NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

Classic Experiments in Molecular Biology

The Transforming Principle: Identifying the Molecule of Inheritance

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Part I – Molecule of Inheritance

If there's inheritance of traits from parents to children, or from "mother cell" to "daughter cells" in mitosis, then some *thing* must be passed from parent to child. We know today that this *thing* is DNA, in the form of chromosomes. However, someone needed to figure that out!

In the 1930s and 1940s, scientists were very interested in identifying the biochemical nature of the "transforming principle." The candidate molecules were DNA, RNA, and protein. These molecules were candidates because we knew that nuclei contained chromosomes which are associated with phenotypes (think Morgan's fruit fly eye color experiments where eye color corresponded to the X- or Y- chromosome content of the fly cells), and isolated nuclei are composed mostly of protein, DNA, and RNA. Most scientists at the time were leaning toward protein being the genetic material because it is the most molecularly diverse of the three.

The investigations into the chemical nature of genetic material were initiated by one very important paper from 1928, written by Fred Griffith at the British Ministry of Health. Griffith was studying the bacterium *Streptococcus pneumoniae*, an important pathogen in the 1920s.

Question

1. Why would studying *S. pneumoniae* be an important topic in the 1920s?

Some forms of *S. pneumoniae* cause disease (pneumonia), others don't. When grown on a laboratory plate, you can make a good guess about the pathogenicity (disease-causing ability) of *S. pneumoniae* because *pathogenic* strains look shiny (smooth) due to a polysaccharide cell coat called a capsule (right side of the picture). The capsule helps the bacteria "hide" from the immune system long enough to cause disease. *Nonpathogenic* strains lack the capsule and appear "rough" on a petri plate (left side of the picture). Generally these colonies are smaller, too.

Griffith used mice as his species for detecting the pathogenicity of the bacteria. Injecting mice with bacteria grown on petri plates either made the mice sick and killed them, or produced no disease.

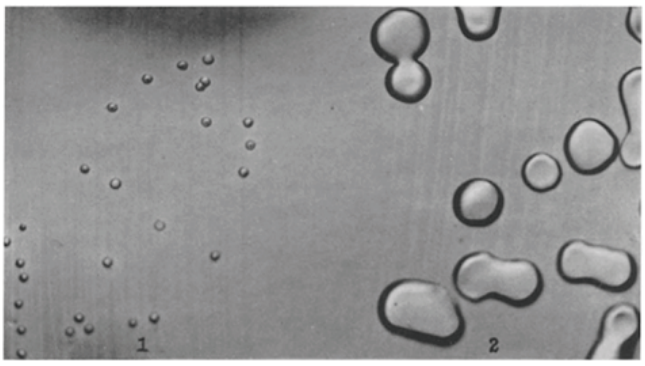
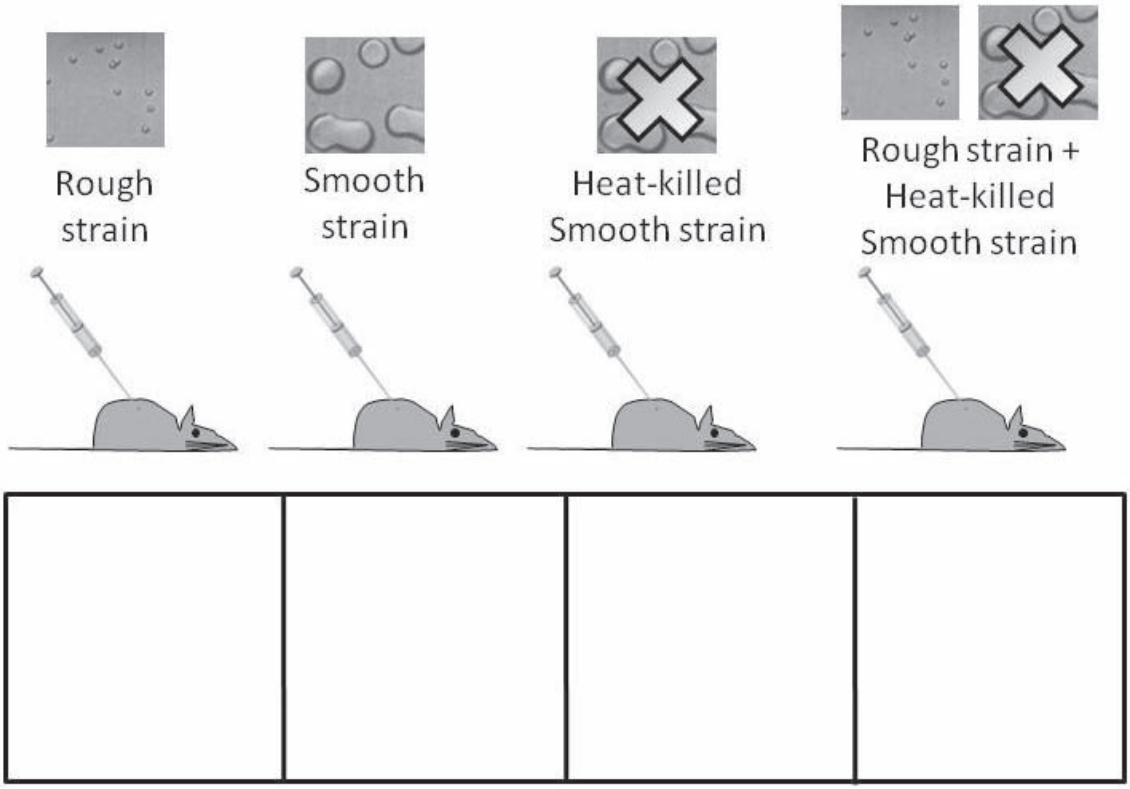


Image credit: Photograph by Joseph B. Haulenbeek, from Avery et al., *Journal of Experimental Medicine* 79 (2): 137–158. ©1944 Rockefeller University Press, used in accordance with the Creative Commons Attribution-Noncommercial-Share Alike 3.0 Unported license.

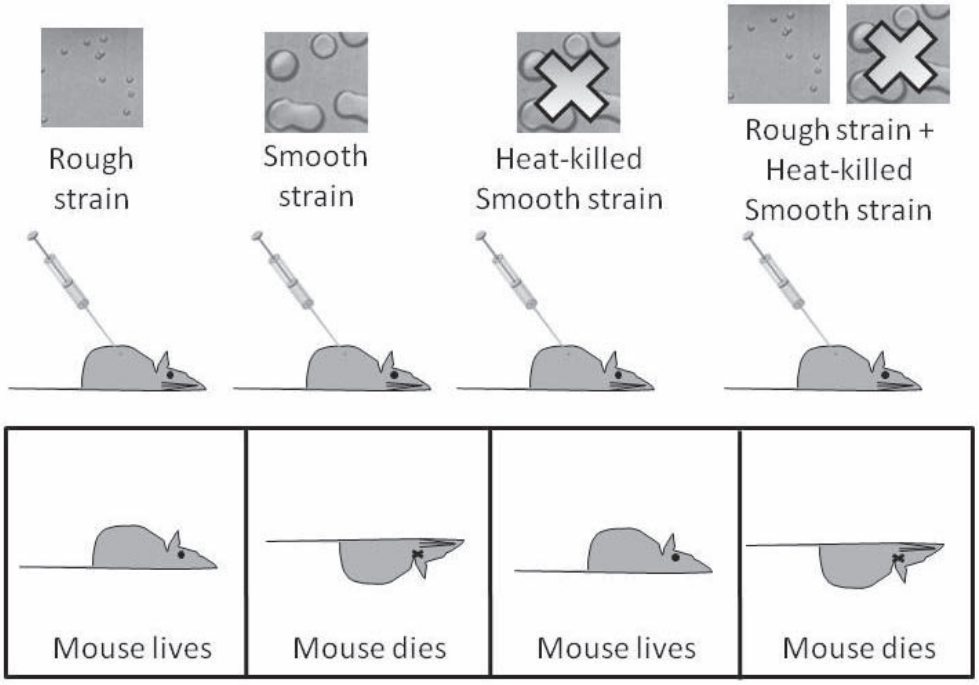
Question

2. Fill out the table below the diagram predicting what you think will happen as a result of each injection (mice live or mice die).



Part II – Results

Here are the actual results of the experiment.



Questions

1. Which of the four treatments are controls? Explain your answer.
2. Which of the results is unexpected?
3. What are *two* hypotheses that might explain the unexpected result? In other words, what might be going on in the system?

Part III – Enzymes as Tools

The properties of the rough strain are its *phenotype*. In the experiment you just read about, the *phenotype* of the living rough strain changed from nonpathogenic to pathogenic. Scientists proposed that it changed because the *genotype* changed. The next set of experiments started with the hypothesis that the *genotype change* was due to some extra genetic material being added to the rough bacteria to change their *phenotype* to a smooth phenotype.

The group of scientists who did the next set of experiments consisted of Oswald Avery, Colin MacLeod, and Maclyn McCarty. Their paper was published in 1944. These scientists had three tools to use in their experiments (in addition to the smooth and rough strains, and mice):

1. Proteases

2. DNase

3. RNase

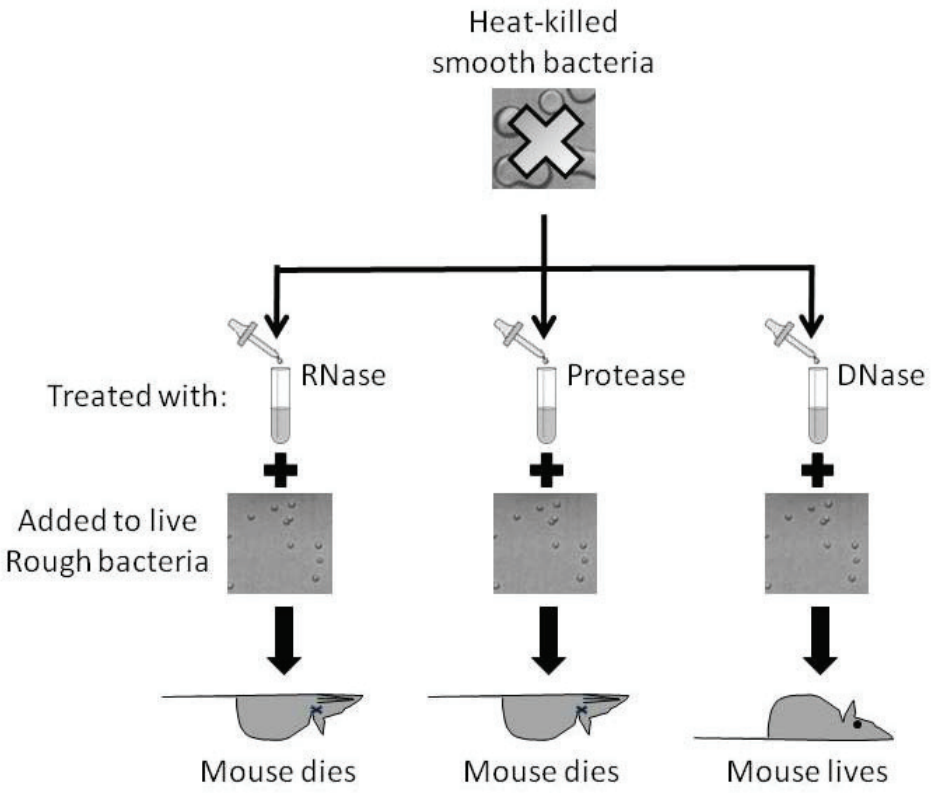
All three of these tools are enzymes, as you can guess because their names end in "ase."

Questions

1. Given the names of these three enzymes, what reaction do you expect each one to catalyze? Write your answers in the space to the right of the name above.
2. How could you treat dead smooth bacteria with these enzymes to determine whether DNA, RNA, or protein is the genetic material?

Part IV –More Results

The scientists treated heat-killed smooth bacteria with either RNase, Protease, or DNase, then combined that reaction with living rough bacteria and injected mice with the mixture. The results are shown in the diagram.



Question

1. What conclusion can be drawn from these data?

Take-Home Assignment

Address the following using a well-constructed essay paragraph. If you use diagrams, you must have text to thoroughly explain the diagrams rather than just drawing a picture.

Describe the experiments by Griffith, Avery, McCarty, and McLeod that determined the role for DNA as the genetic material (include the logic behind the experiment).

References

Avery, O.T., CM. MacLeod, and M. McCarty (1944). 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. *Journal of Experimental Medicine* 79 (2): 137–158.

Griffith, F. (1928). The significance of pneumococcal types. *Journal of Hygiene* 27 (2): 113–59.

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