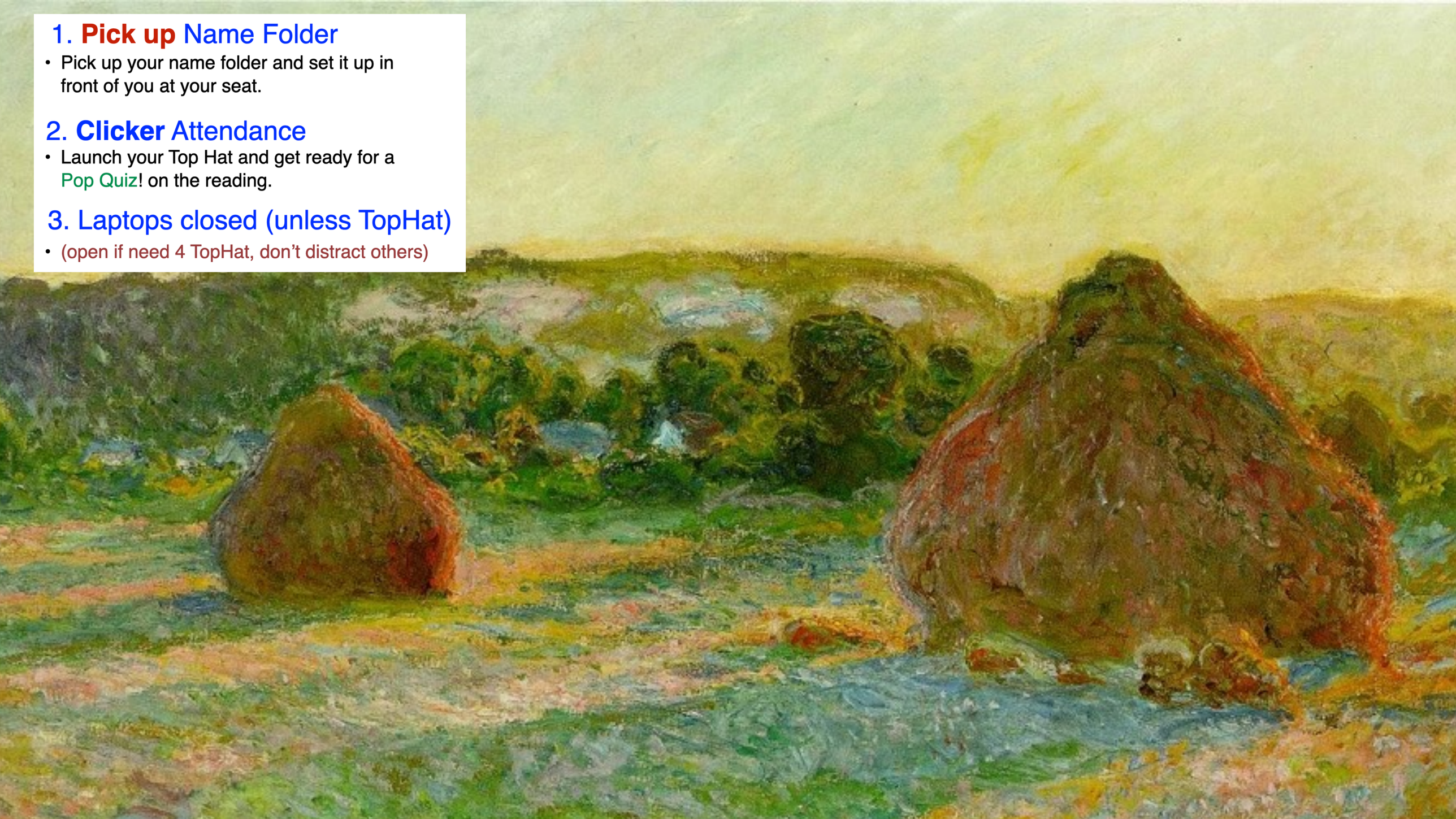

1. **Pick up** Name Folder

- Pick up your name folder and set it up in front of you at your seat.

2. **Clicker** Attendance

- Launch your Top Hat and get ready for a Pop Quiz! on the reading.

3. Laptops closed (unless TopHat)

- (open if need 4 TopHat, don't distract others)

1. **Pick up** Name Folder

- Pick up your name folder and set it up in front of you at your seat.

2. **Clicker** Attendance

- Launch your Top Hat and get ready for a Pop Quiz! on the reading.

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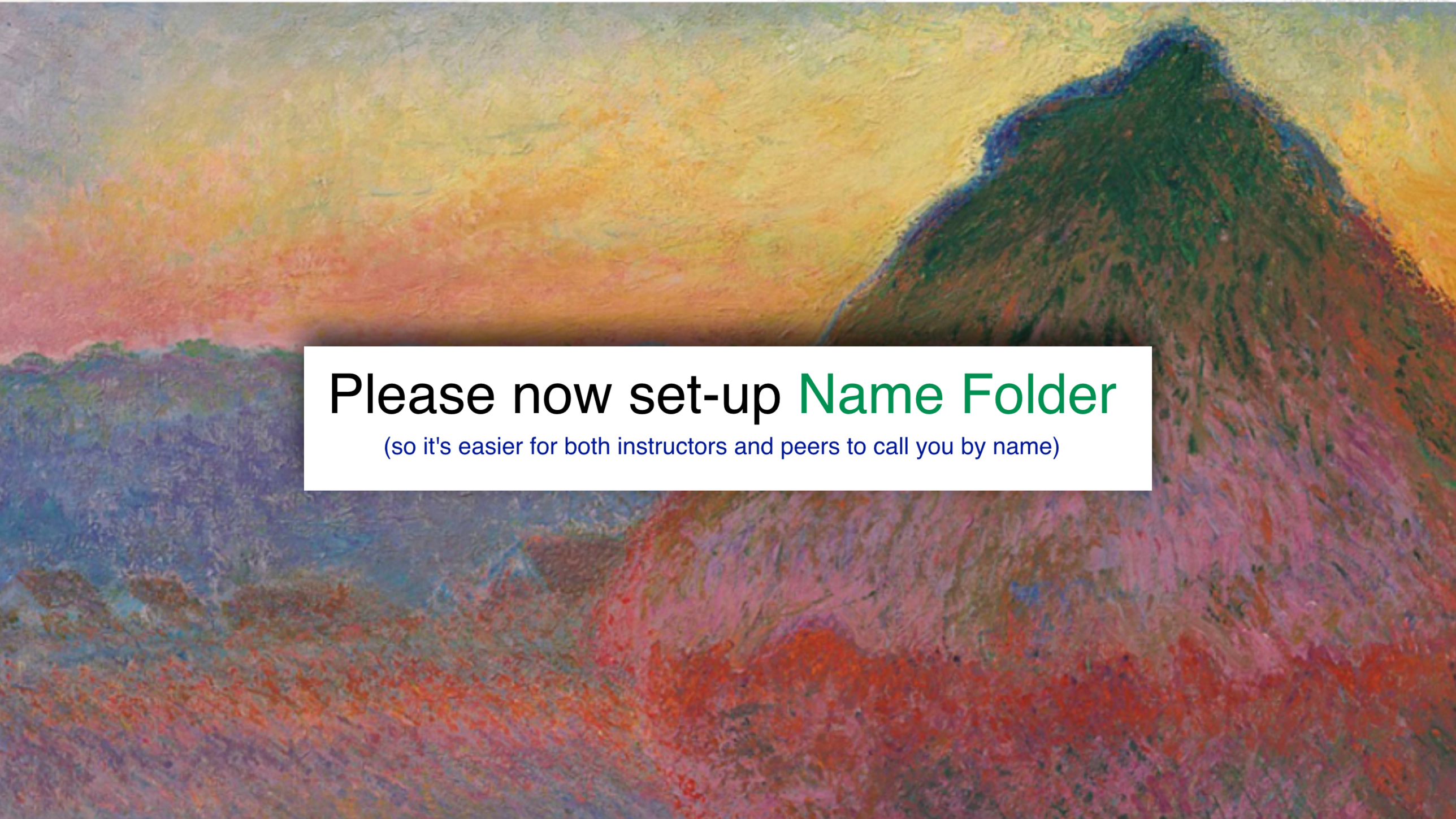


Please now set-up Name Folder

(so it's easier for both instructors and peers to call you by name)

Remind me to stop with 5 minutes left, to do **Announcements**

Wait, so what do you to learn this semester...?

Thinking of what you want to get out of your college education and this course, which of the following is **most important to you**?

a) Acquiring information (facts, principles, concepts)

b) Learning how to use information and knowledge in new situations

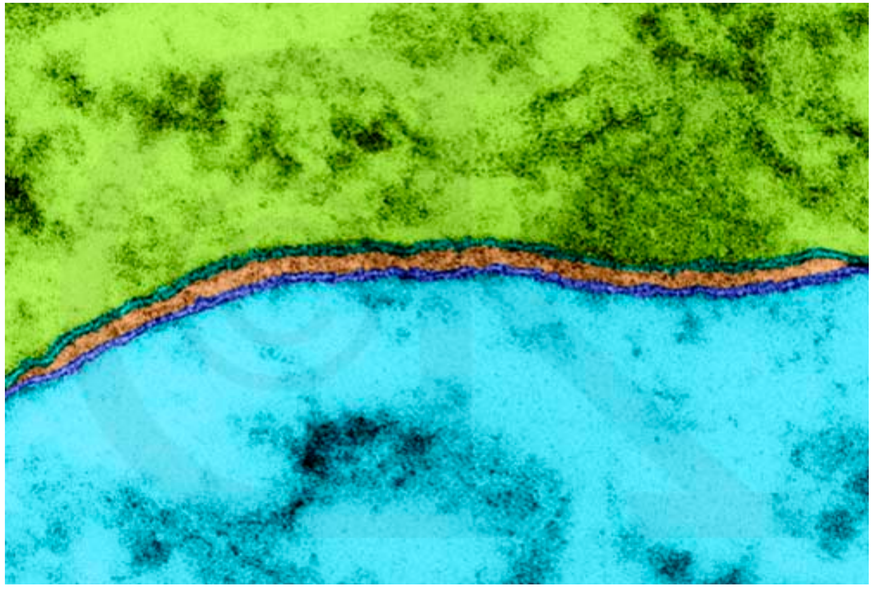
c) Developing lifelong learning skills

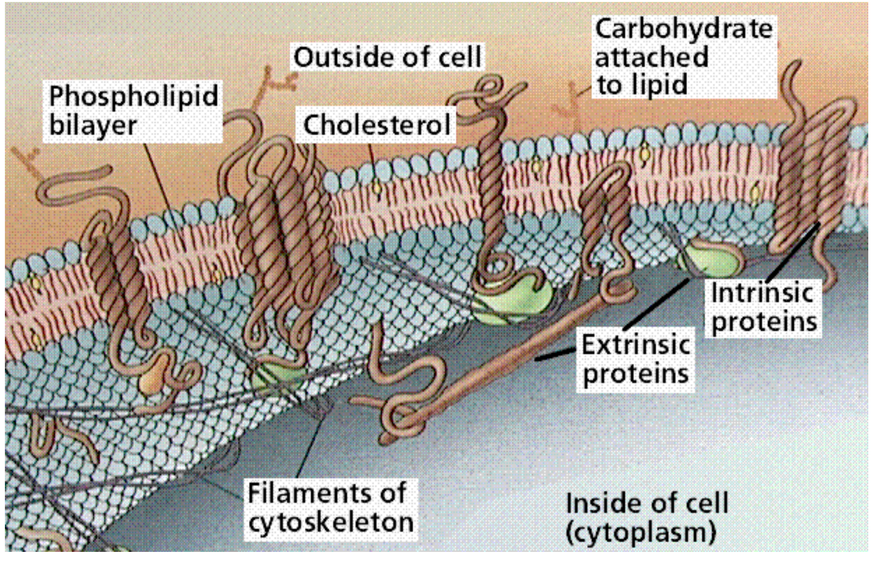
Of these three goals, which one do you think you can make headway on **outside of class** by your own reading and studying?

a) Acquiring information (facts, principles, concepts)

b) Learning how to use information and knowledge in new situations

c) Developing lifelong learning skills





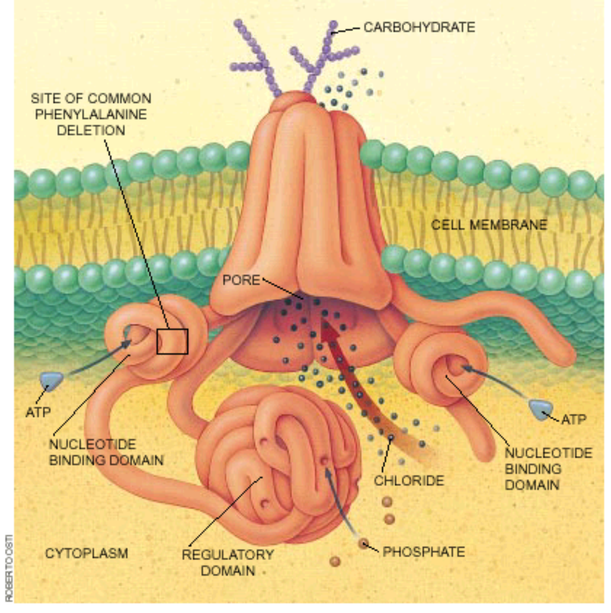
ABC Transporter Family

Clinical Relevance

MDR- Cancer

SUR- Diabetes

CFTR- Cystic Fibrosis



“Pop Quiz”: **Reward** for those who remember or wrote in notebook.
(clicker questions, 60 seconds each, handwritten notes can be used)

Where are the CFTR channels found normally [in a healthy person]?

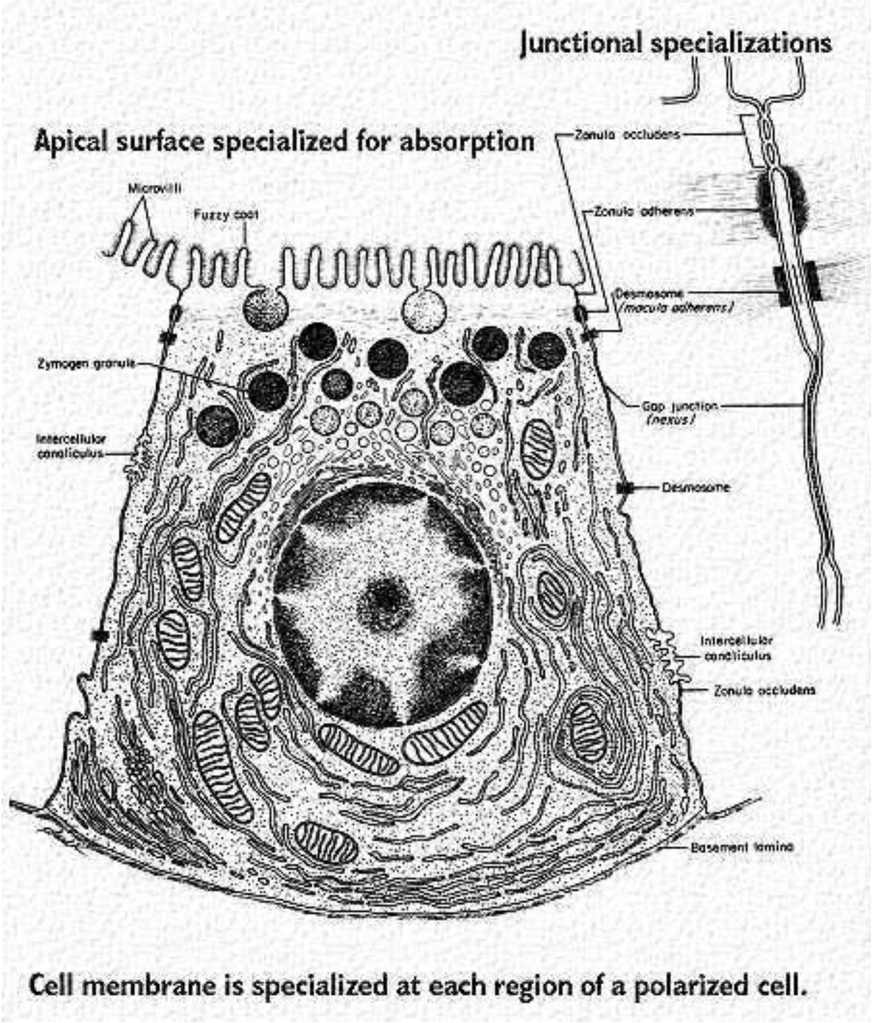
A. the apical surface ->

B. inside the ER

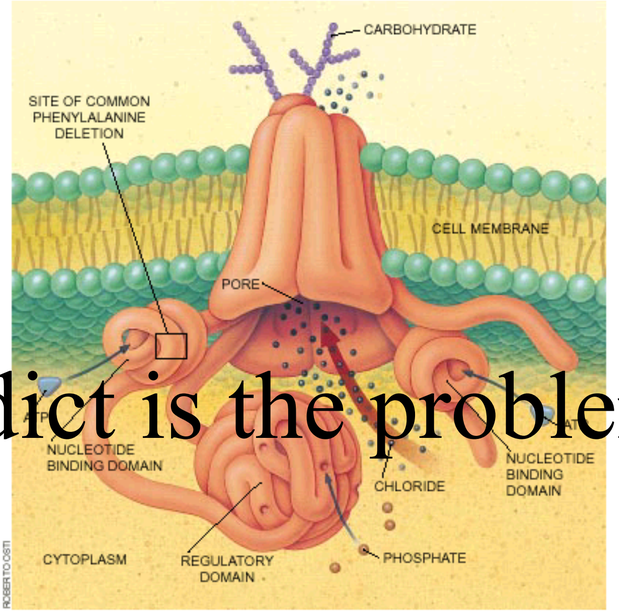
C. the lateral surface ->

D. in the lysosome

E. the basal surface ->



So what do you predict is the problem?



A. The deletion alters gating, thus blocking the CFTR.

B. The deletion alters ATP binding, thus stopping CFTR.

C. The deletion alters the folding, but CFTR still works.

D. None of the above cause the disease.

How many CFTR channels are on the surface of a cell of a CF patient?? (normal=100)

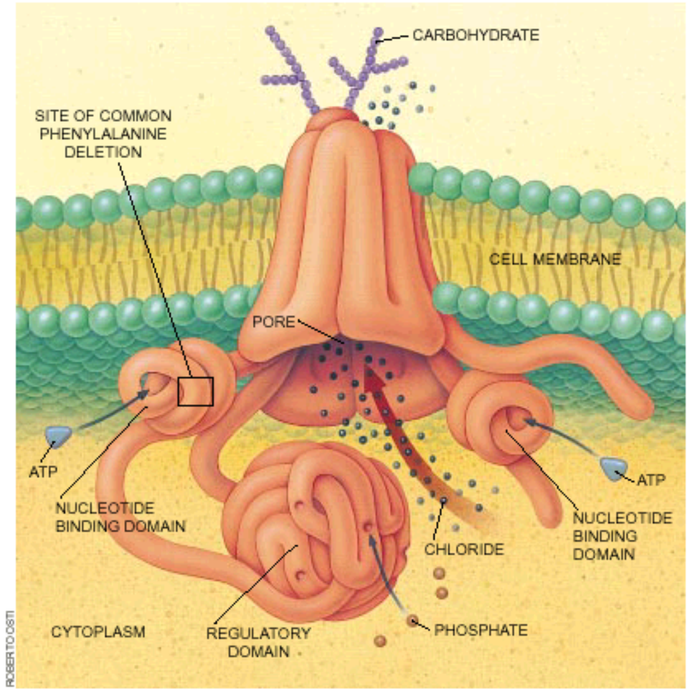
A. 50

B. 25

C. 10

D. 5

E. 0



How many CFTR channels are on the surface of a cell of a person who is a **CF carrier** [heterozygote]?? (normal=100)

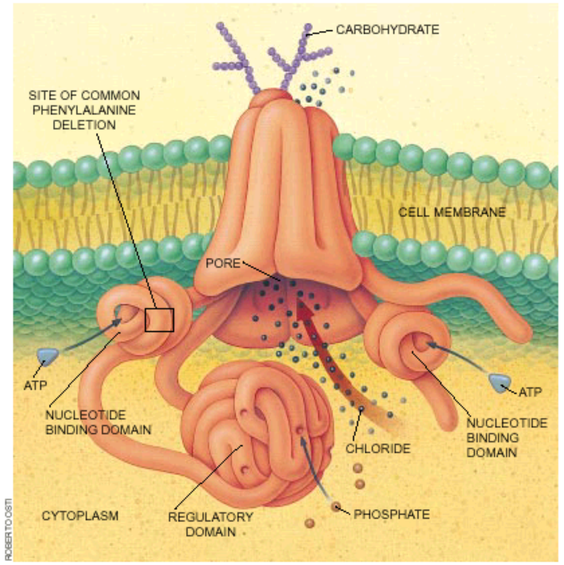
A. 50

B. 25

C. 10

D. 5

E. None of the above are correct.



Predict

If you have a cell that produces **0 mRNAs** from its CFTR gene, ***how many*** CFTR proteins will that cell make?

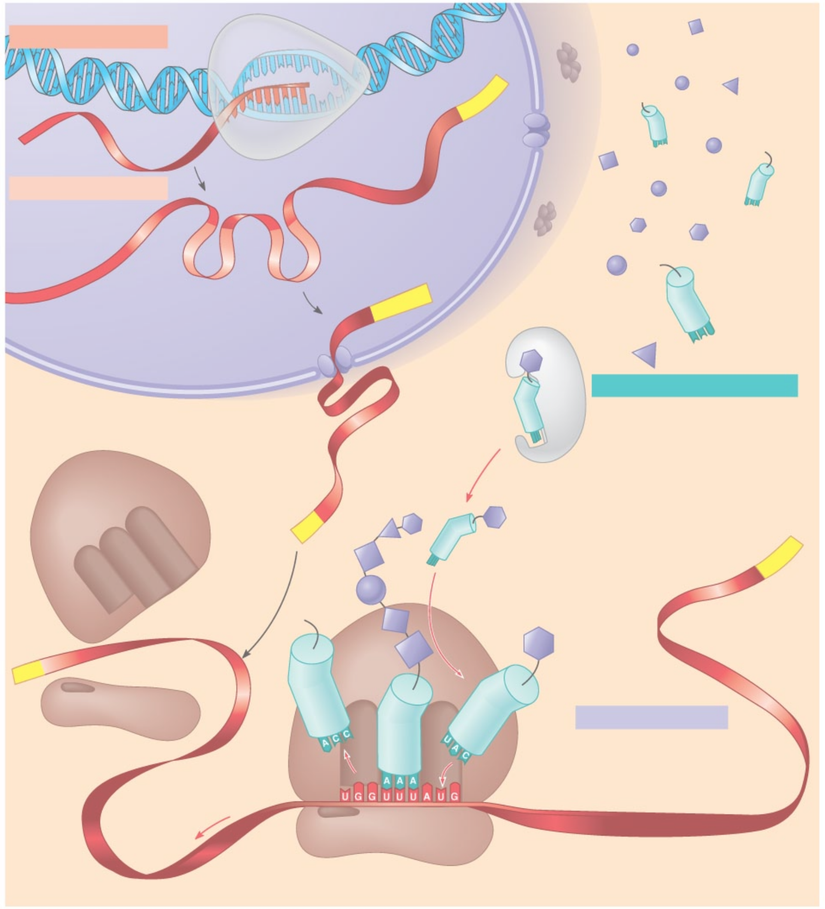
A. 50

B. 25

C. 10

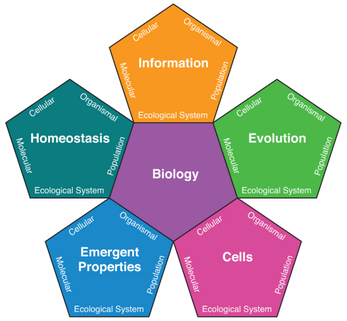
D. 5

E. 0



Back to Today’s reading…

Integrating Concepts in Biology



Chapter 1:
Heritable Material

1.1 What is biological information?
1.2 What is the heritable material?

by A. Malcolm Campbell, Laurie J. Heyer, & Christopher Paradise

Budgeting homework time (70 min): Ch. 1, section 1.2 is approximately 2600 words in length. At what's considered slow reading speed, 200 words per minute, reading section 1.2 should take 13 minutes. But when done properly, when you pause to review figures, read and think about a few of the Integrating Questions, and take careful notes, if you focus (avoid distraction) it should take you approx. 70 minutes.

1. _____ For the first lecture, read the 1-page **Foreword** written by the very famous Dr. Bruce Alberts, review the Student Resources in **Chapter 0**, and then begin reading **Chapter 1: Heritable Material** of our textbook, Integrating Concepts in Biology (ICB). Read the single Introduction page, and the short section 1.1 of Chapter 1, but you do not need to take notes on any of those pages.

2. _____ Then slowly read the section we will discuss most during lecture, section 1.2 "What is the heritable material?" As you read section 1.2 on your computer or tablet be sure to **take handwritten notes in your lecture notebook** (handwritten notes lead to much greater learning[2]).

3. _____ **Try to answer at least one Integrating Question (IQ) in each set**. As you read the ICB textbook always attempt to answer at least one of the yellow **Integrating Questions** each time you get to a set of them. It will help you test yourself to determine if you got the meaning, or not, while reading the last few paragraphs. Just like taking handwritten notes, this too will greatly increase your learning. If you desire a high grade in the course, try to answer more IQs.
   NOTE: Assume you will be asked a question in lecture which is directly from one of the IQs.

4. _____ **Trifecta**: **Prepare to explain (aloud) Figures 1.2, 1.3 and Table 1.1 in class**. As you read a section from the ICB textbook always attempt to pause and study **each figure/drawing/table** that is discussed. Some of them are just pictures or drawings and may not require lots of thinking, but others are graphs or tables that contain actual data from research experiments. Spend more time looking at these. In class, during lecture, students will be randomly chosen to explain a Figure or Table aloud (LA will hand you a microphone) so prepare for when your name is called to be sure you are ready. *Some students avoid stress by just writing out in their notebook an explanation of the Purpose, Methods and Findings of each data figure* (we call these three things *the Trifecta*). If it's already written down then you can just read aloud what you wrote, like: "Purpose: Dr. Griffith wanted to determine...., Methods: his group worked with mice and pneumonia bacteria called...., Findings: in the end they found evidence that ...".

1.2

Lecture 2 LB-145 Ch. 1 Heritable Material

L.O. • Interpret data showing that DNA is heritable material + protein is not.
° Evaluate experimental design + analyze data from research on DNA as info.

Dr. Fred Griffith British Ministry of Health 1920s

→ pandemic of the time was pneumonia caused by bacterium Streptococcus pneumoniae. 1920-1927 he collected 278 isolates from patients. Way to diagnose pneumonia, 1. inject mouse with patient's saliva or mucus → mouse die? 2. spread on petri dish with red growth media examine appearance of colonies that grew.

Figure 1.2 Photographs of S. pneumoniae Rough R + smooth S strains (non pathogenic / pathogenic → kills mice)

✗ did many replications of experiments to be sure no contamination

• Griffith eventually hypothesized: Rcells + "S factor" (protein) → S cells ("transformation" / "transformed")

Figure 1.3 illustration of experimental design

4 treatment strategies heat (steam) kills pneumoniae

Positive control → S cells + mouse = dead mouse + live S cells
Negative " → heat killed S cells + mouse = live mouse + no cells
→ R cells + mouse = live mouse + live R cells
→ dead S + R cells + live mouse = dead mouse + S cells

IQs 1. Positive vs Negative controls which, why?
2. Which experiment showed S factor, is it DNA or protein?

✗ Griffith thought S factor may be the heritable material for everything

BOLD

S-factor has to be CHO, PRO, nucleic, lipids - only things in bacteria

MATH supported proteins because 20 combinations nucleic only 4

LOCATION could separate bacteria into cell wall/mem vs cytoplasm (location)

$ all cytoplasm not S factor! cell wall/mem = Yes, wash → No! proteins (not nucleic acids) DNA RNA floating free

IQs 3. Math 4. loosely attached 5. solubility of nucleic acids

16 years later...

Oswald Avery MD in 1904 Brookly NY research like med faculty retired in 1943 THEN he got to work full time on research!

Picked up Griffith's work + developed a protocol to purify Something that always made R cells → S cells

METHODS / FIGURE 1.4?

1. Grind up S cells in buffer to extract soluble material (10 mL)
2. Add 50 ml ethanol to extract, mix, chill 8 hrs → white fluffy strings
3. Centrifuge 60 mL to pellet, pour off ethanol, let pellet dry
4. Dissolve + resuspend pellet in 10 mL buffer
5. Add sterile soln to R cells → incubate 37C for day → spread petri

EQ

7. Since S factor from soluble material thus might be?

Yet was it pure 100% DNA? or also had proteins?
tests said no detectable proteins BUT lots DNA
so also compared chemical composition of "S factor"

Table 1.1 Four samples of S factor vs pure DNA

• Then also added proteases (trypsin + chymotrypsin)
yet S factor soln still worked

• Then RNase, still unaffected

• Then DNase → stopped S factor from working ✓ best evidence

Never use term "prove" in science yet can disprove

Skeptics said DNase altered trace protein shape
Still not everyone convinced

What defines you as a human being? Why is every human different, even “identical” twins? Your body contains 10 to 50 trillion cells. Each cell contains instructions for the processes and functions of a human body. The information to carry out these functions is encoded in your deoxyribonucleic acid (DNA), half of which you inherited from each of your parents. What evidence supports the claim that DNA is the heritable material? How does DNA relay its information to the next generation? For many years, scientists mistakenly thought that protein was the heritable material. However, over many years of clever and now famous experiments, the evidence mounted in favor of DNA and against protein as the carrier

1.2 What is the heritable material?

- Context: Genetic information is passed from one generation to the next.
- Major themes: Heritable information provides continuity of life and information can be expressed and regulated without loss of content.
- Bottom line: DNA probably is the heritable material, not proteins.

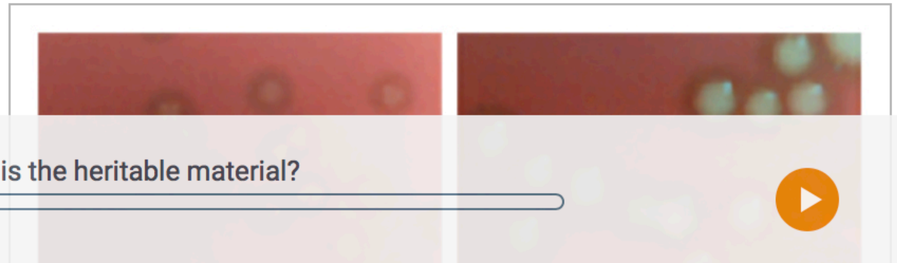
Biology Learning Objectives

- Interpret data showing that DNA is the heritable material and protein is not.
- Evaluate experimental design and analyze data from research on DNA as molecular information.

Science attempts to understand the physical world by answering questions through experimentation. For example, why do children often look like their parents? Why do adults give rise to the same species? Our first case study centers on the question, "What is the heritable material that is passed from one generation to the next?"

Sometimes, great science arises from an astute observation and a simple question. Dr. Fred Griffith was a medical officer in the British Ministry of Health during the 1920s. One of the major health threats at that time was pneumonia caused by the bacterium *Streptococcus pneumoniae*. Between 1920 and 1927, Griffith collected samples from patients and performed experiments on 278 isolates of pneumonia bacteria. At that time, the way to diagnose pneumonia consisted of two procedures: 1) inject a mouse with a patient's saliva or mucus to see if the mouse died of pneumonia; and 2) spread the saliva or mucus on a Petri dish containing red growth media and examine any **colonies** that grew (Figure 1.2).

While conducting these tests, Griffith noticed *S. pneumoniae* could be classified into two **strains,** which he called rough (R) and smooth (S). These two strains of bacteria could be distinguished visually. He first tried many experiments to make sure he had not contaminated his samples. He also discovered an interesting **correlation:**



2020

1. What plague swept the world?

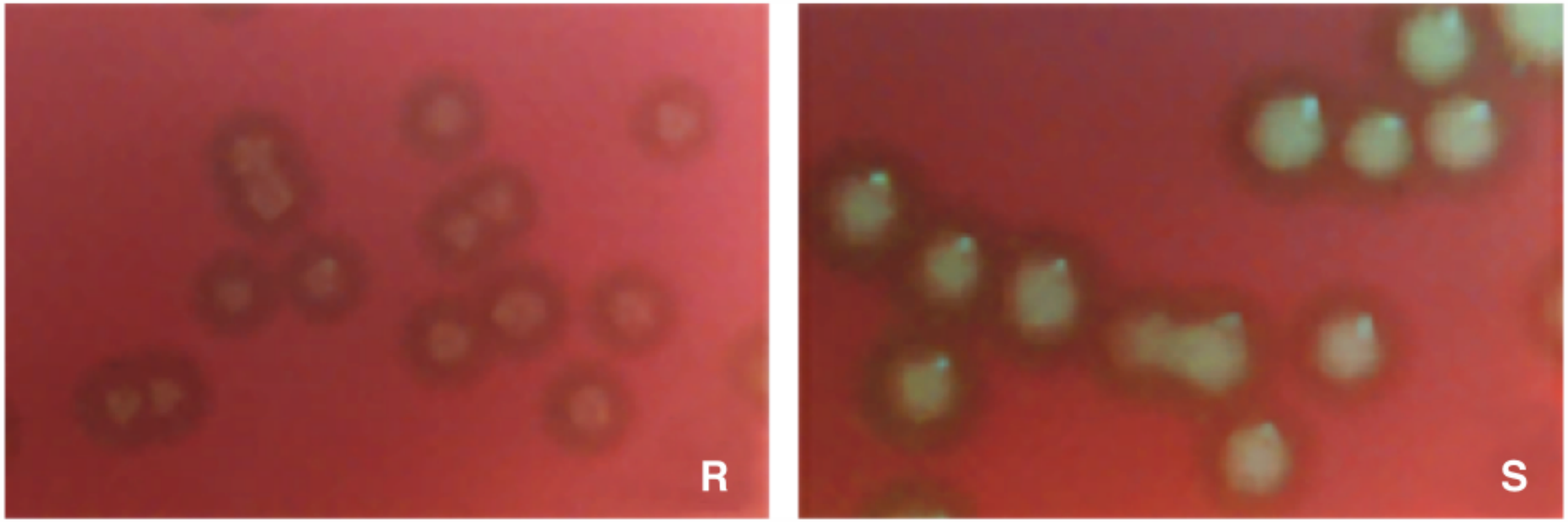
2. How did doctors diagnose you had it?

1920

1. What plague swept the world?

2. How did doctors diagnose you had it?

Trifecta (purpose, methods, findings)

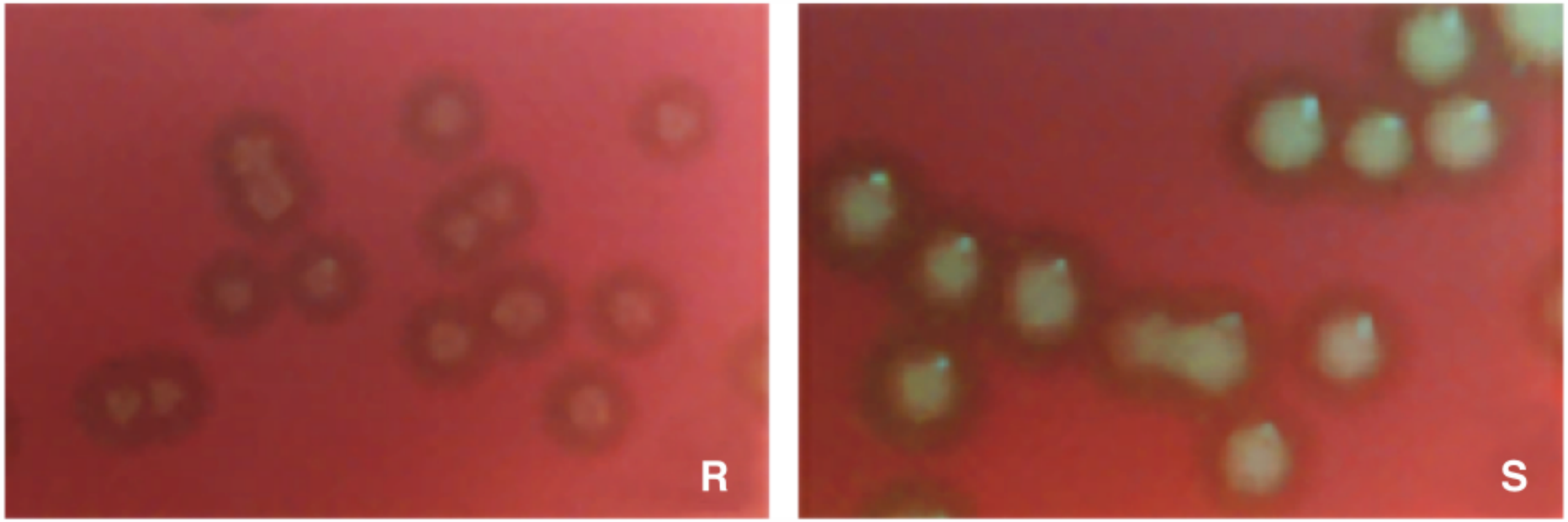


Griffith, 1928

Fig. 1.2

from Belanger et al. 2004

Photographs of Pneumococcus Strains



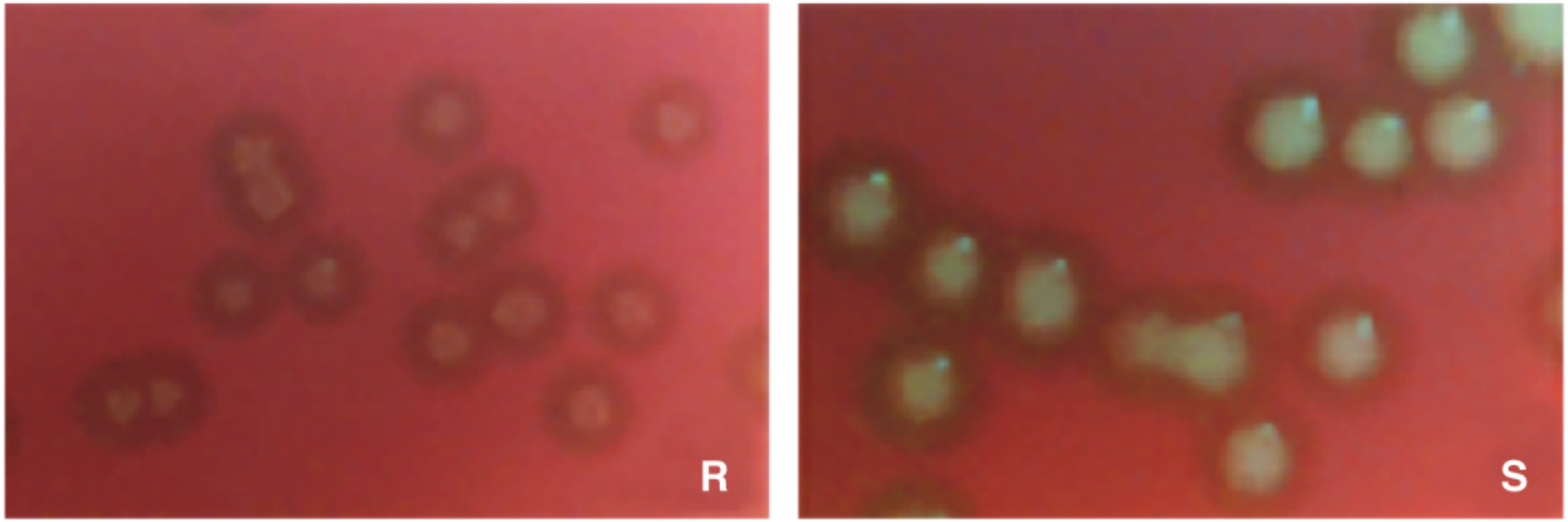
Griffith, 1928

Fig. 1.2

from Belanger et al. 2004

Photographs of Pneumococcus Strains

R strain → S strain



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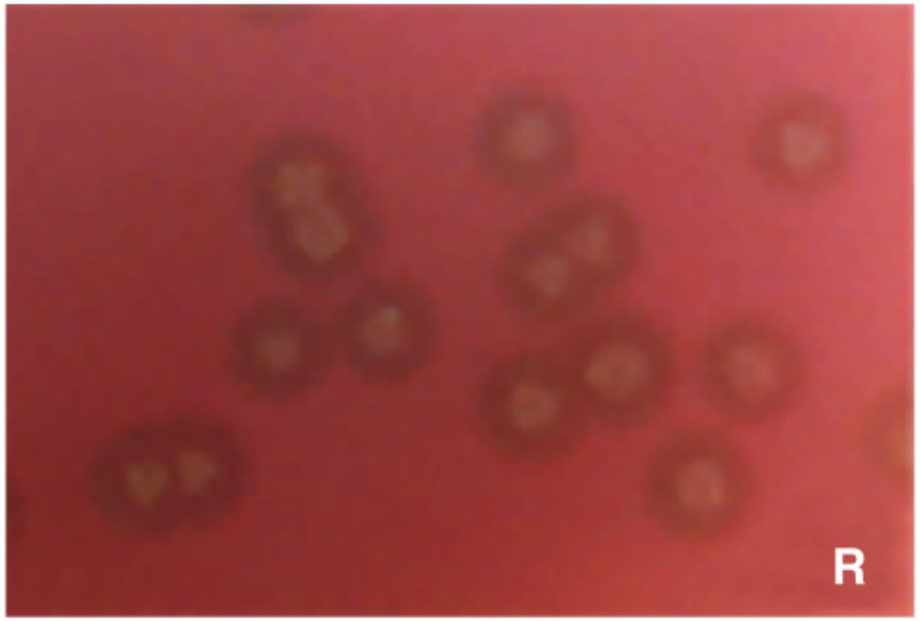
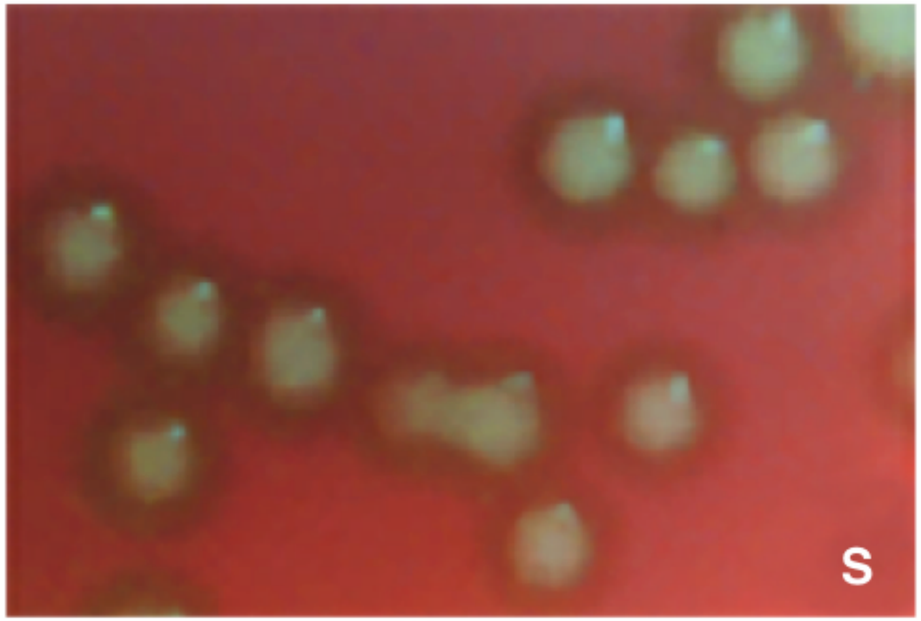
R strain → S strain





harmless

lethal

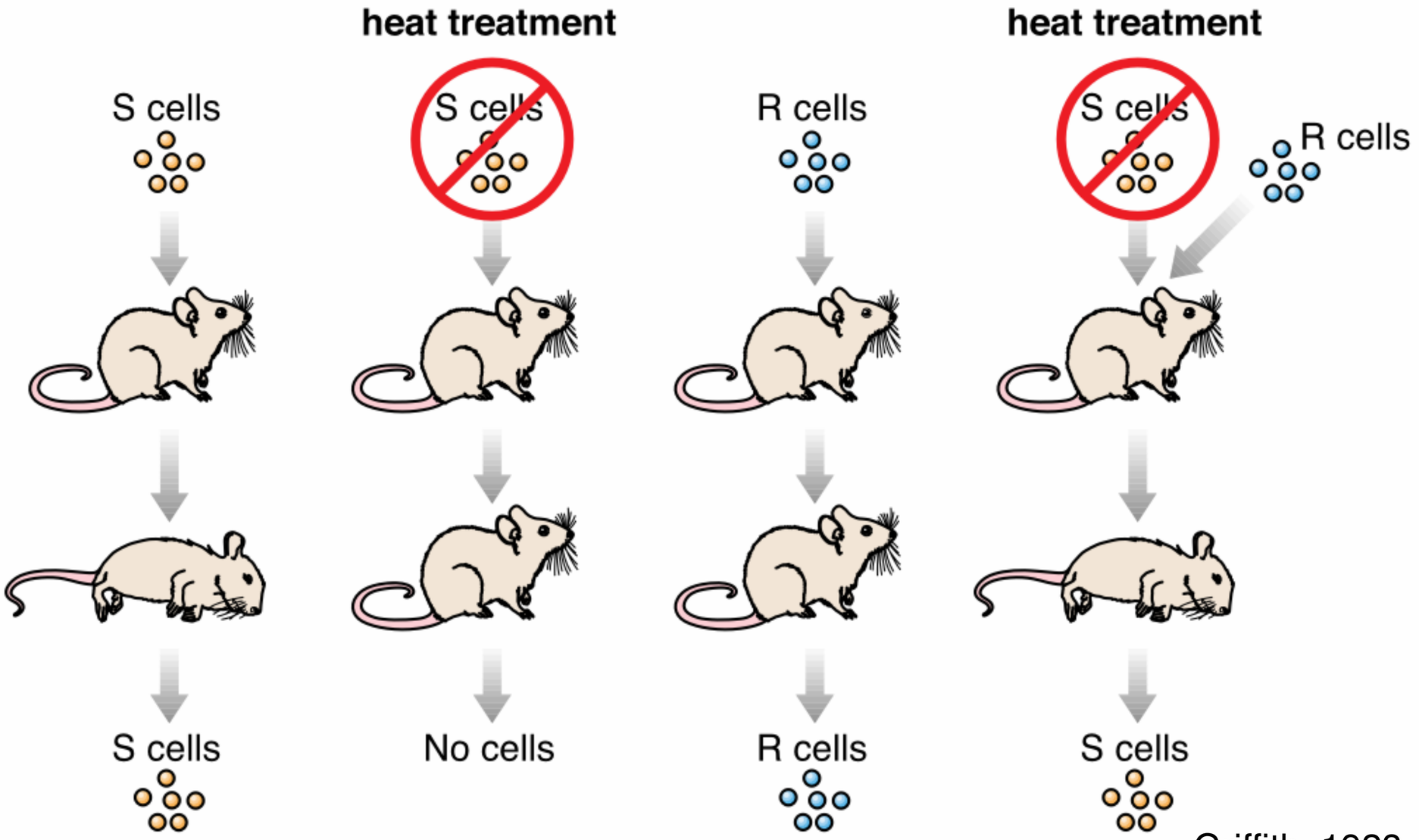
Griffith, 1928

Fig. 1.2

from Belanger et al. 2004

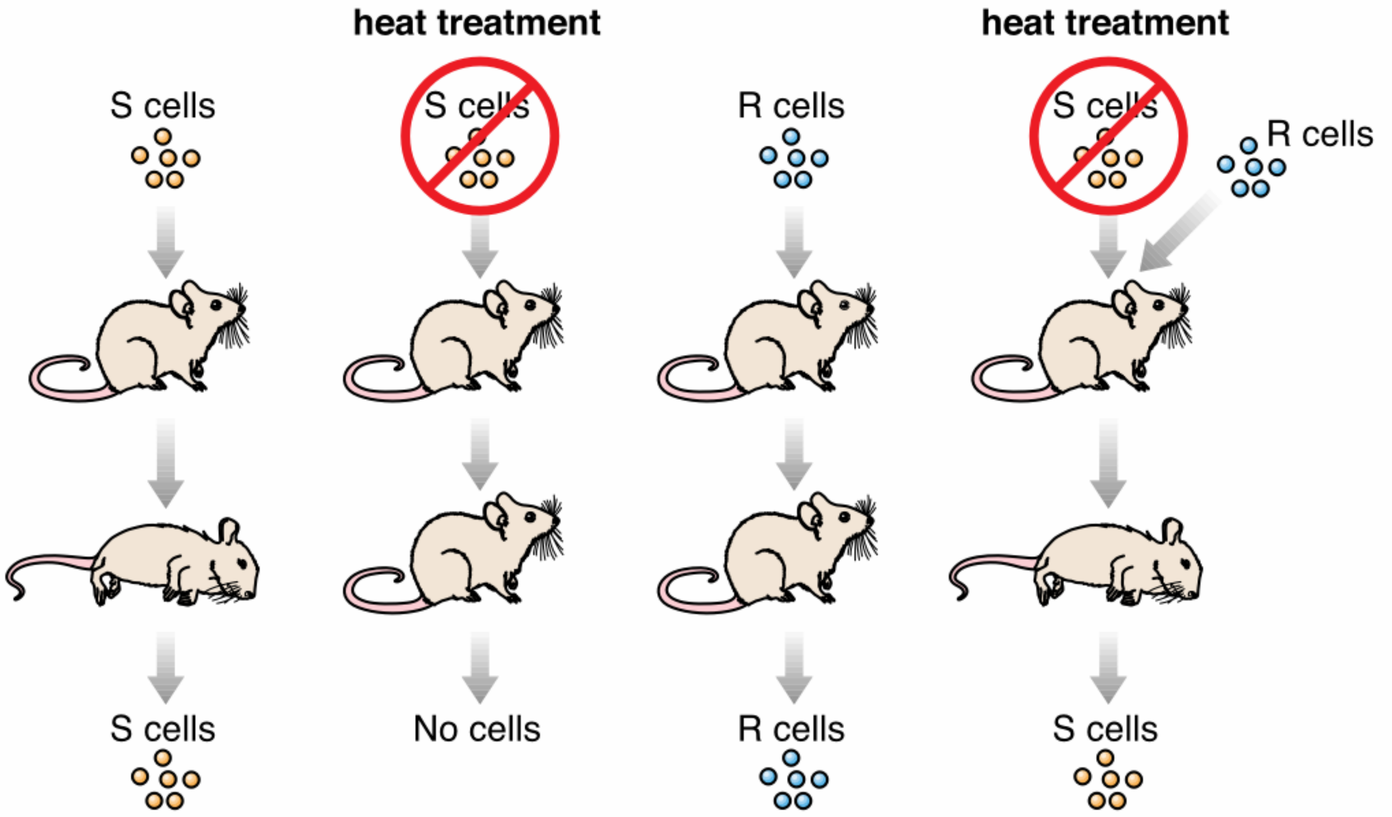
Griffith's work in the 1920s was fighting pneumonia

Trifecta (purpose, methods, findings)



Griffith, 1928

Fig. 1.3

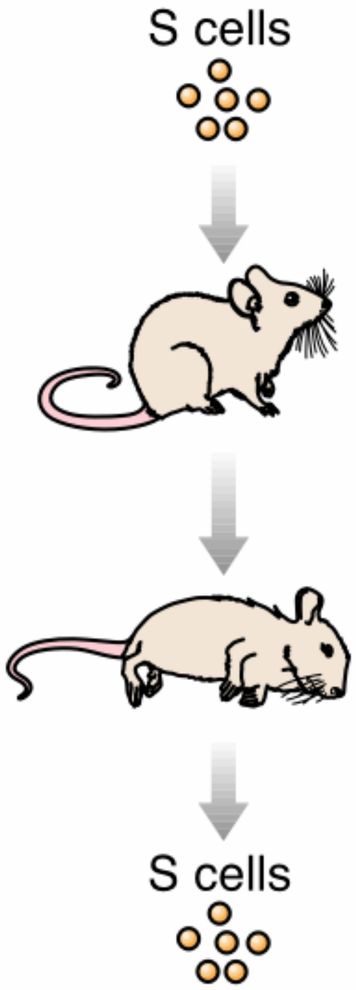


Integrating Questions

1. Identify the positive and negative controls in Figure 1.3. Is it always clear when to call a control either positive or negative?
2. Which of the four experiments demonstrates the existence of an "S factor?" Can you use Griffith's data to determine whether DNA or protein is the heritable material?

Fig. 1.3

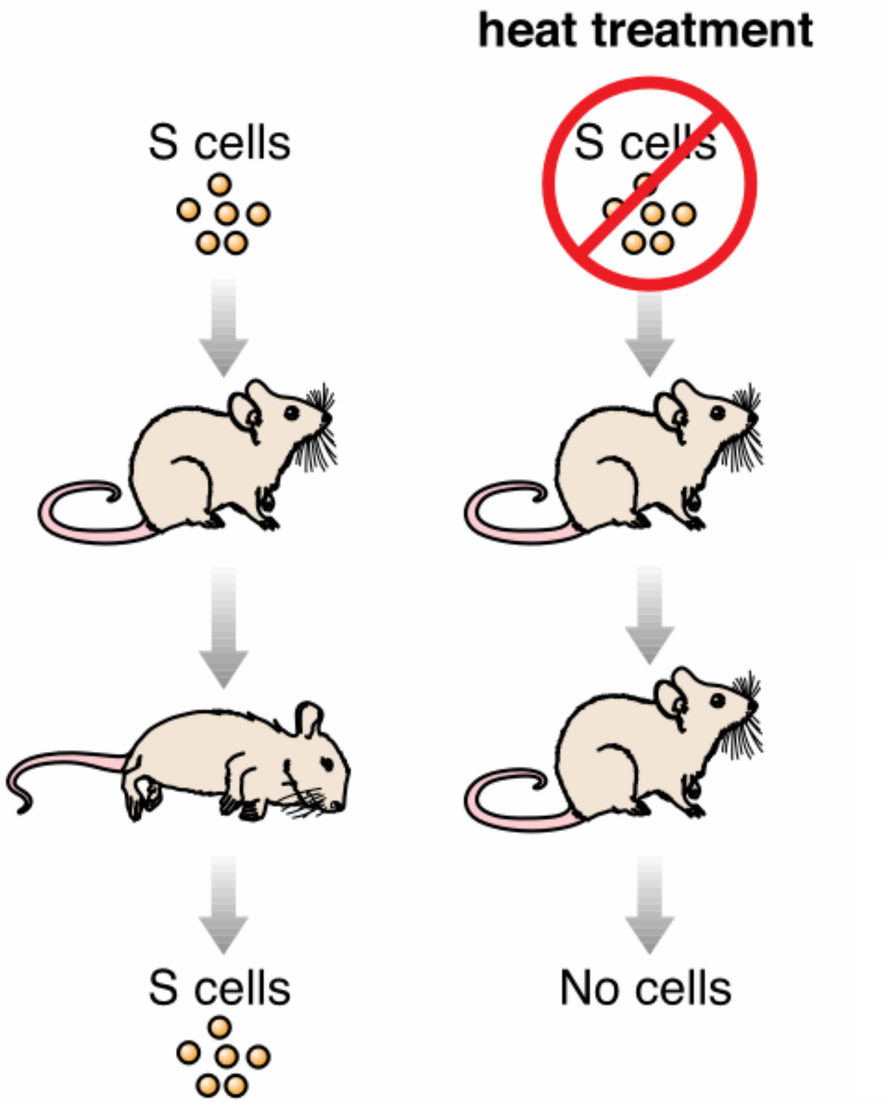
Griffith's Experiments



Griffith, 1928

Fig. 1.3

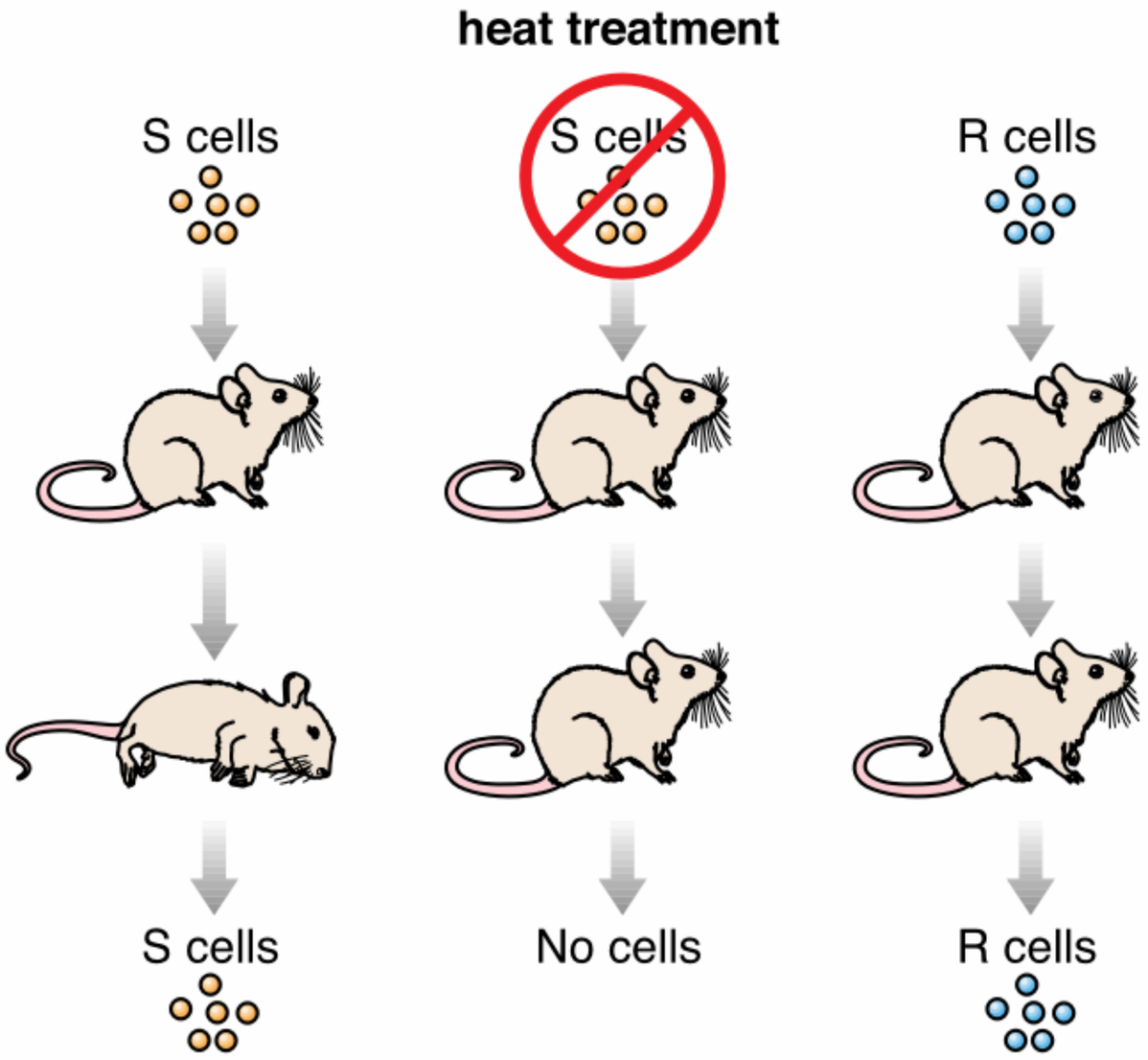
Griffith's Experiments



Griffith, 1928

Fig. 1.3

Griffith's Experiments



Griffith, 1928

Fig. 1.3

Griffith's Experiments

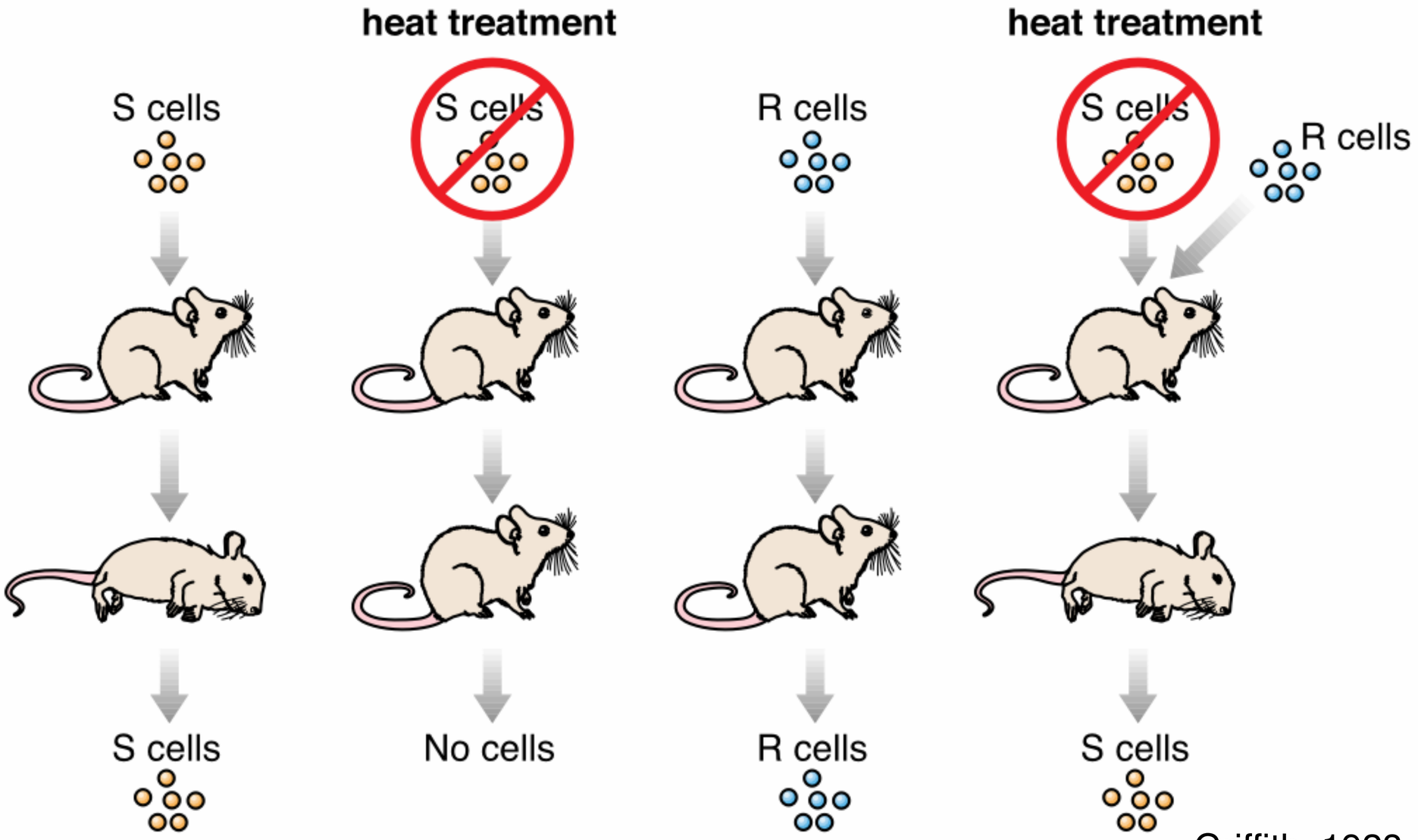


Fig. 1.3

Avery worked in the 1940s to learn what was the transforming factor (genetic material)

his age wind down their careers, but Avery would launch his most significant research and publish a groundbreaking result 40 years after earning his medical degree.

Avery addressed the open question Griffith left hanging: Is protein really the heritable material? Avery and his collaborators developed a **robust protocol** to convert R cells to S cells that worked better than Griffith's protocol:

1. Grind up S cells in buffer to extract all soluble material (10 mL).
2. Add 50 mL ethanol to the extract. Mix and store in a refrigerator for 8 hours. A white fluffy web of stringy material will appear that looks like a tangle of silk thread (Figure 1.4A).
3. The next morning, **centrifuge** the mixture (60 mL) to **pellet** the white stringy material. Pour off the ethanol, and allow the white pellet to dry.
4. Dissolve the pelleted material in 10 mL buffer.
5. Add the sterile solution from step 4 to R cells and incubate at 37° C for a day.
6. The next day, spread the cells from step 5 onto agar plates, and look for the transformation from R to S colonies (see Figure 1.4B). These S cells could have been injected into mice to demonstrate lethality, but out of concern for the animals, investigators in the 1940s had stopped using live mice for the pneumonia test.

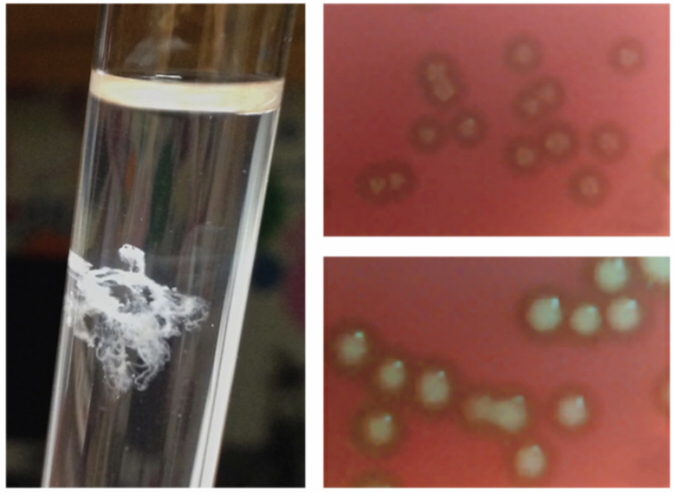


Figure 1.4 The heritable material produces S cells from R cells. **A,** Modern photograph of transforming factor precipitate. Note the wiry white strands in the tube. **B,** Photographs showing the original R cells (top) that were transformed into S cells (bottom). A. Original photo. Photo by Abagael Slattery, Davidson, NC B. From Belanger, Aimee E. *et al.* 2004. Figures 3A and 3B. Belanger, Aimee E. *et al.* 2004. Pyruvate oxidase is a determinant of Avery's rough morphology. Journal of Bacteriology. 186: 8164 – 8174.

Integrating Questions

6. Where is the S-factor in Avery's protocol? Hypothesize what the white stringy material is in Figure 1.4A. (You may have performed a similar procedure during a lab at some point in your education.)
7. If the heritable material was isolated from mostly cytoplasm in the absence of cell wall/membrane, what is the likely source of heritable material? Apply Avery's protocol to hypothesize what Griffith was washing off from his cell wall/membrane material.

Avery's team precipitated the transforming S-factor after using buffer to remove it from the cell wall/membrane. However, they could not be certain the water-soluble DNA was pure, because some proteins are also water soluble. Chemical tests developed in the 1930s helped Avery's team

Trifecta (purpose, methods, findings)

Table 1.1 Comparison of four independent preparations of transforming factor *vs* purified DNA.

sample #	% nitrogen, N	% phosphorus, P	N/P ratio
37	14.21	8.57	1.66
38B	15.93	9.09	1.75
42	15.36	9.04	1.69
44	13.40	8.45	1.58
pure DNA	**15.32**	**9.05**	**1.69**

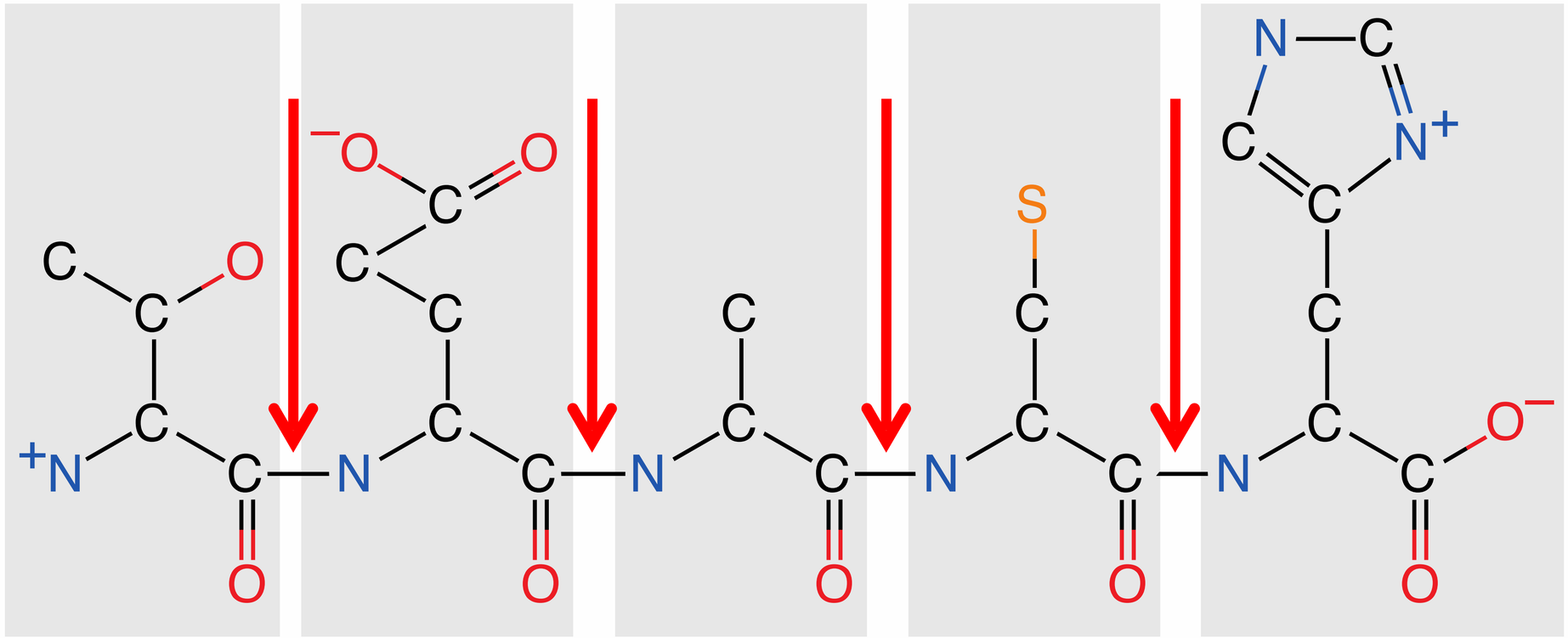
*from Avery, *et al*., 1944. Table I.

Avery, 1944

Table 1.1

Which enzyme cuts Amino Acids?

Protease



peptide bonds

Fig. 1.5A

Which enzyme cuts?

DNase

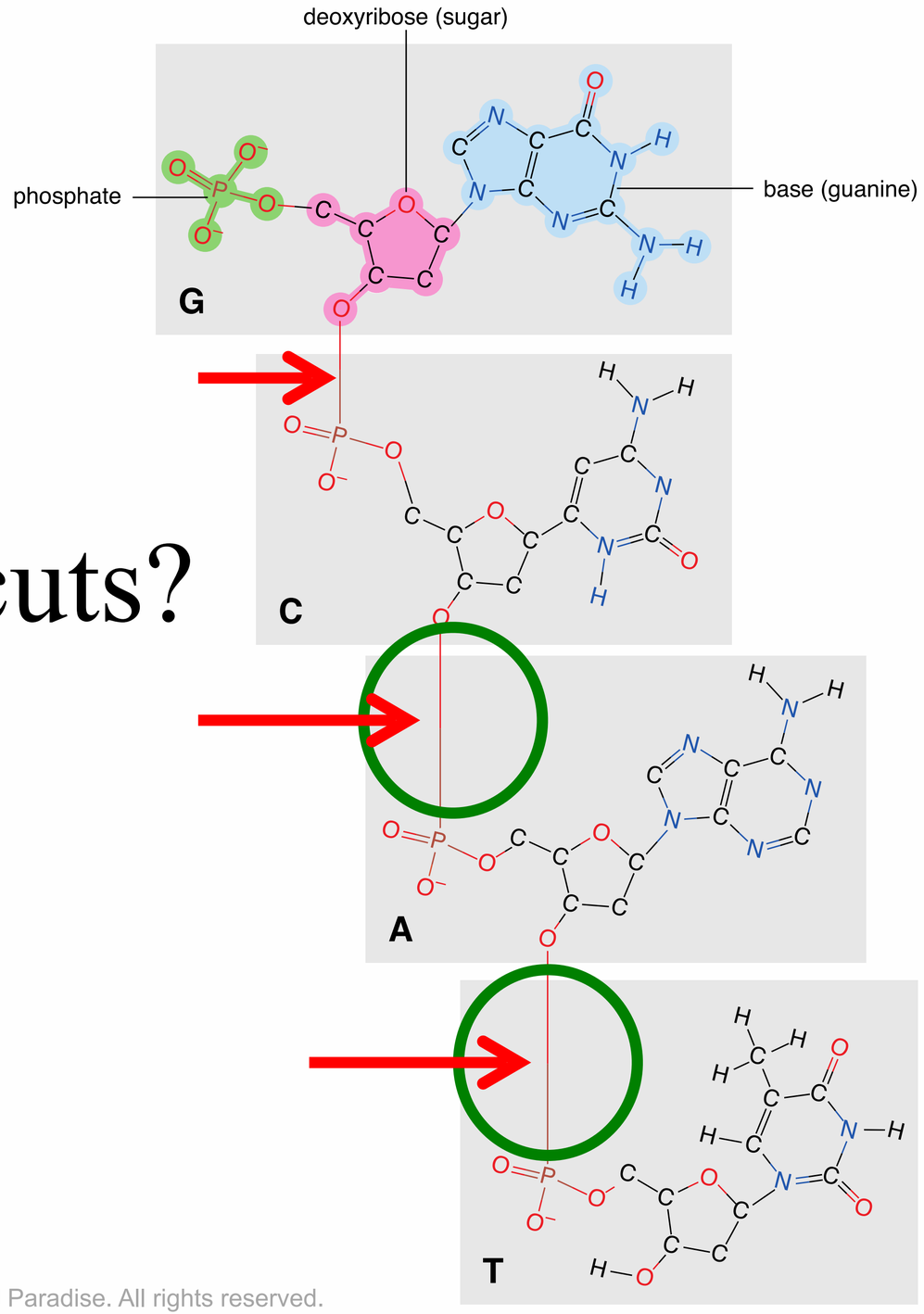
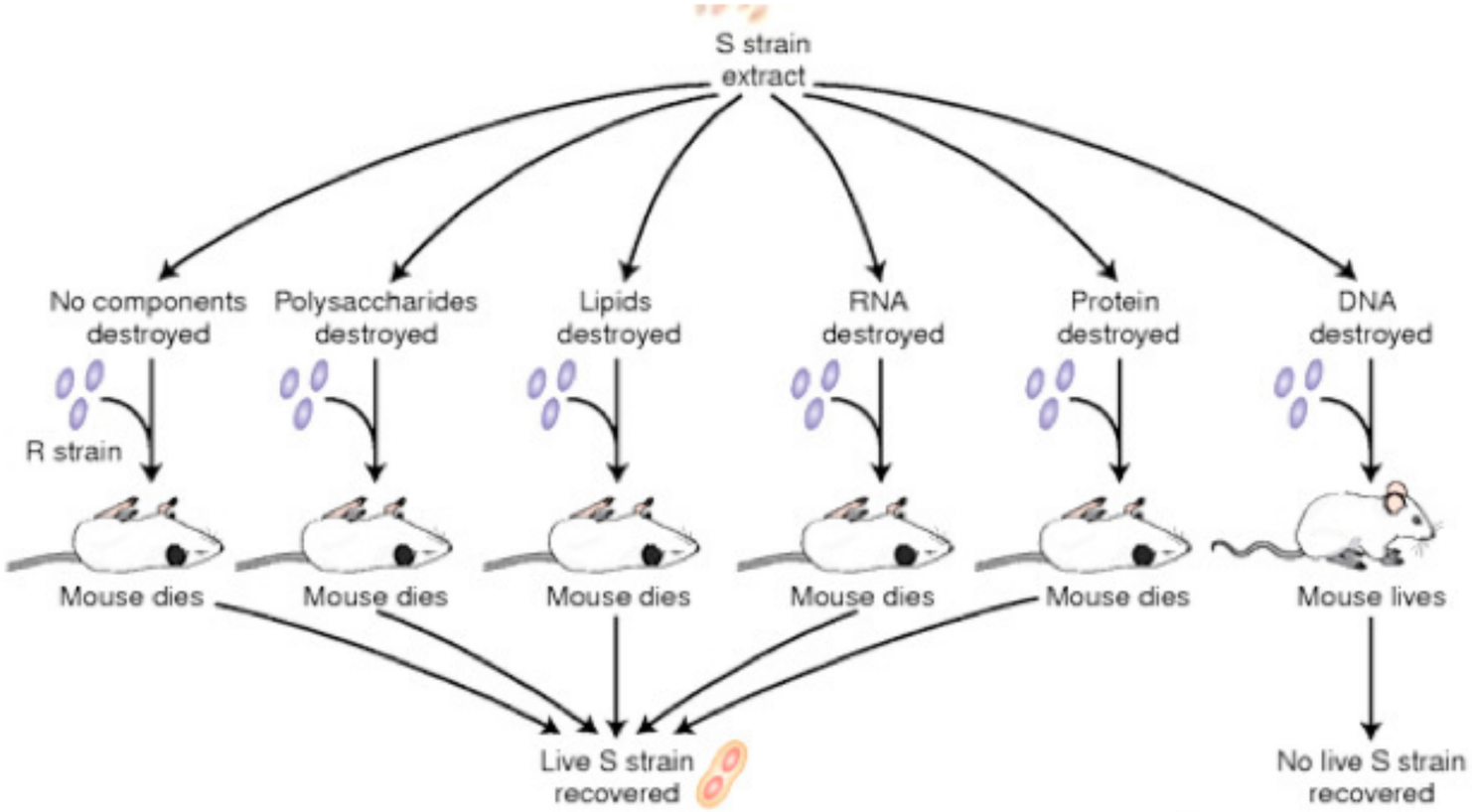


Fig. 1.5B

Avery's experiments (1944)



Q. How do these findings by Avery help determine which chemical is the heritable material?

Review Questions

1. Summarize the key experiments demonstrating that DNA is the heritable material and protein is not.
2. Use Figure 1.5 to identify the 5' and 3' ends of DNA.
3. Explain why it is impossible to prove a negative. Define the word “proof” as used in popular culture. Explain why the term “proof” is inappropriate for science.
4. Which should you trust more when reading a scientific paper, the authors’ interpretation as presented in the written text, or the data presented in figures and tables? Explain your answer.

Announcements

1. **Opera**: When you get to the Opera or Theater late what happens?
2. **Advice: Prof likes to see that you are serious in early weeks**
3. **Contract (p17):** signed and submitted by next Friday 5pm
4. Why do we use **Random calling?**
5. **Next lecture is ONLINE "lecture 3" on TopHat** due Sunday night**.**
6. **TopHat clicker questions** gain points if answered correctly (but only need to get 70% on them correct to earn 4.0 grade**)**
7. **Office Hours**- M/W 2:00-3:00pm, if there's a line, 10-minute limit.

Questions?

Grades (second page of syllabus)