"Welcome to Mars"
LB144-Pandemic edition

Pop Quiz!

Test Your Knowledge

Griffith conclude?

1:00

What did Griffith conclude was the heritable material based on his work with R & S strains

All results

A	DNA
B	RNA
C	protein
D	lipid

Math proof? 1:00

What math proof did Griffith incorporate into his conclusion that protein was heritable material?

All results

A	Protein lacks Phosphates
B	DNA lacks Nitrogens
C	DNA is in cytoplasm not cell wall
D	20 amino acids makes better code than 4 nucleotides

Everyone convinced? 1:00

Were all Biologists convinced by Avery's work that DNA was the heritable material?

All results

A	Yes, the N/P ratio was very compelling
B	Yes, he had proven heritable material was DNA
C	No, people are resistant to change
D	No, skeptics were not convinced by these data

END

Pop Quiz!

(Preparing for) **Tuesday's lecture:**

Budgeting homework time (60 min): Chapter 1, has a cover page, section 1.1 is 660 words, and section 1.2 on Drs. Griffith and Avery is 1725 words in length. While this is about 2300 words in total, thus the reading would be estimated to take 12 minutes. Yet careful reading and notetaking takes time and it has four data figures. While the Trifectas are easy to prepare for, Table 1.1 may be more difficult.

1. _______ **For Tuesday's lecture,** start **Chapter 1: Heritable Material** by reviewing the cover page and reading the short section 1.1: "What is biological information?" No notes needed.

2. _______ **Now slowly carefully read** section 1.2: "What is the heritable material?" and take careful handwritten notes in your lecture notebook.

3. _______ **Try to answer some Integrating Questions** and **Review Questions**.

4. _______ (Trifecta): **Prepare to explain (aloud) Figures 1.2, 1.3, 1.4 and Table 1.1 in class** (Purpose, Methods, Findings).

Chapter 1: Heritable Material

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 of genetic information. One of the most famous discoveries in science was the double helix structure of DNA. DNA's structure helps explain how your DNA replicates itself to produce the next generation. Chemical modifications to DNA can lead to differences among individuals, including some we can observe and some that make us sick. In Chapter 1, you will explore and interpret the original data from experiments that led to our current understanding of DNA as heritable information. Genetic information defines you as a human being and differentiates you as an individual. The five sections of Chapter 1 focus on information at the molecular level.

Dog breeds vary in phenotype, but they are all the same species. A is courtesy Kevin G. Smith, Davidson, NC. B - D are courtesy Abbye W. Stooksbury, Marietta, GA.

you are here		Big Ideas of biology				
		Information	Evolution	Cells	Homeostasis	Emergent Properties
levels of the biological hierarchy	molecules	1	4	7	10	13
	cells	2	5	8	11	14
	organisms I	3	6	9	12	15
	organisms II	16	19	22	28	25
	populations	17	20	23	29	26
	ecological systems	18	21	24	30	27

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Opening Figure

courtesy Kevin G. Smith and Abbye W. Stooksbury

Four Breeds of One Species

Slight differences in genetic information leads to different phenotypes.

Opening Figure

courtesy Kevin G. Smith and Abbye W. Stooksbury

1.1 What is biological information?

- Context: Introduce the Big Idea of Information as a critical part of life.
- Major themes: Heritable information provides continuity of life, and non-heritable information is transmitted within and between biological systems.
- Bottom line: Biological information takes many forms and is transmitted to others.

Biology Learning Objective

- Categorize different forms of biological information.

Biology is the study of life. You have learned this definition, but what does *life* really mean? If you look up the word *life,* Webster's dictionary tells us life is the quality that distinguishes a vital functional being from a dead body. In other words, life is not death. Frankly, this definition of life is not very informative; biology is the study of a quality that is not death. Most people mistakenly think of biology (and science in general) as a compilation of facts or a vocabulary list. In reality, science is a process of discovery based on observation and experimentation. Through the science of biology in this book, you will discover information that exists in nature and decipher information that characterizes the quality of life. Professional biologists are not paid to memorize facts already discovered. As a biologist, a student of life, your charge is to discover different layers of information represented in living organisms, regardless of their size or complexity. You will explore the Big Idea of Information at different levels of biological organization that are assembled into the quality that distinguishes life from death.

If you look up the word **information** in a dictionary, you will find many definitions, but two are particularly relevant: 1) communication or reception of knowledge; 2) signal representing data that justifies a change. One aspect of biological information is the transmission of knowledge to other living beings. Sharing ideas is commonplace for humans, and most people consider the communication of knowledge to be a uniquely human trait. But restricting information to human communication is a misconception (Figure 1.1). Information can be conveyed between monkeys, dogs, bees, plants, predators and their prey, and even bacteria. A very famous example of information as communicated knowledge is called

Biological Information

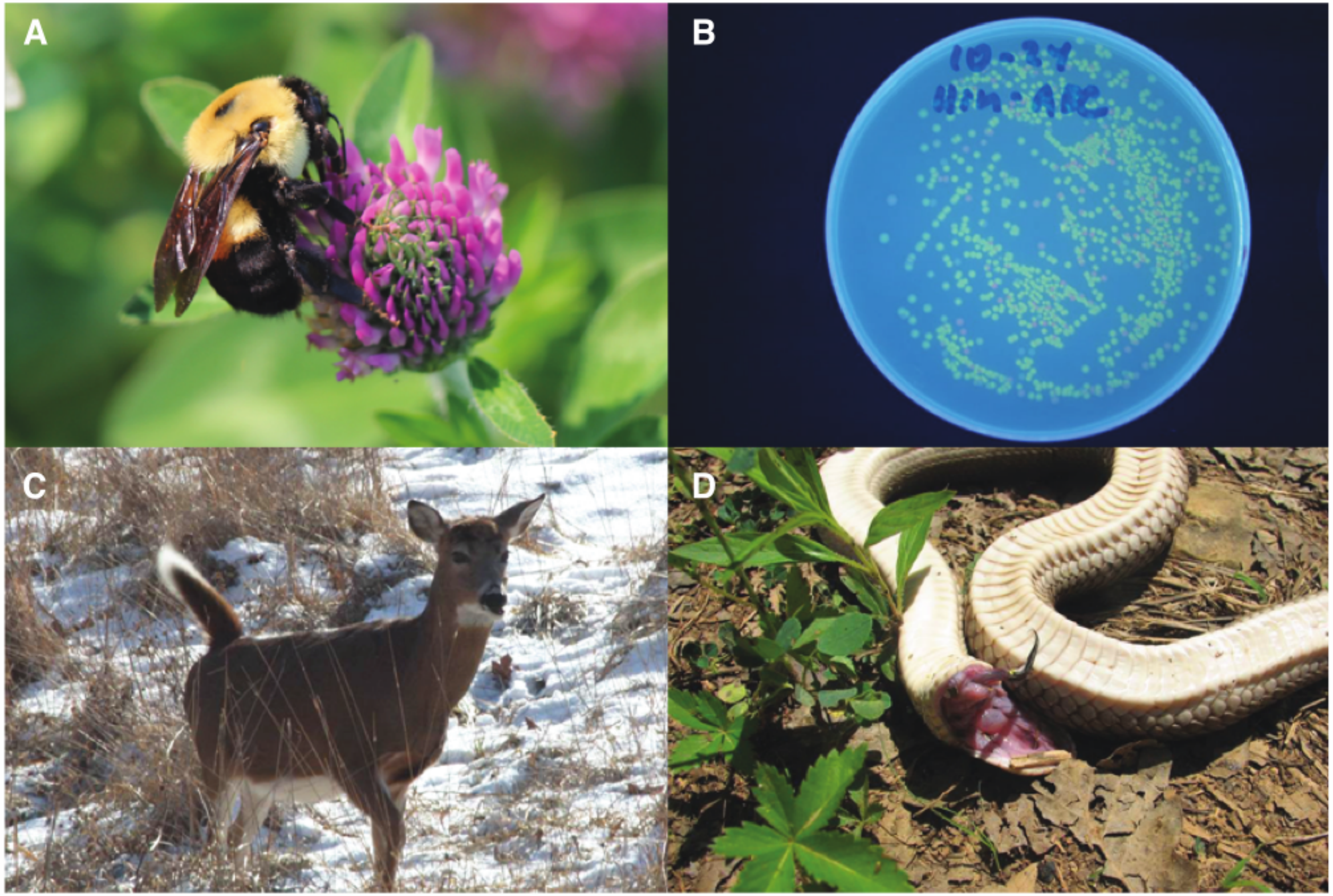


Fig. 1.1

courtesy Chris Paradise, Todd Eckdahl, and Travis Mohrman

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.

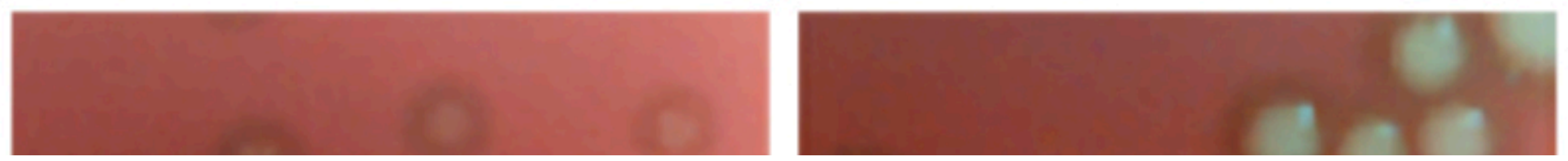
Biology Learning Objectives

- 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.

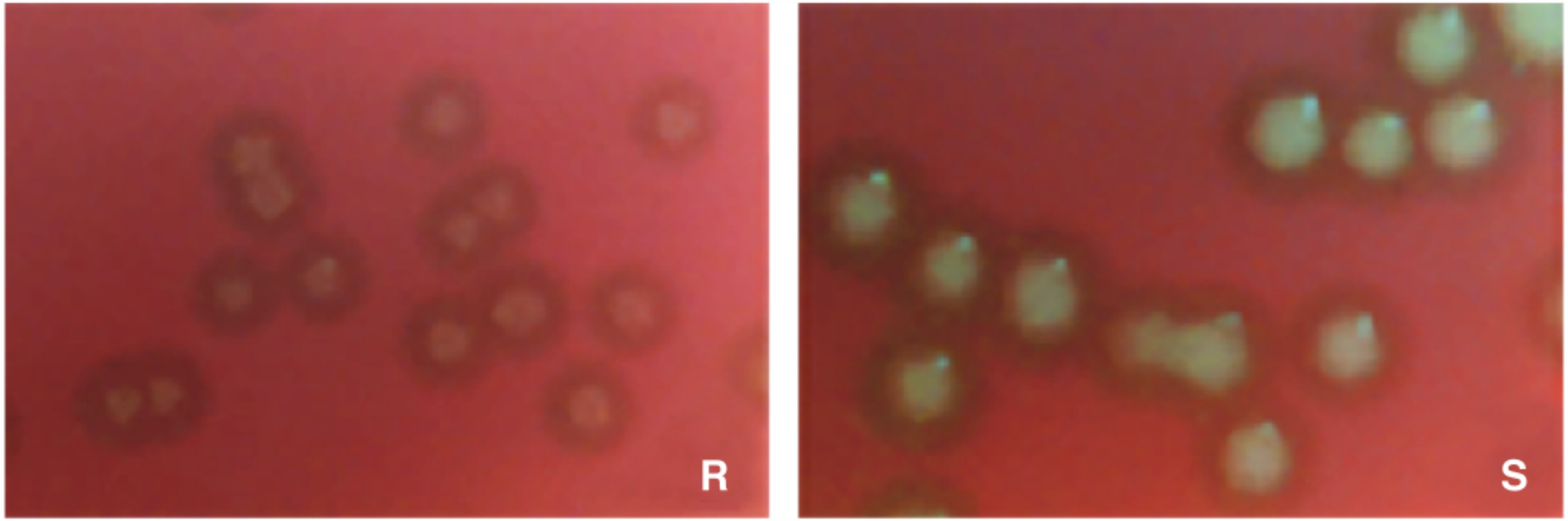
Science attempts to understand the physical world by answering questions through experimentation. For example, why do children often look like their parents? Why do adults give rise to the same species? Our first case study centers on the question, “What is the heritable material that is passed from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



Trifecta (purpose, methods, findings)

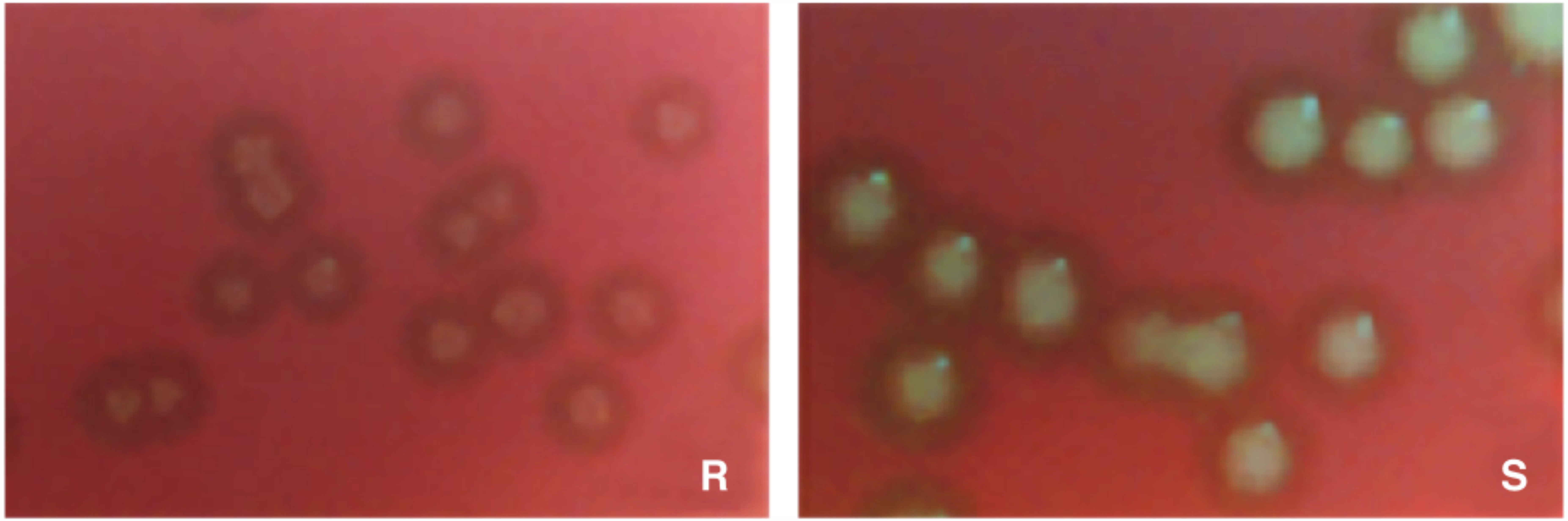


Griffith, 1928

Fig. 1.2

from Belanger et al. 2004

Photographs of Pneumococcus Strains



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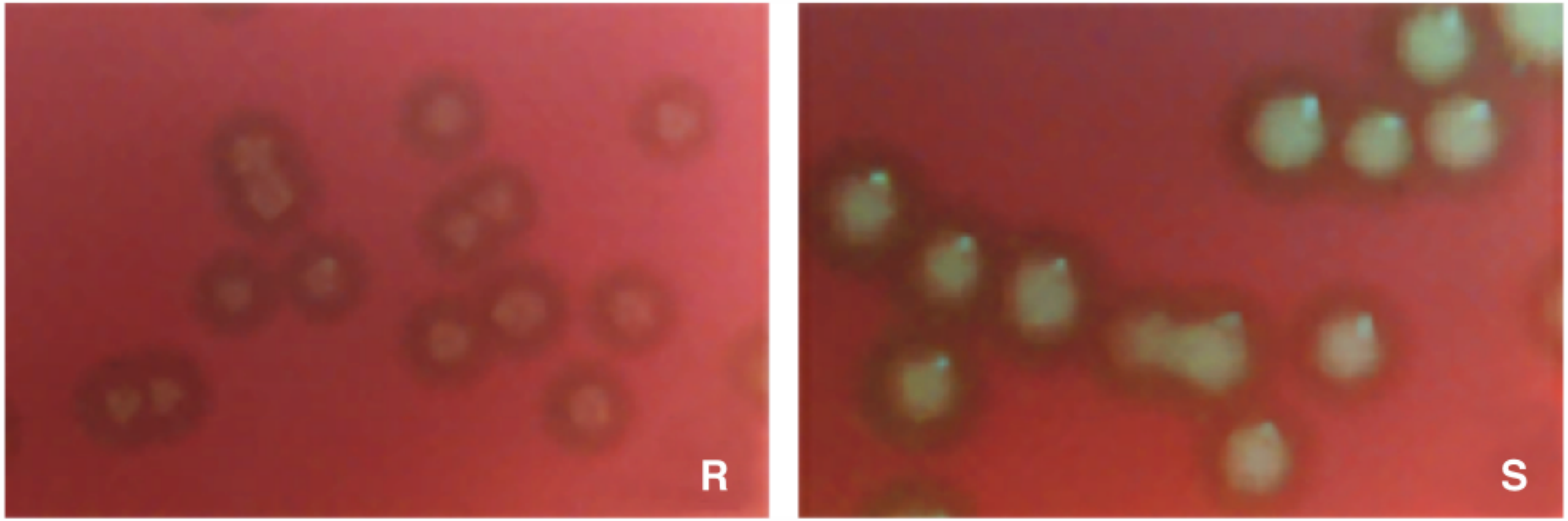
Photographs of Pneumococcus Strains

R strain → S strain



Griffith, 1928

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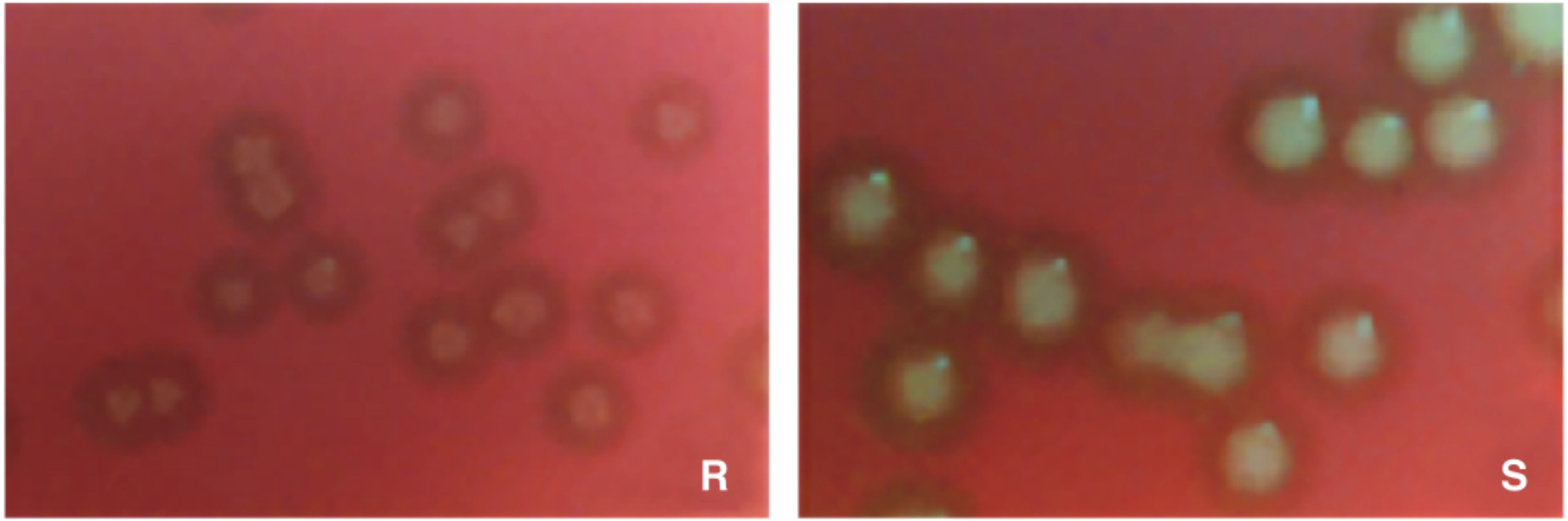


harmless lethal

Griffith, 1928

Fig. 1.2

from Belanger et al. 2004

Griffith's work in the 1920s was fighting pneumonia

Trifecta (purpose, methods, findings)

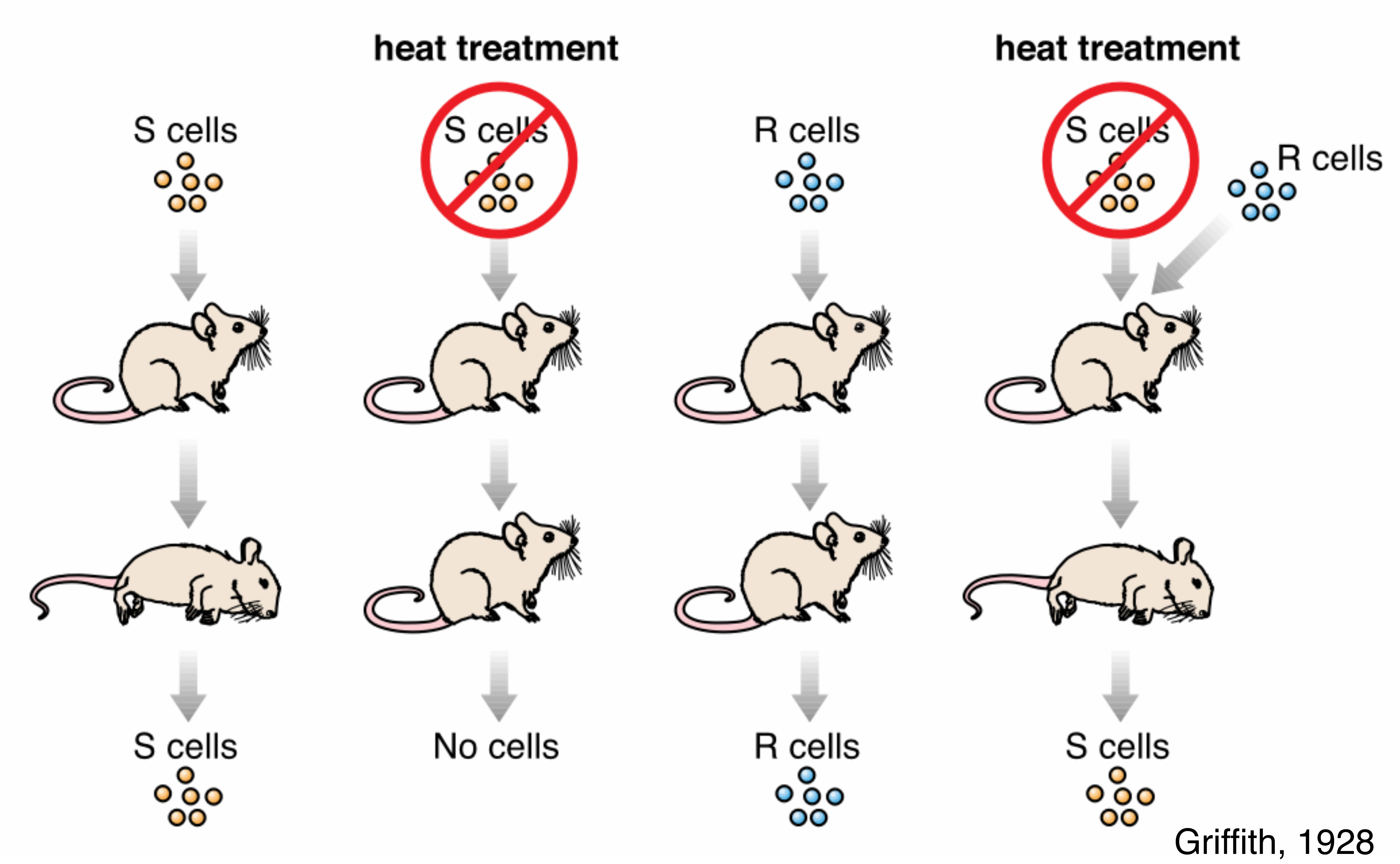


Fig. 1.3

Griffith's Experiments

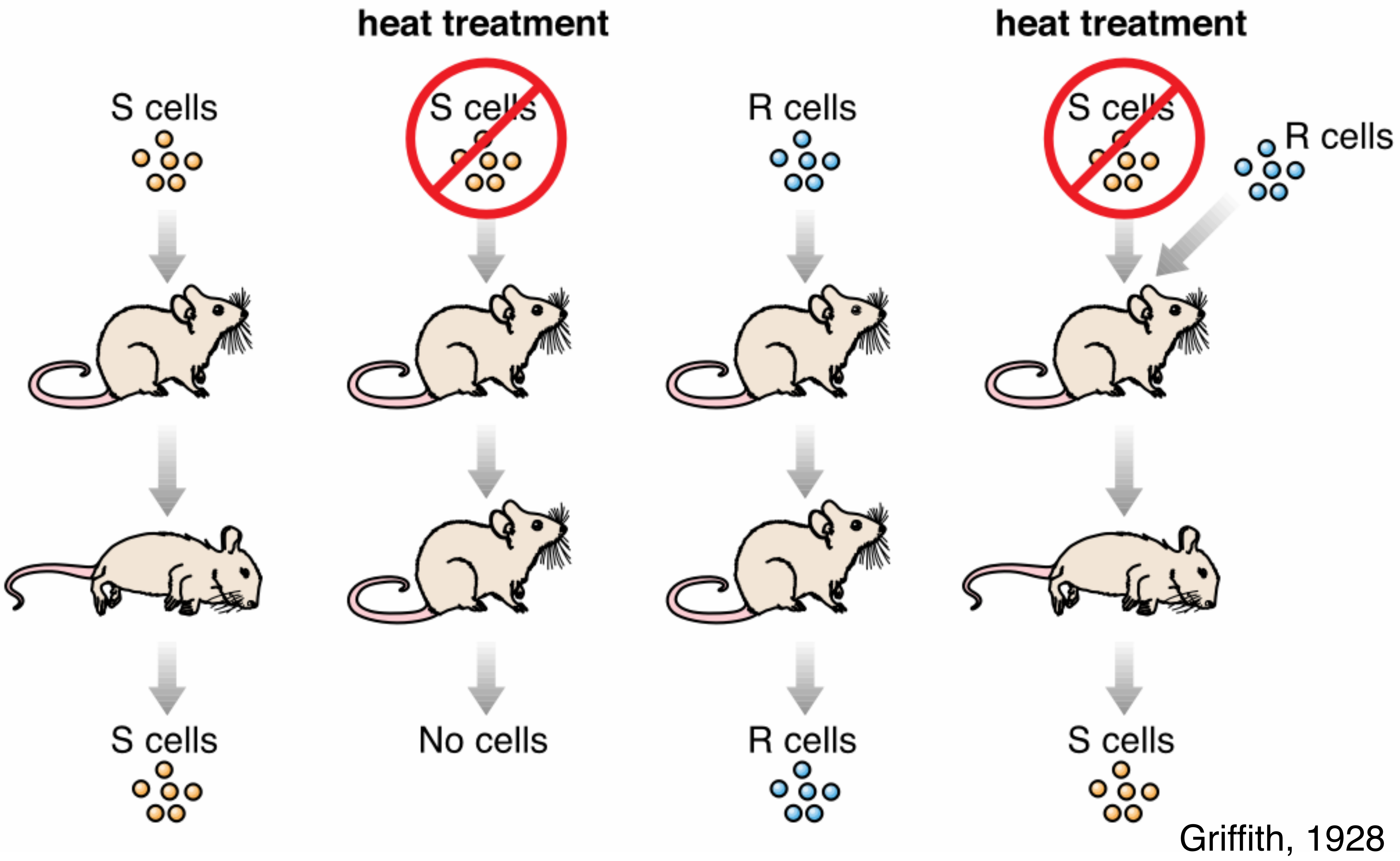
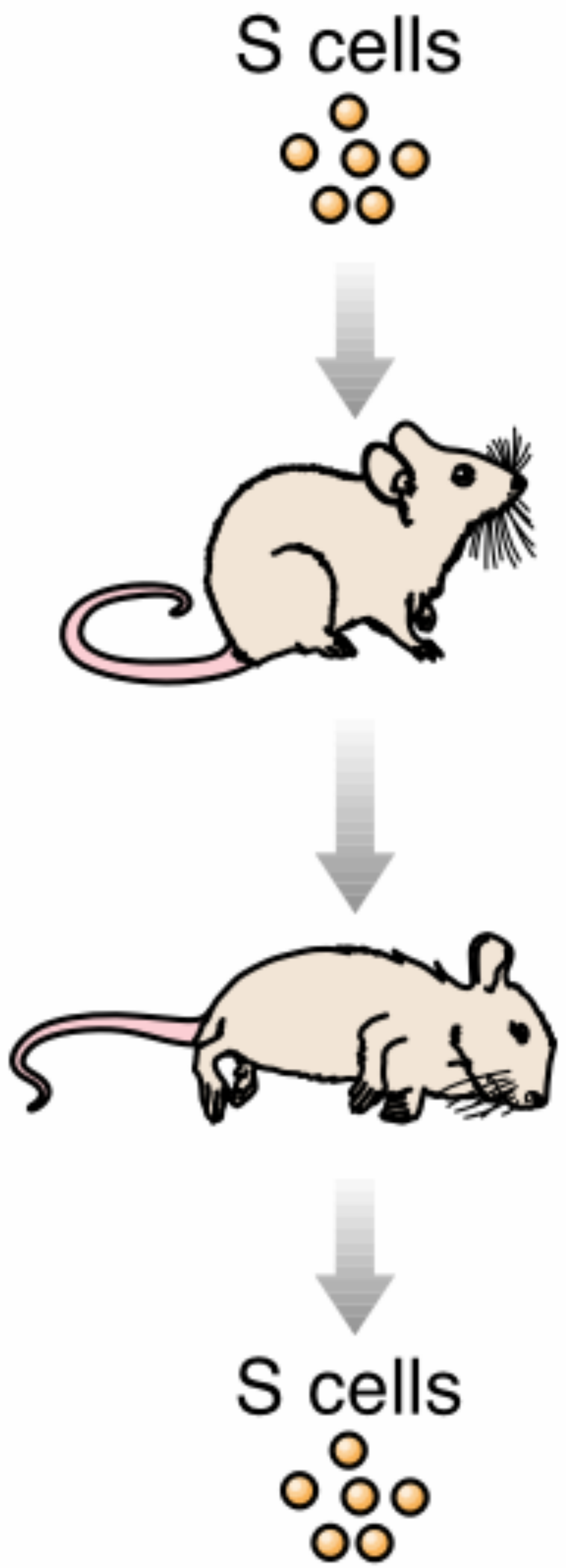


Fig. 1.3

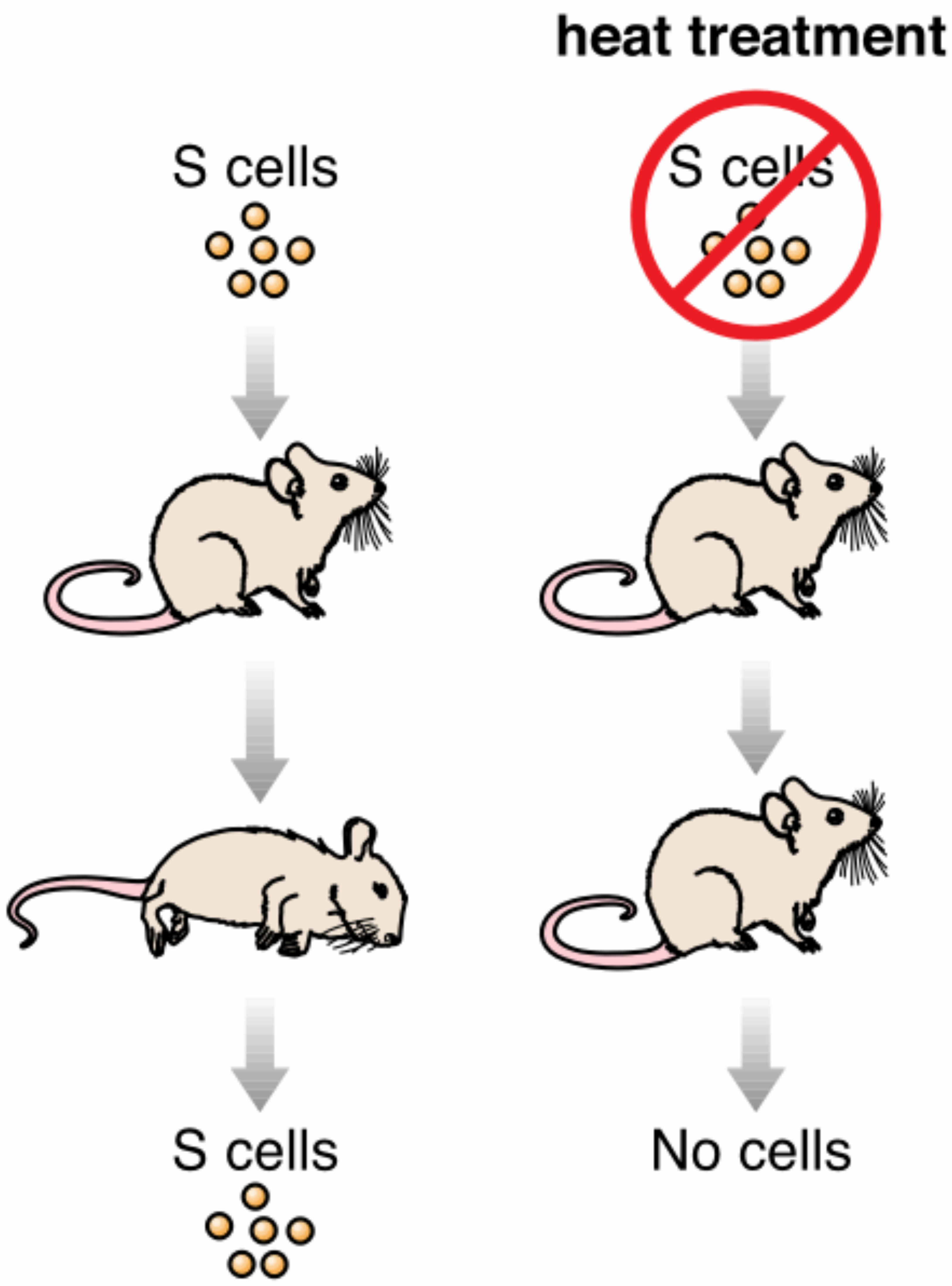
Griffith's Experiments



Griffith, 1928

Fig. 1.3

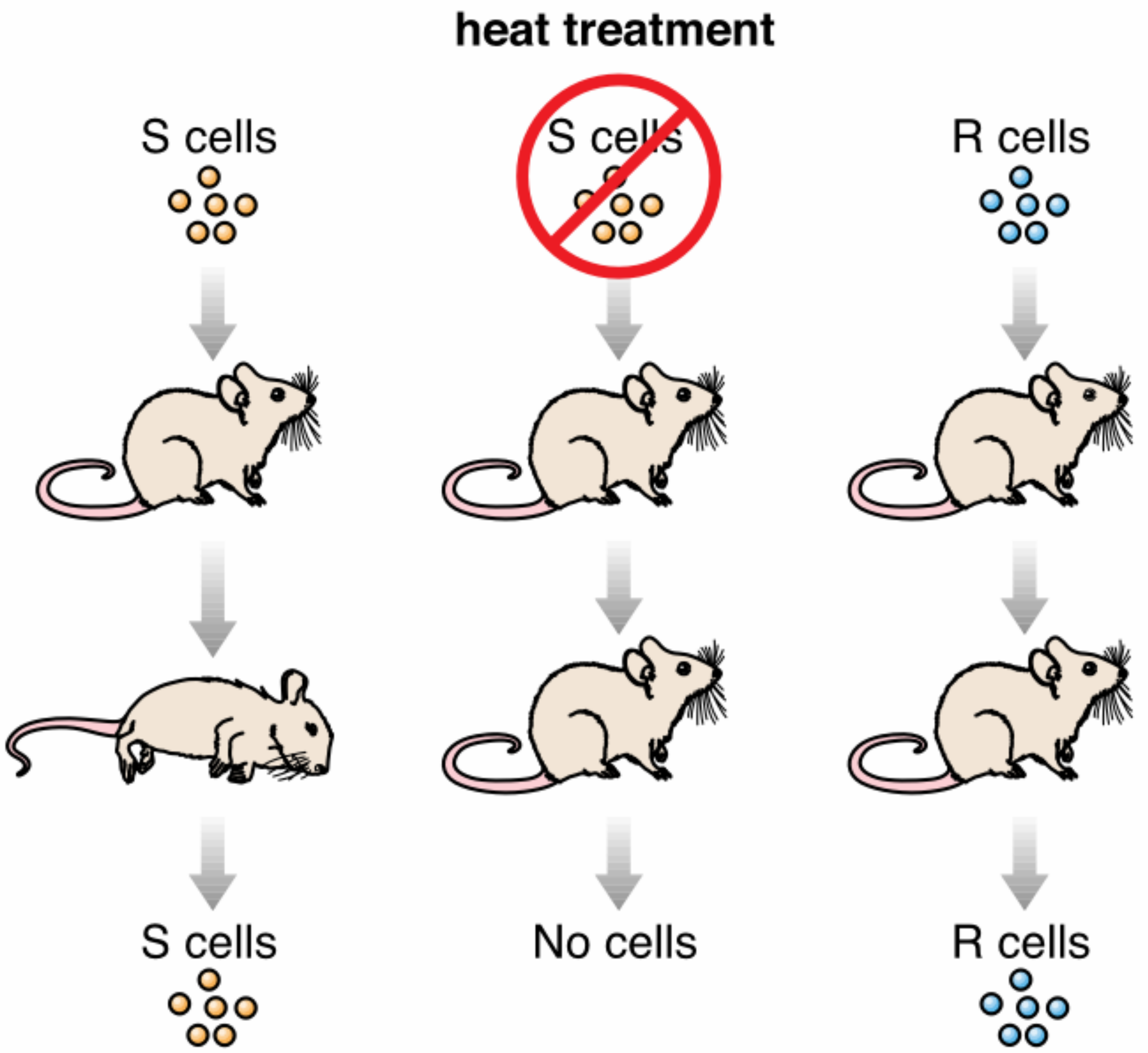
Griffith's Experiments



Griffith, 1928

Fig. 1.3

Griffith's Experiments



Griffith, 1928

Fig. 1.3

Griffith's Experiments

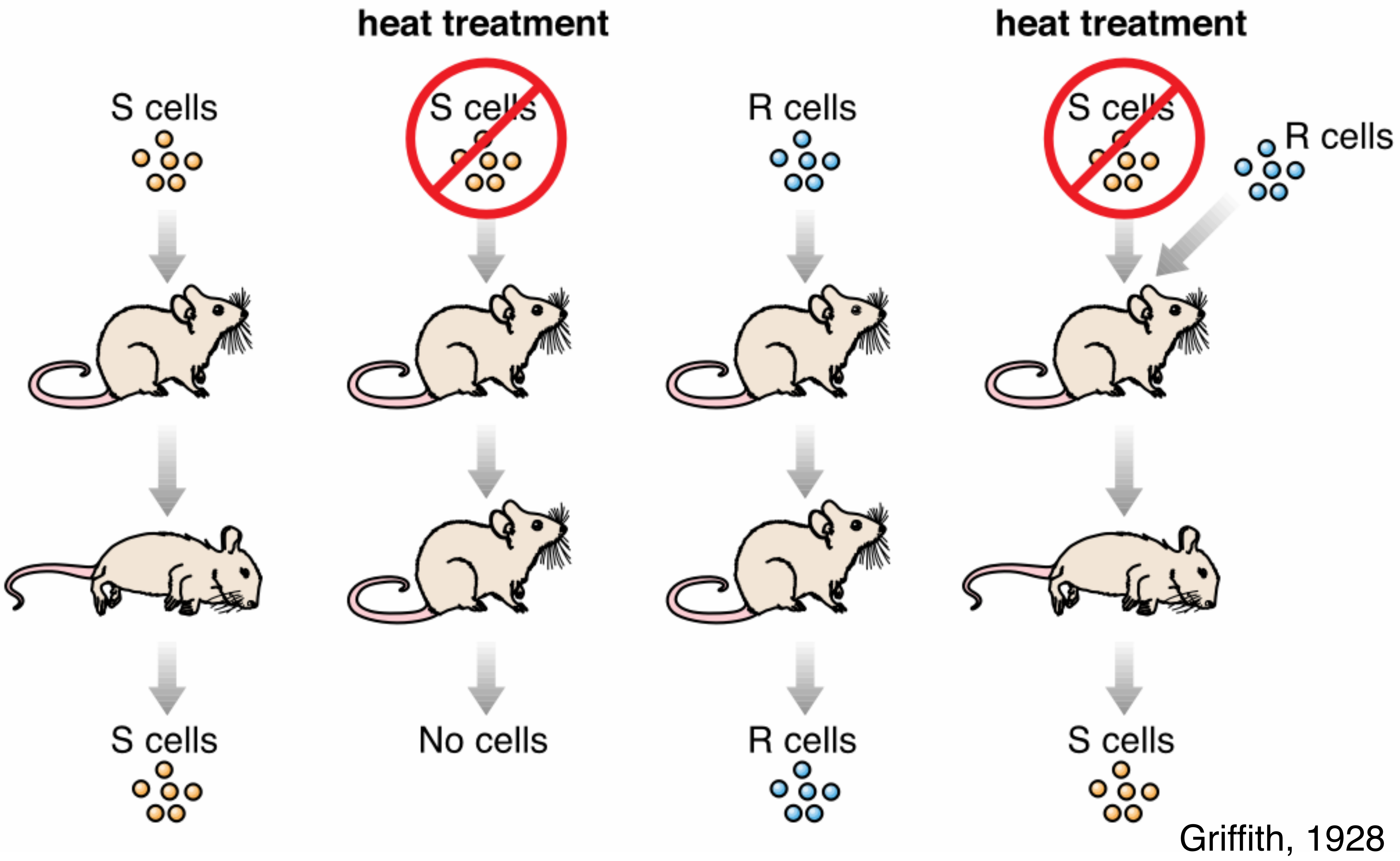


Fig. 1.3

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?

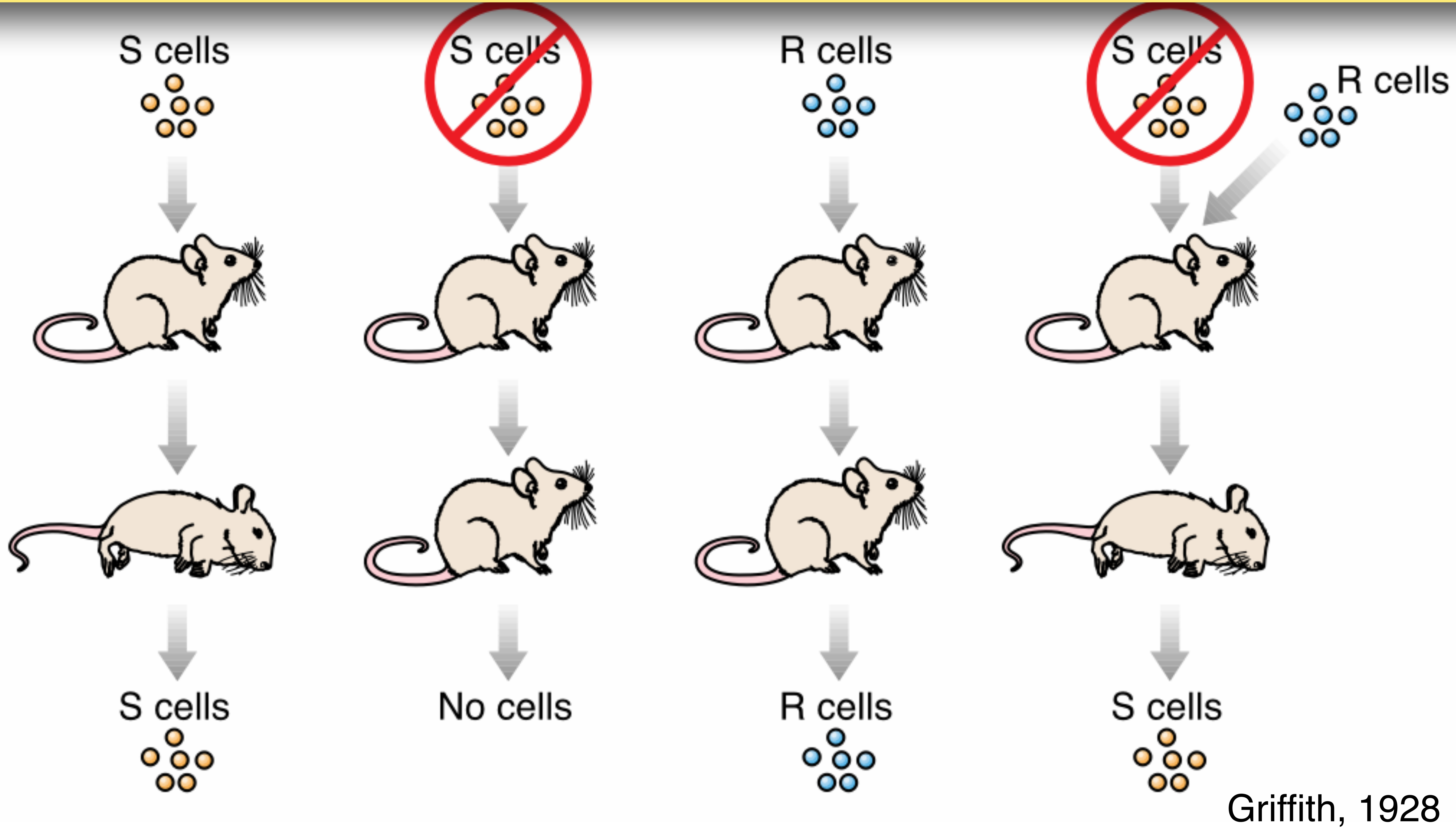


Fig. 1.3

Integrating Questions

3. Summarize how biologists used mathematics to draw the reasonable conclusion that proteins would be a better heritable material than DNA.

VOLUME XXVII JANUARY, 1928 No. 2

THE SIGNIFICANCE OF PNEUMOCOCCAL TYPES.

BY FRED. GRIFFITH, M.B.

(*A Medical Officer of the Ministry of Health.*)

(*From the Ministry's Pathological Laboratory.*)

CONTENTS.

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

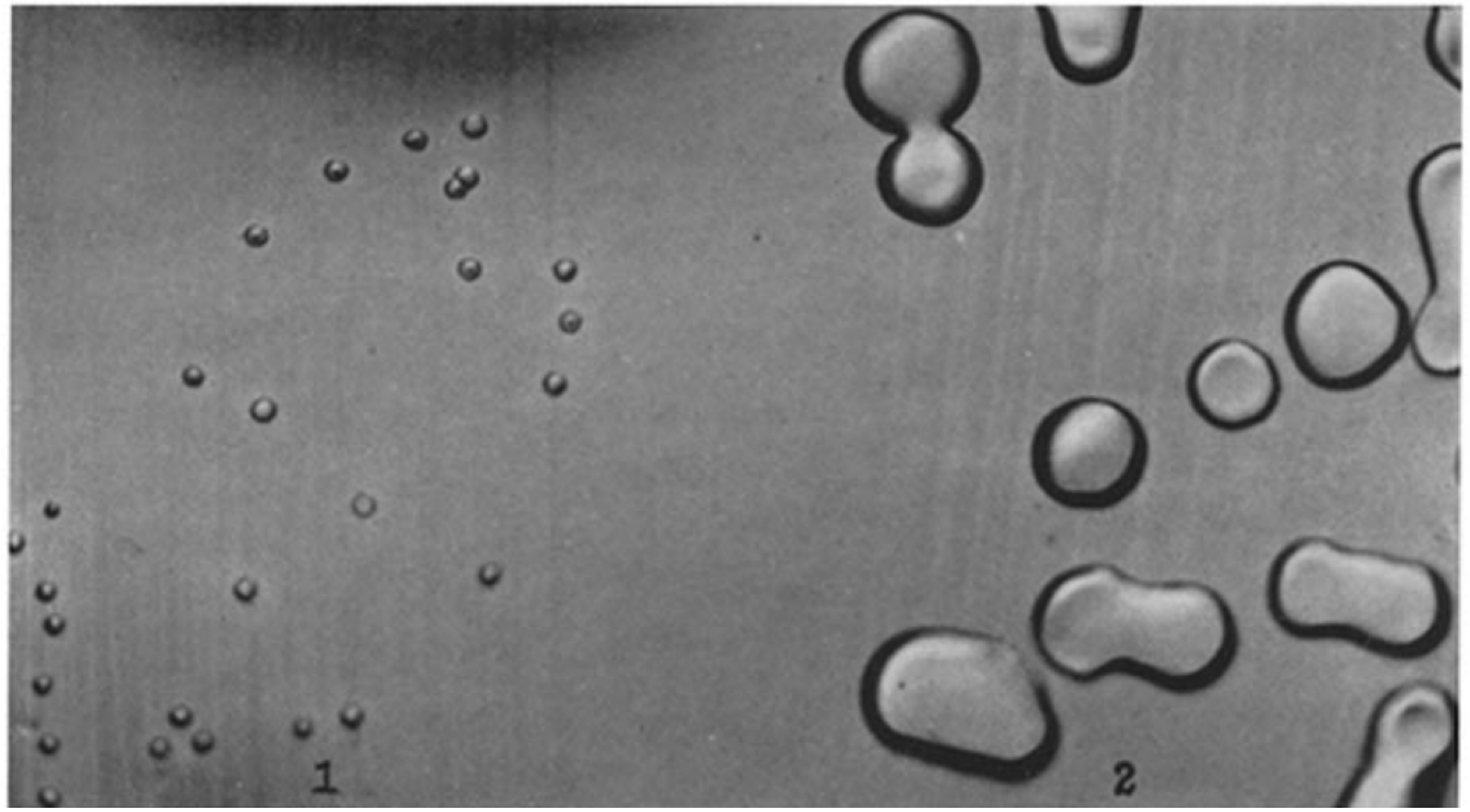
STUDIES ON THE CHEMICAL NATURE OF THE SUBSTANCE INDUCING TRANSFORMATION OF PNEUMOCOCCAL TYPES

Induction of Transformation by a Desoxyribonucleic Acid Fraction Isolated from Pneumococcus Type III

By OSWALD T. AVERY, M.D., COLIN M. MacLEOD, M.D., and MACLYN McCARTY,* M.D.

(*From the Hospital of The Rockefeller Institute for Medical Research*)

Plate 1



The photograph was made by Mr. Joseph B. Haulenbeek.

Fig. 1. Colonies of the R variant (R36A) derived from Pneumococcus Type II. Plated on blood agar from a culture grown in serum broth in the absence of the transforming substance. ×3.5.

Fig. 2. Colonies on blood agar of the same cells after induction of transformation during growth in the same medium with the addition of active transforming principle isolated from Type III pneumococci. The smooth, glistening, mucoid colonies shown are characteristic of Pneumococcus Type III and readily distinguishable from the small, rough colonies of the parent R strain illustrated in Fig. 1. ×3.5.

JOURNAL OF BACTERIOLOGY, Dec. 2004, p. 8164–8171 Vol. 186, No. 24
0021-9193/04/$08.00+0 DOI: 10.1128/JB.186.24.8164–8171.2004

Pyruvate Oxidase Is a Determinant of Avery's Rough Morphology

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Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Indiana

Received 13 July 2004/Accepted 10 September 2004

In pioneering studies, Avery et al. identified DNA as the hereditary material (A. T. Avery, C. M. MacLeod, and M. McCarty, J. Exp. Med. 79:137–158, 1944). They demonstrated, by means of variation in colony morphology, that this substance could transform their rough type 2 *Streptococcus pneumoniae* strain R36A into a smooth type 3 strain. It has become accepted as fact, from modern textbook accounts of these experiments, that smooth pneumococci make capsule, while rough strains do not. We found that rough-to-smooth morphology conversion did not occur in rough strains R36A and R6 when the ability to synthesize native type 2 capsule was restored. The continued rough morphology of these encapsulated strains was attributed to a second, since-forgotten, morphology-affecting mutation that was sustained by R36A during strain development. We

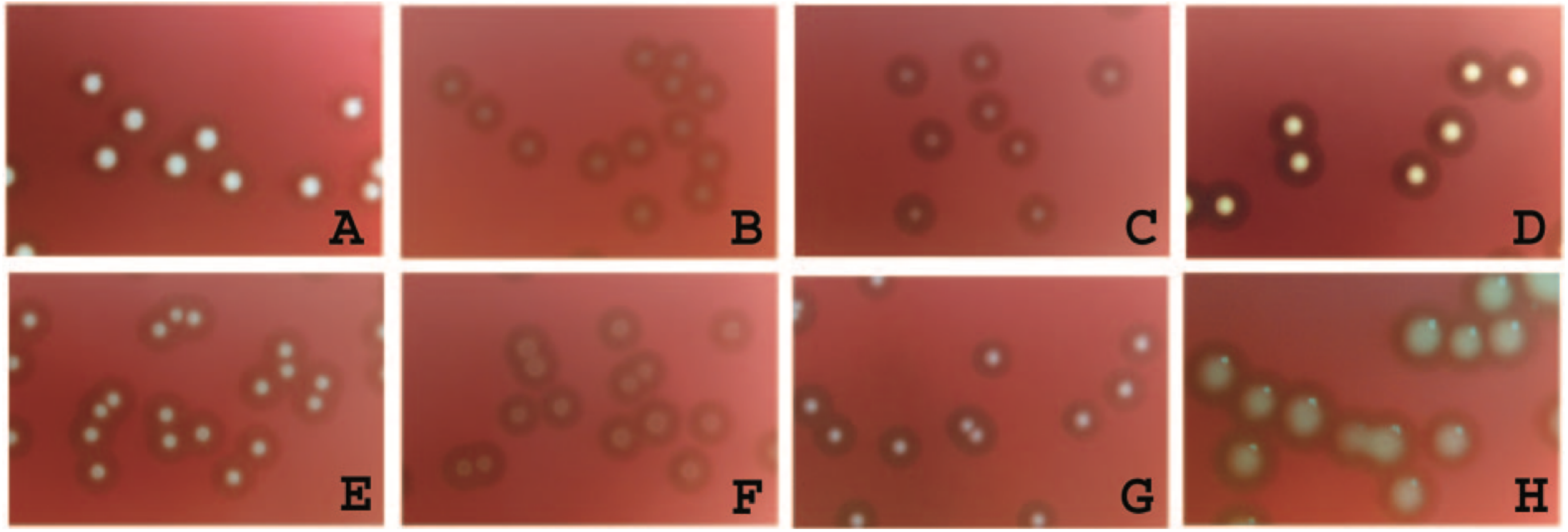

FIG. 3. Colony morphology of various *S. pneumoniae* strains grown on blood agar. (A) D39; (B) R6; (C) AB2; (D) AB7; (E) AB28; (F) R36A; (G) AB14; (H) AB15.

If grading this Methods section…?

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^{o} 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.

STUDIES ON THE CHEMICAL NATURE OF THE SUBSTANCE INDUCING TRANSFORMATION OF PNEUMOCOCCAL TYPES

INDUCTION OF TRANSFORMATION BY A DESOXYRIBONUCLEIC ACID FRACTION ISOLATED FROM PNEUMOCOCCUS TYPE III

BY OSWALD T. AVERY, M.D., COLIN M. MACLEOD, M.D., AND MACLYN McCARTY,* M.D.

(From the Hospital of The Rockefeller Institute for Medical Research)

PLATE 1

(Received for publication, November 1, 1943)

Biologists have long attempted by chemical means to induce in higher organisms predictable and specific changes which thereafter could be transmitted in series as hereditary characters. Among microörganisms the most striking example of inheritable and specific alterations in cell structure and function that can be experimentally induced and are reproducible under well defined and adequately controlled conditions is the transformation of specific types of Pneumococcus. This phenomenon was first described by Griffith (1) who succeeded in transforming an attenuated and non-encapsulated (R) variant derived from one specific type into fully encapsulated and virulent (S) cells of a heterologous specific type. A typical instance will suffice to illustrate the techniques originally used and serve to indicate the wide variety of transformations that are possible within the limits of this bacterial species.

Griffith found that mice injected subcutaneously with a small amount of a living R culture derived from Pneumococcus Type II together with a large inoculum of

for desoxyribonucleic acid is strongly positive. The orcinol test (Bial) for ribonucleic acid is weakly positive. However, it has been found that in similar concentrations pure preparations of desoxyribonucleic acid of animal origin prepared by different methods give a Bial reaction of corresponding intensity.

Although no specific tests for the presence of lipid in the purified material have been made, it has been found that crude material can be repeatedly extracted with alcohol and ether at −12°C. without loss of activity. In addition, as will be noted in the preparative procedures, repeated alcohol precipitation and treatment with chloroform result in no decrease in biological activity.

Elementary Chemical Analysis.[1]—Four purified preparations were analyzed for content of nitrogen, phosphorus, carbon, and hydrogen. The results are presented in Table I. The nitrogen-phosphorus ratios vary from 1.58 to 1.75 with an average value of 1.67 which is in close agreement with that calculated

TABLE I

Elementary Chemical Analysis of Purified Preparations of the Transforming Substance

Preparation No.	Carbon	Hydrogen	Nitrogen	Phosphorus	N/P ratio
	per cent	*per cent*	*per cent*	*per cent*	
37	34.27	3.89	14.21	8.57	1.66
38B	—	—	15.93	9.09	1.75
42	35.50	3.76	15.36	9.04	1.69
44	—	—	13.40	8.45	1.58
Theory for sodium desoxyribonucleate.....	34.20	3.21	15.32	9.05	1.69

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.

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.
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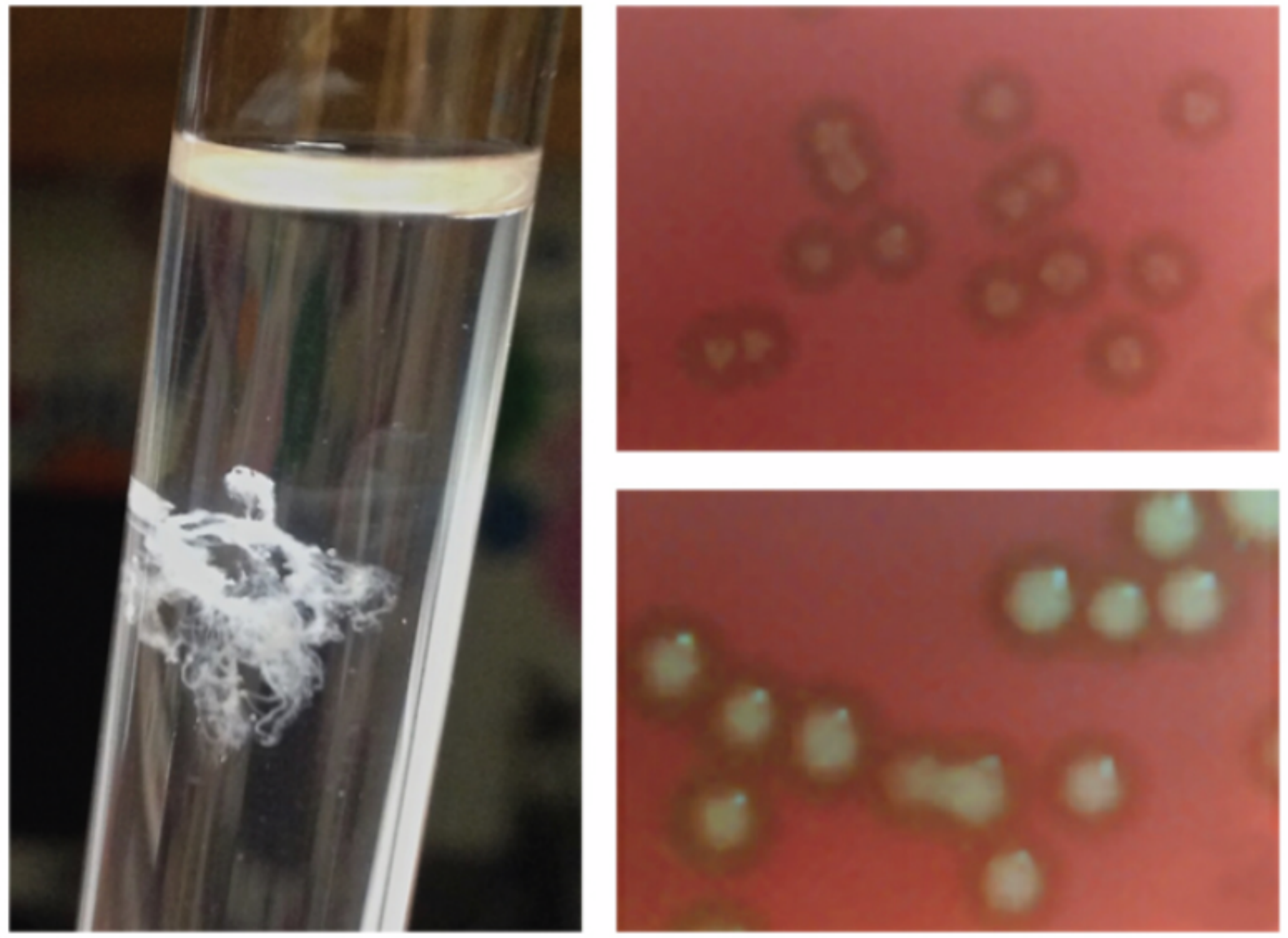
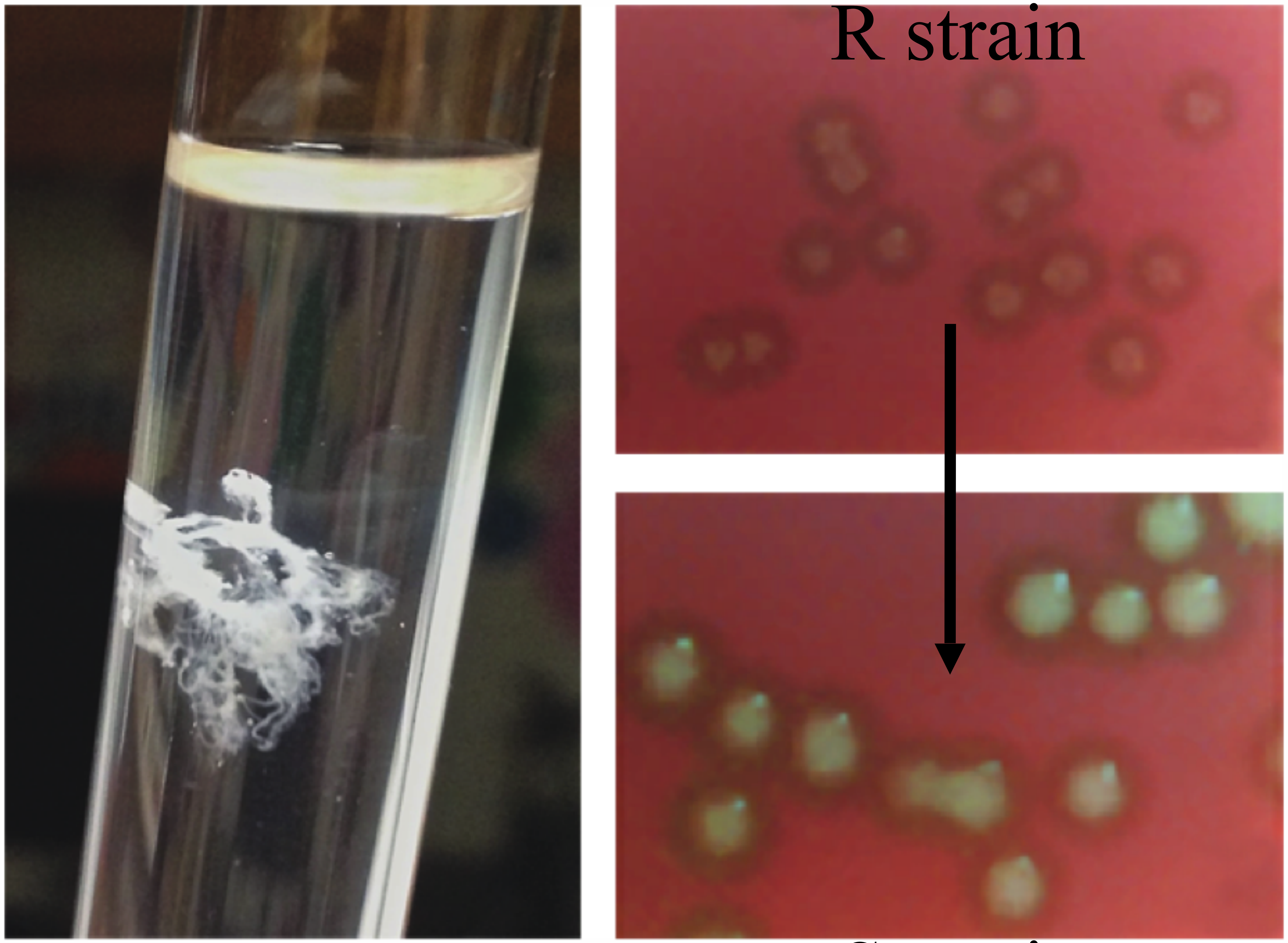


A B

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.

Cell Extract Determines Phenotype



A B

S strain

Avery, 1944

Fig. 1.4

courtesy of Abagael Slattery and from Belanger et al. 2004

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

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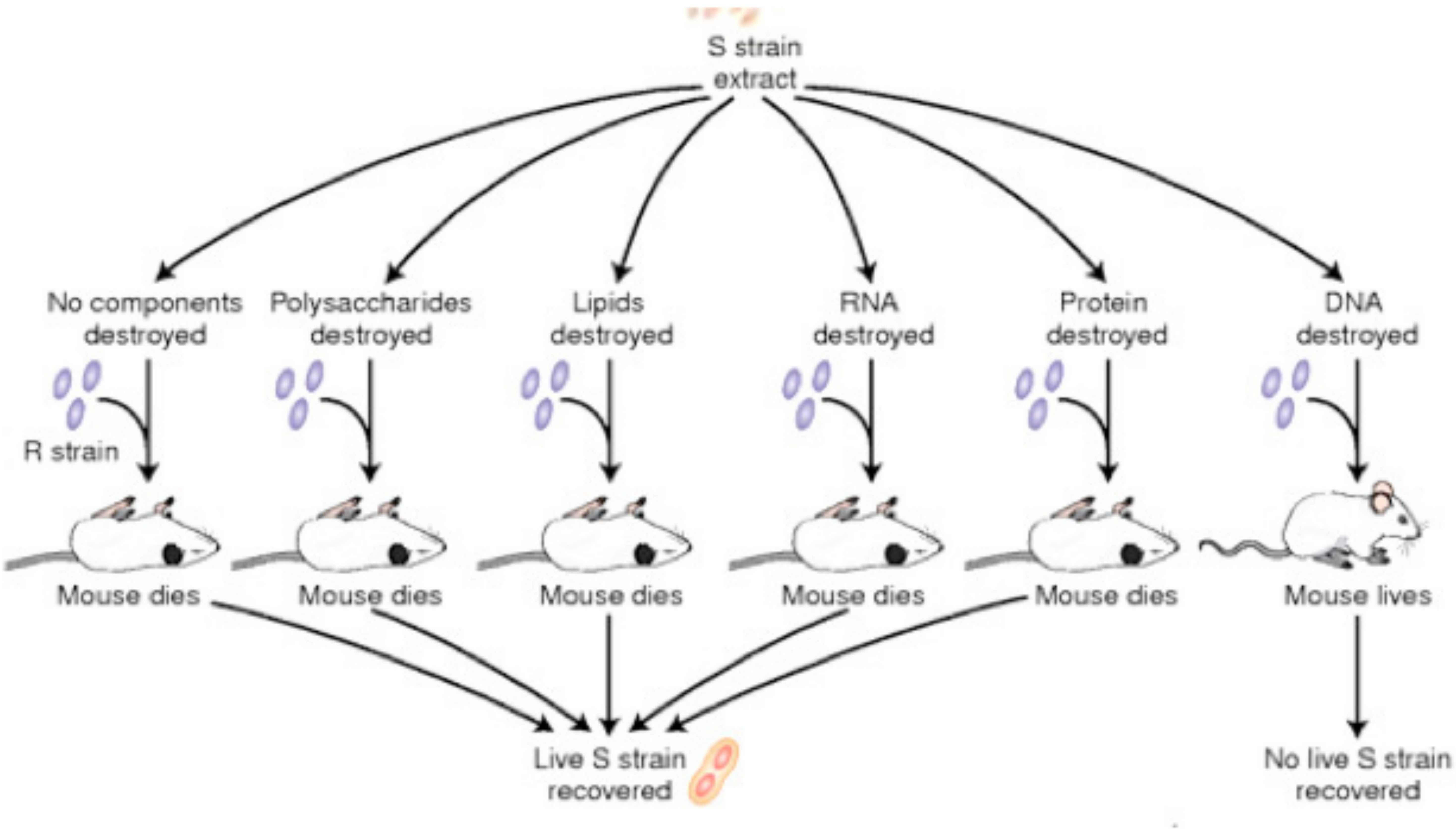
nitrogen/phosphorous ratios of transforming factor ≈ DNA

Table 1.1

Avery’s experiments (1944)



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

“Welcome to Mars”
LB144-Pandemic edition