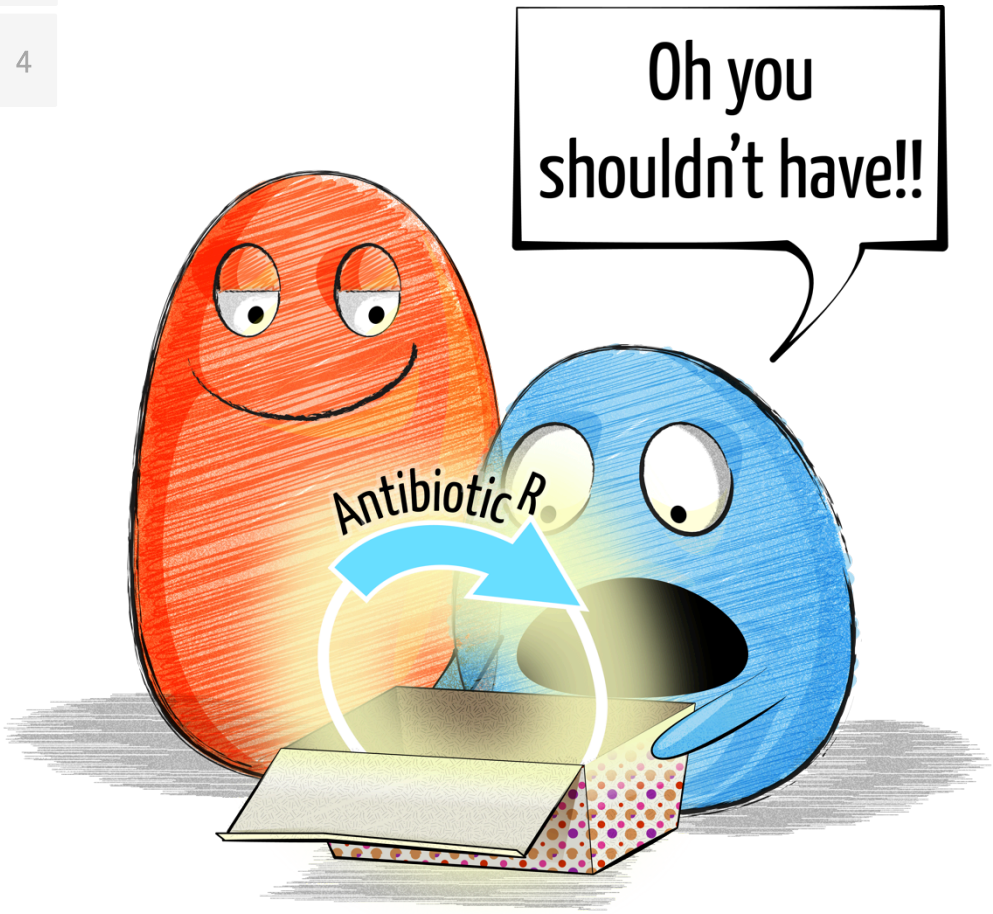


Replication errors create diversity within a population



Resistant mutant

Bacteria "share" genes via horizontal gene transfer



Many important genes for antibiotic resistance can be found on

PLASMIDS

mobile DNA elements that can easily jump between species

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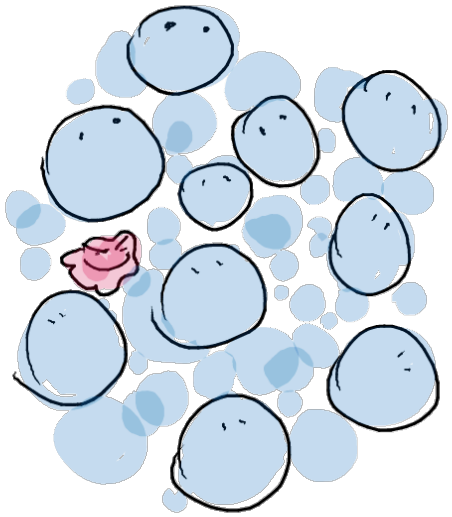
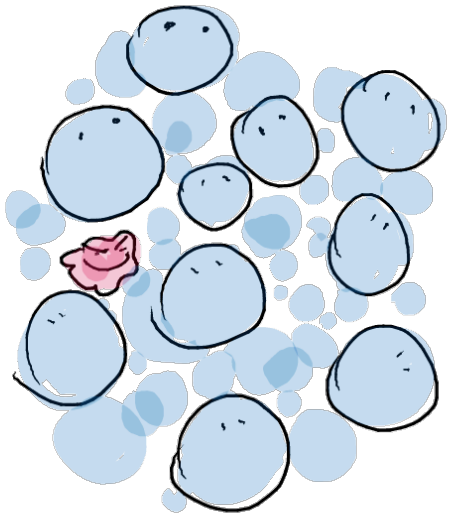
Antibiotics kill off the sensitive cells, allowing resistant cells to take over



Initial **sensitive** population with rare **resistant** cell

Antibiotics kill off the sensitive cells, allowing resistant cells to take over



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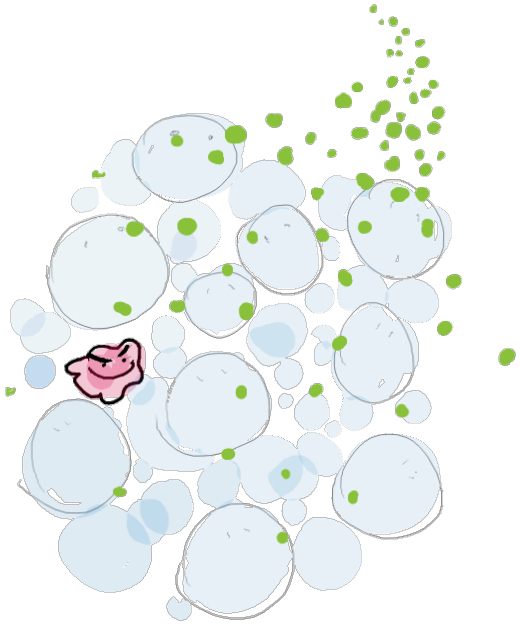

Antibiotics kill **sensitive** cells, but not **resistant** cells

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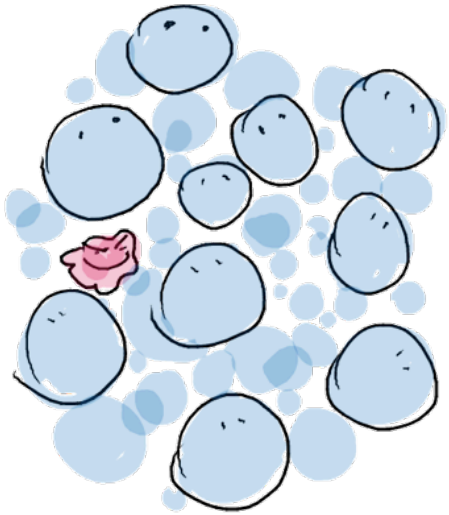
Antibiotics kill off the sensitive cells, allowing resistant cells to take over



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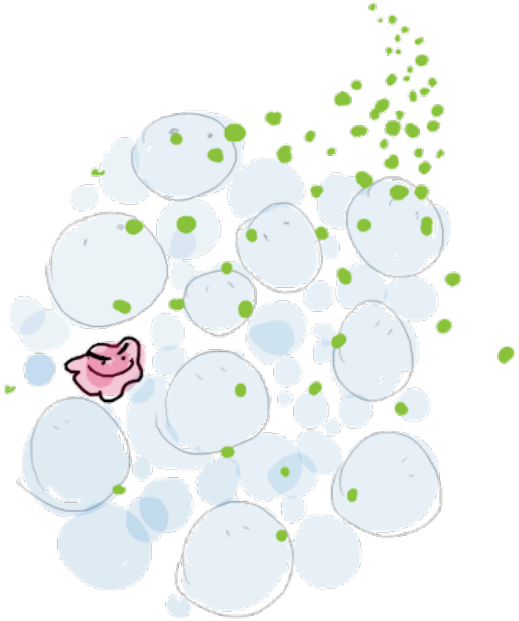
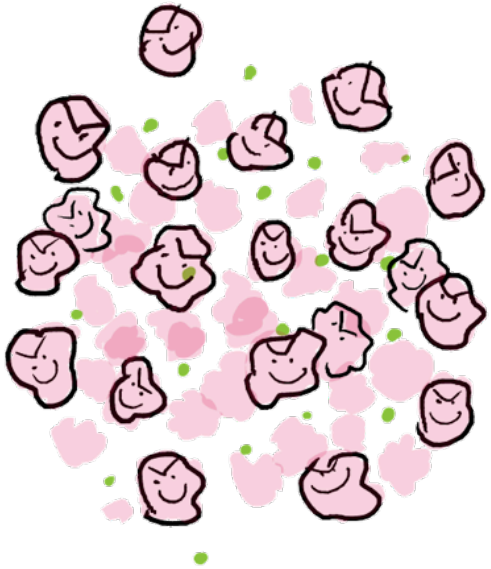


Antibiotics kill **sensitive** cells, but not **resistant** cells



Resistant cells take over the population

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Questions?

Battle Plan

1. Understanding the enemy
2. Attack and counterattack
3. **Intelligence from the frontlines**
   - Better Stewardship
   - New antibiotics
   - Diagnostics
4. Join the fight

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Conserve what we have left: better Stewardship

~90% of antibiotics used in the US are for agricultural production[1]

Antibiotics used as growth promoters in livestock production:

- Bambermycin
- Lasalocid
- Monensin
- Salinomycin
- Virginiamycin
- Bacitracin

1. Union of Concerned Scientists. 2001
2. Reinhardt, Merck Veterinary Manual, 2012

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Conserve what we have left: better Stewardship

Antibiotic use in agriculture has been shown to generate

resistant bacteria

which can then **spread to humans**

In 2013, the FDA imposed voluntary guidelines for phasing out certain antibiotics in livestock feed

Wegener, Curr Opinion in Microbiol. 2003
Knox, npr.org, 2012
Carlet, Antimicrobial Resistance and Infectino Control, 2012

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Conserve what we have left: better Stewardship

As much as

50%

of antibiotics prescriptions are unnecessary or misused

Hospitals are working to:

- Make sure to culture bacteria for identification before starting antibiotic treatment
- Give clear dosage and duration instructions
- Reassess effectiveness in 2-3 days

CDC Report on antibiotic resistance, 2013

Battle Plan

1. Understanding the enemy
2. Attack and counterattack
3. **Intelligence from the frontlines**
   - Better Stewardship
   - New antibiotics
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4. Join the fight

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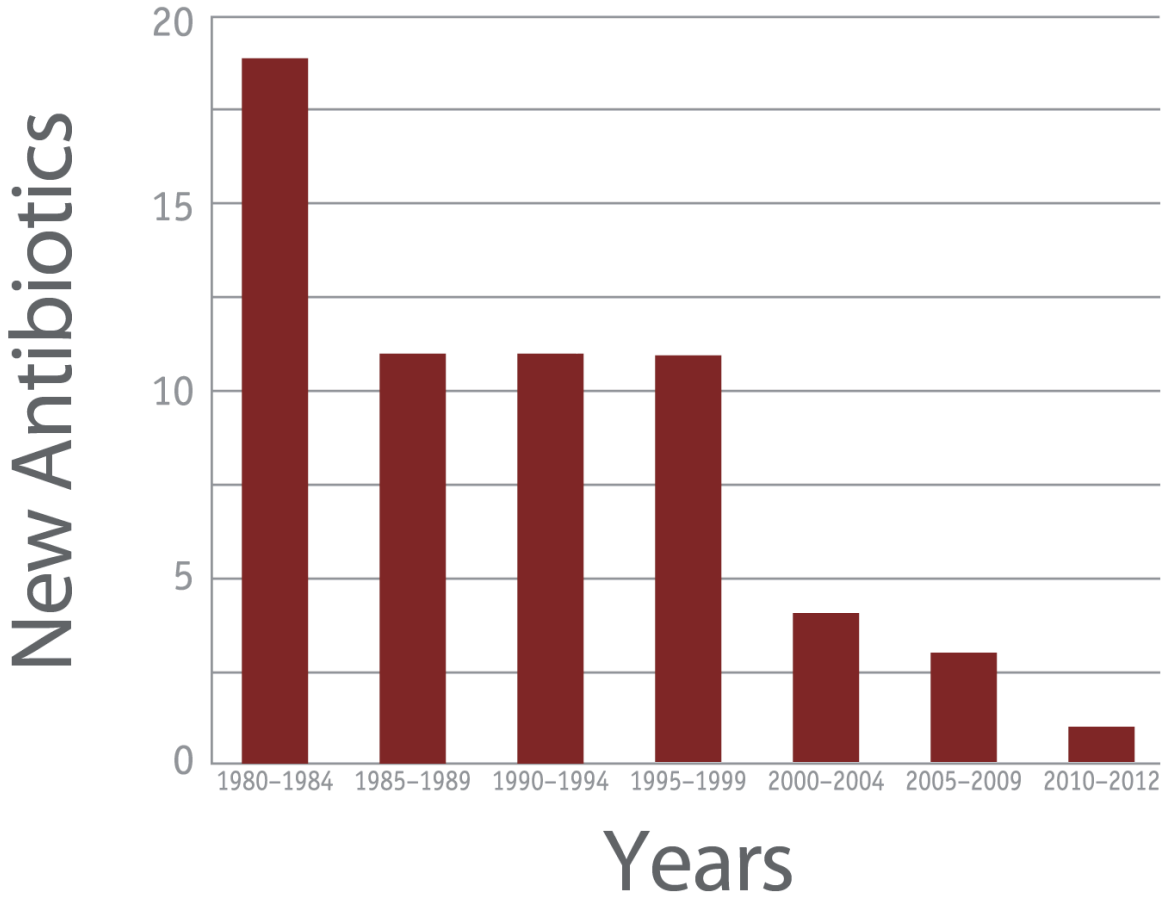
We are discovering fewer and fewer antibiotics



Graphics and data adapted from CDC Report on Antibiotic Resistance, 2013

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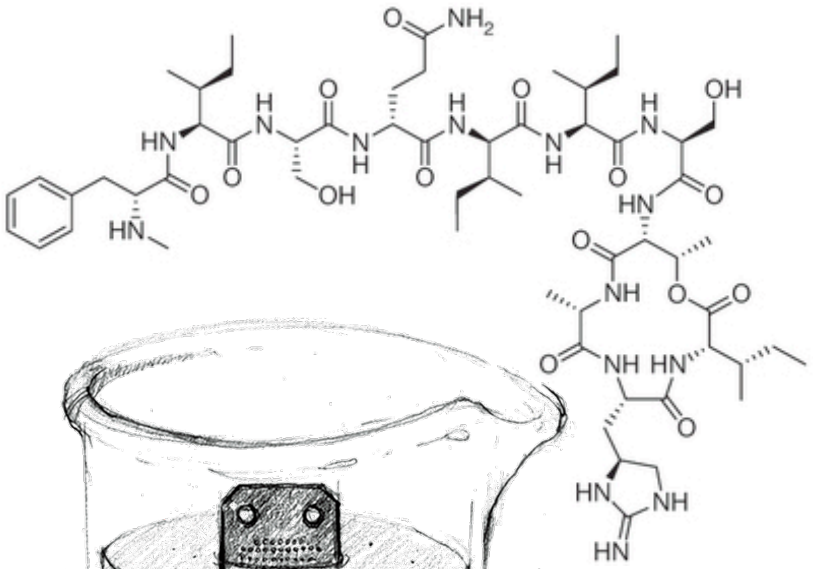
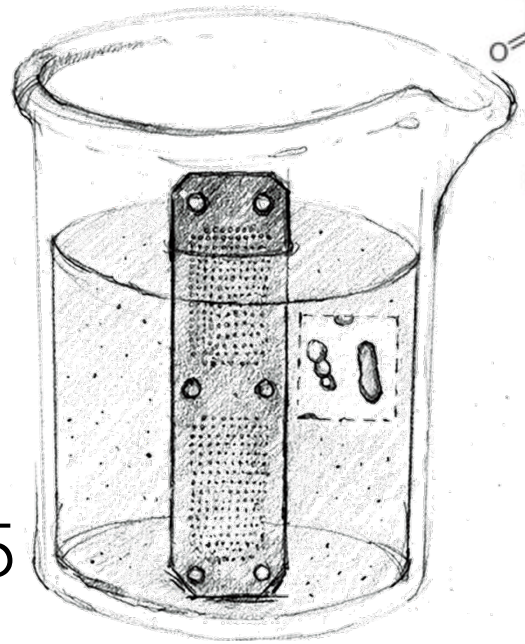
Sorting through dirt for new antibiotics

- Through millenia of microbial warfare, soil bacteria have developed the majority of antibiotics
- Many microbes need "support" from the soil community to grow and are difficult to grow in the laboratory
- The "iChip", introduced in 2010, can grow previously uncultured bacteria



Teixobactin, 2015



Nichols et al, ACM, 2010
Ling et al, Nature, 2015

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New diagnostics for fast detection

- Many pathogens grow very slowly in the lab
- Knowing what antibiotics they are resistant to is time-sensitive
  - Don't waste time using the wrong antibiotics
  - Don't allow further resistance to develop
- New methods for fast diagnosis based on detection of microbial DNA can significantly speed up this process

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Battle Plan

1. Understanding the enemy
2. Attack and counterattack
3. Intelligence from the frontlines
4. **Join the fight**

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The CDC recommends:

Tactic #1

Prevent infections by practicing good hand hygiene

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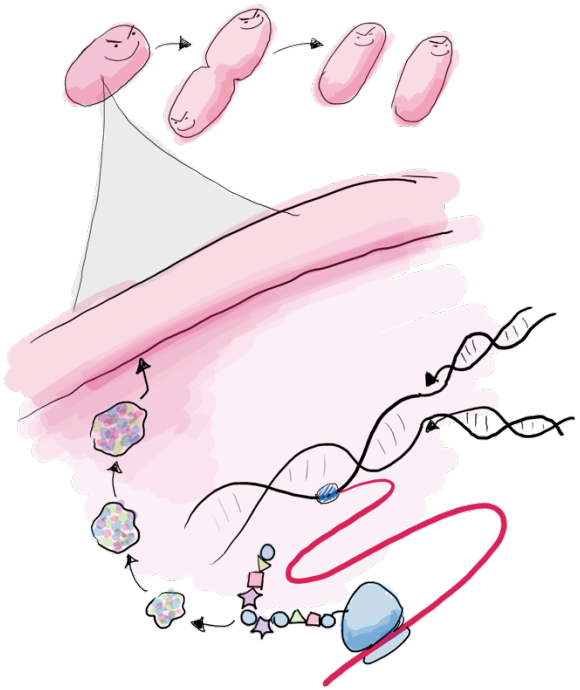
The CDC recommends:

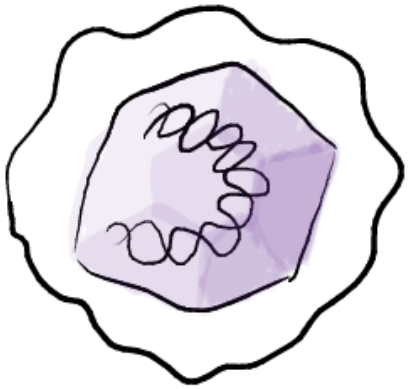
Tactic #2

DO NOT ask for antibiotics when your doctor thinks you do not need them (ex. viral infections)

Antibiotics cannot kill viruses



Bacteria: complex cell with DNA replication, transcription, translation



Virus: a packet of DNA

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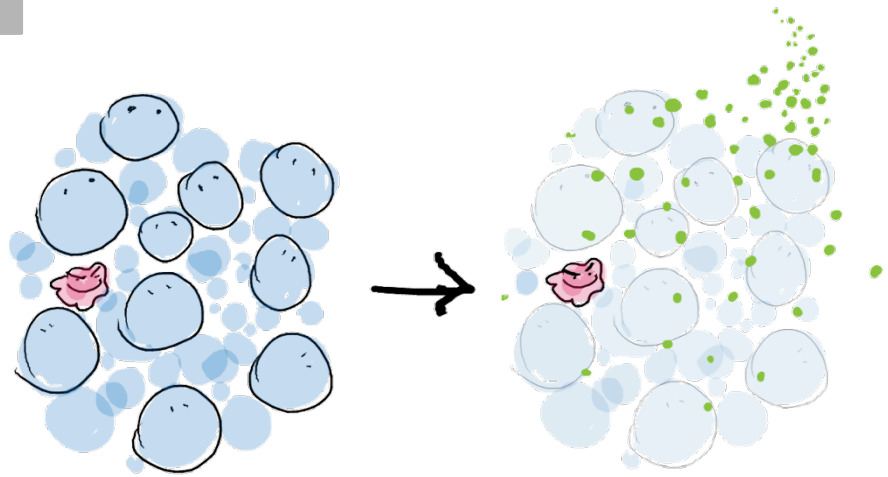
The CDC recommends:

Tactic #3

Always use antibiotics for full duration prescribed

What doesn't kill you makes you more resistant



Initial **sensitive** population with rare **resistant** cell

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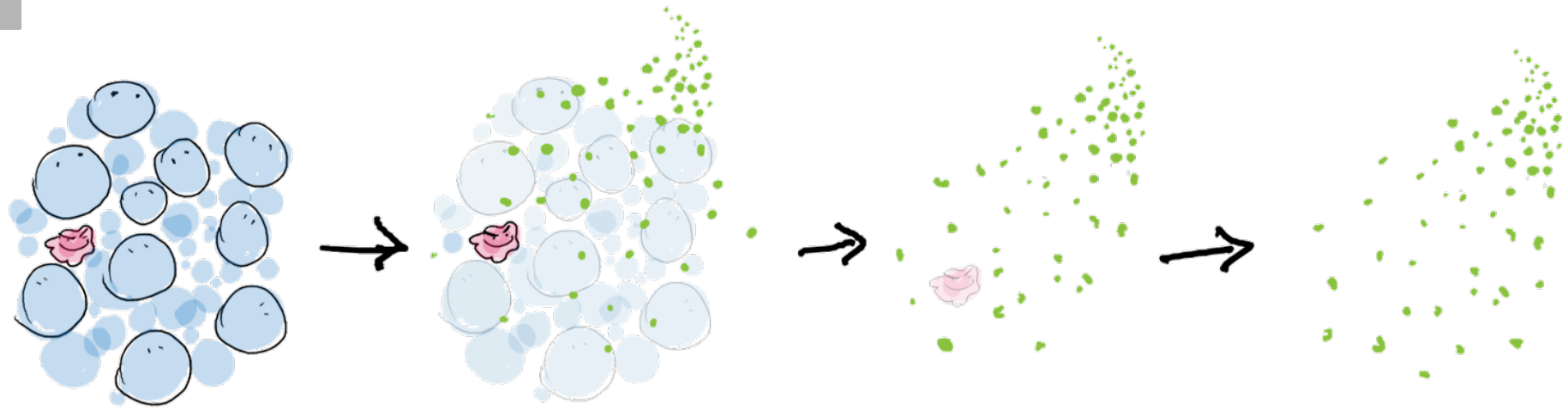
What doesn't kill you makes you more resistant



Initial **sensitive** population with rare **resistant** cell

Antibiotics kill **sensitive** cells quickly, and **slightly resistant** cells slowly. Therapy eventually eradicates all cells.

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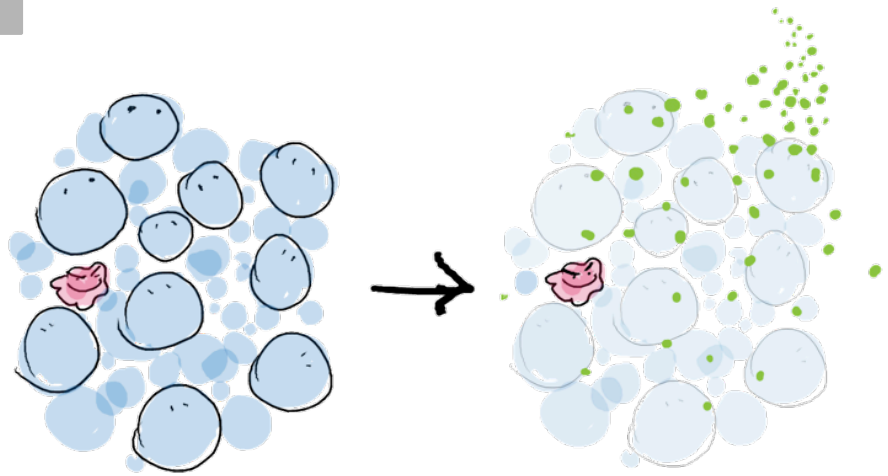
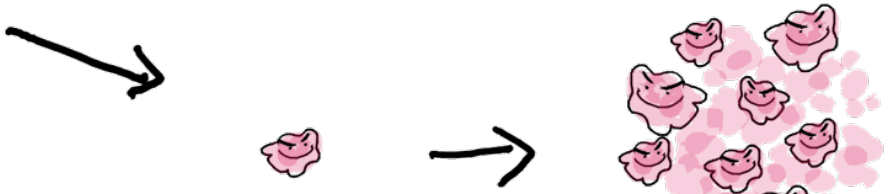
What doesn't kill you makes you more resistant



Premature end of **antibiotics** therapy allow **slightly resistant** cells to take over, and possibly gain increased resistance



Initial **sensitive** population with rare **resistant** cell

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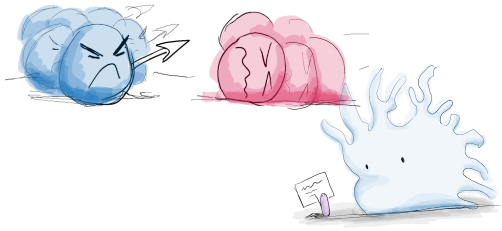
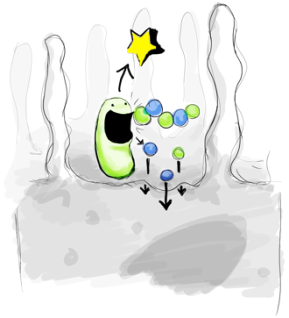
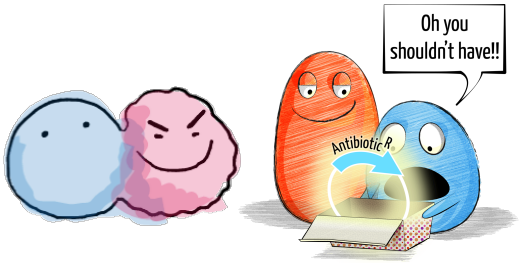
Battle Plan

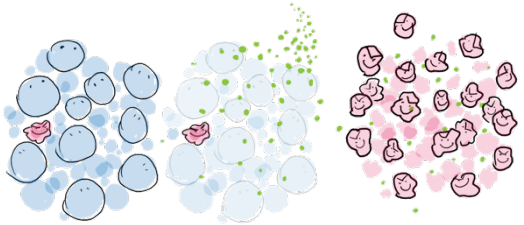
1 **Understand the enemy**





2 **Attack and counterattack**

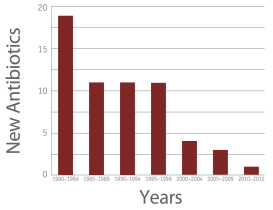




3 **Intelligence from the frontlines**

90% **Livestock**

50% **Incorrect**



4 **Join the fight**

1. DO Wash your hands
2. DON'T take antibiotics for viral infections
3. DON'T skip prescribed antibiotics

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Thank you!

SITN would like to acknowledge the following organizations for their generous support of this event.

Harvard Integrated Life Sciences

HILS

addgene

The nonprofit plasmid repository