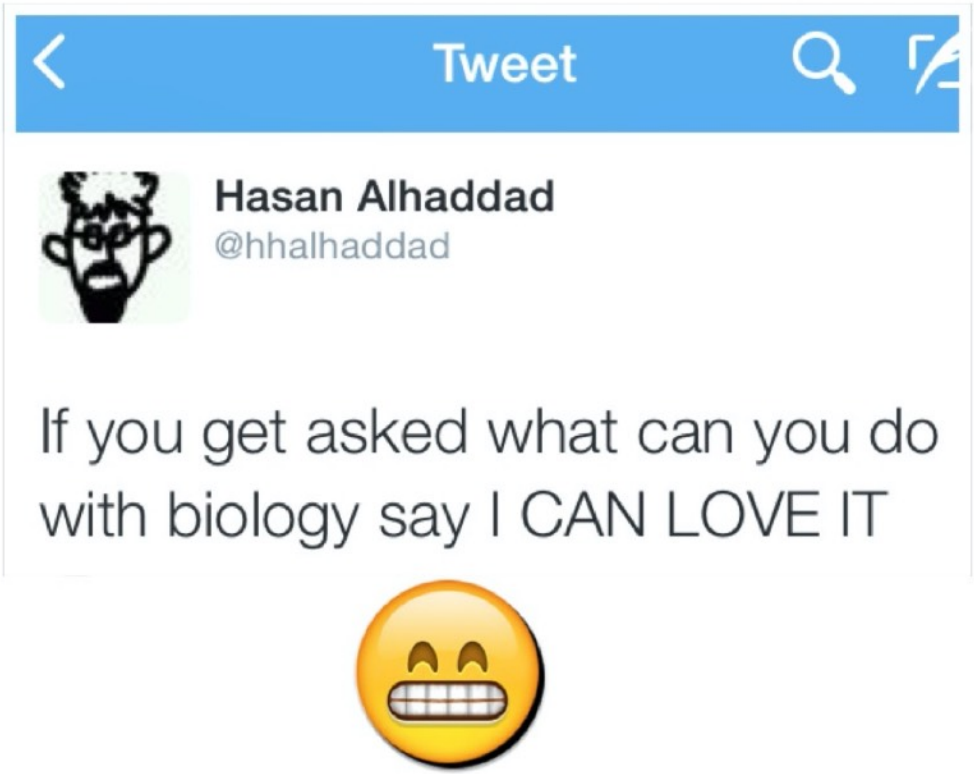
Lecture 3:

The identity and location of the genetic material

Course 281

Introduction to Molecular Biology

Lessons for life

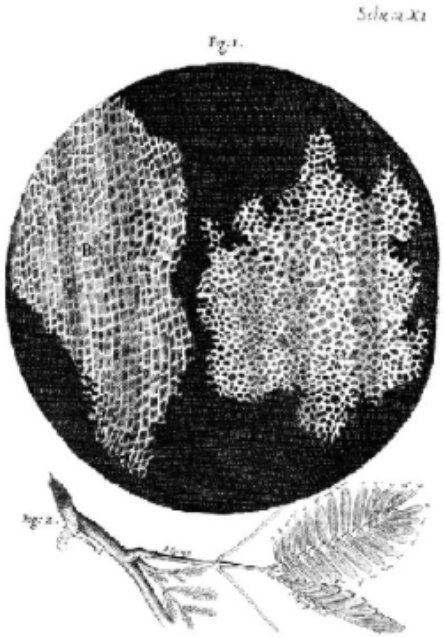


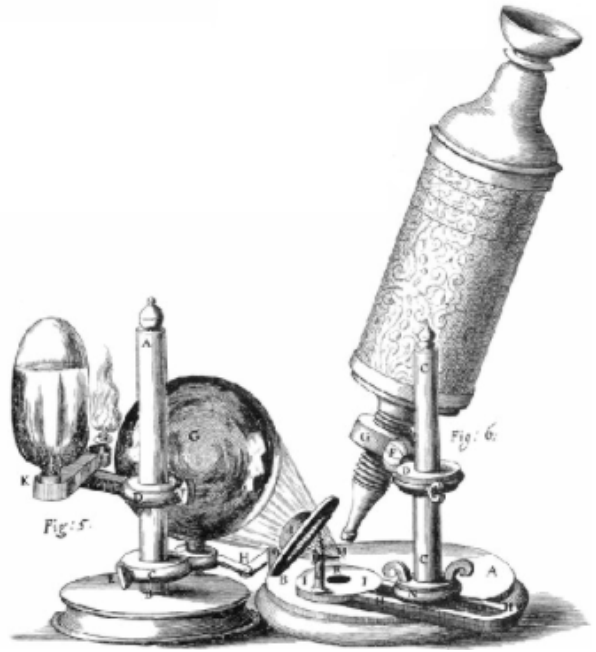
Aims

- Introduce the experiments that led to discovering the identity of the genetic material.
- Explain the progression of scientific thought and evidence associated with DNA discovery.
- Explain when the lines of evidence were sufficient to conclude DNA is the genetic material.

The cell

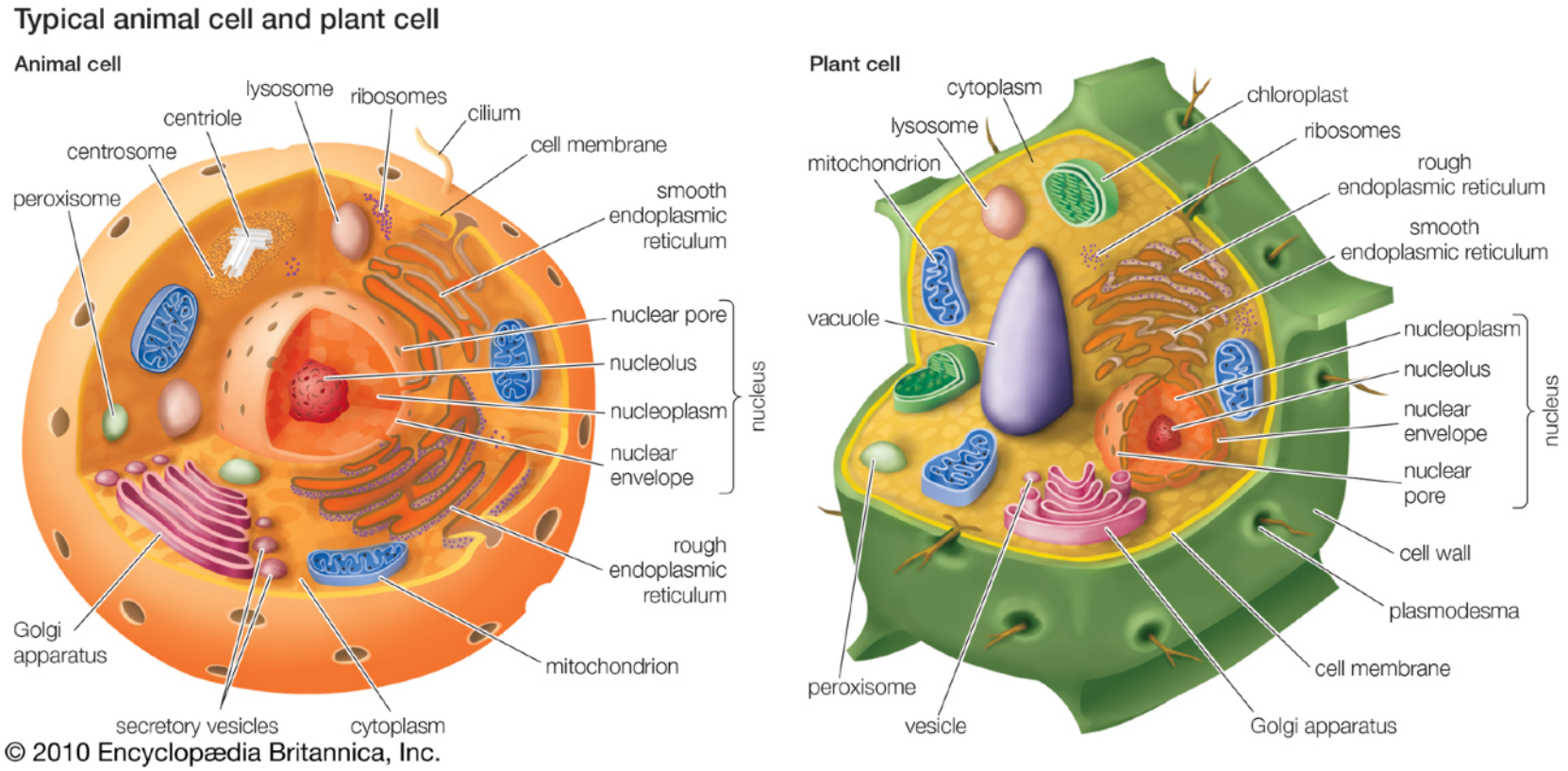
especially to the then radical new cell theory. Back in 1663, the English natural philosopher Robert Hooke had looked at cork, a tree-bark, through an early microscope. He observed the regular, empty spaces in the cork, which reminded him of the rows of tiny rooms in which monks lived, so he dubbed them 'cells'. The name





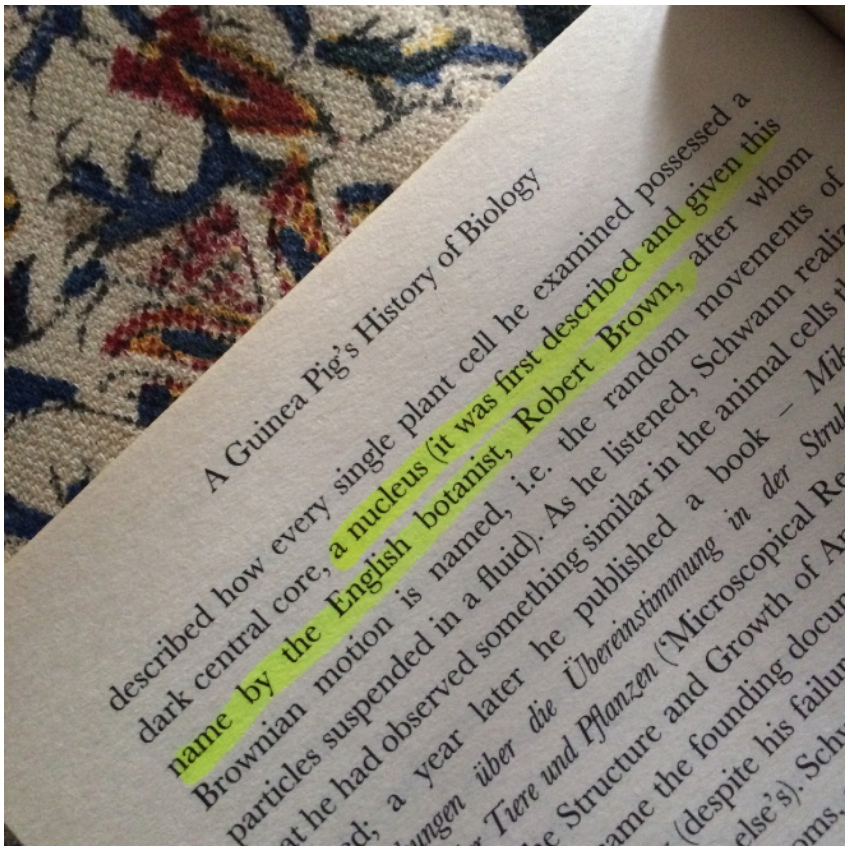
Cells

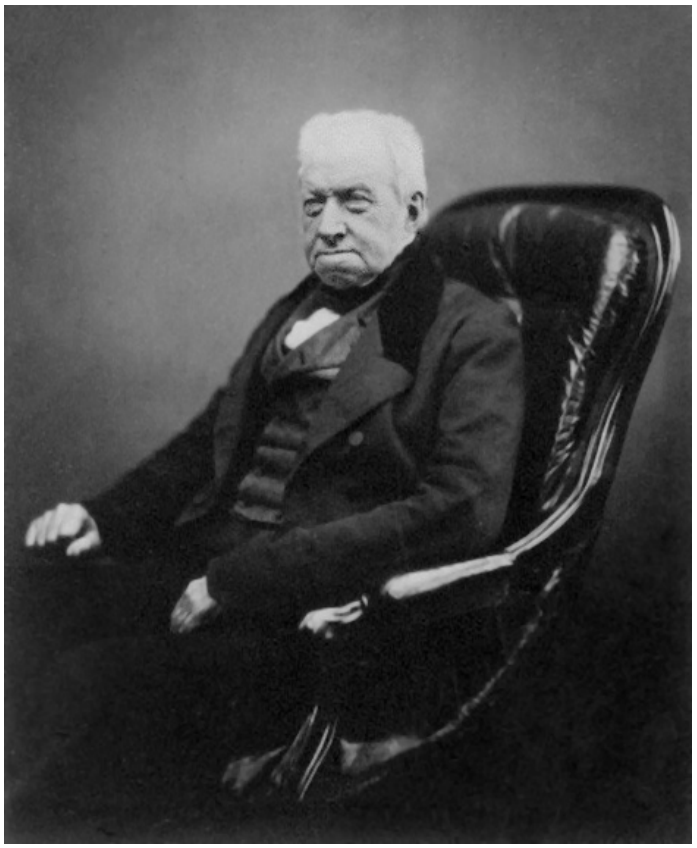
Mid 1800s, animals and plants are made of cells. Cells divide but do not know how.



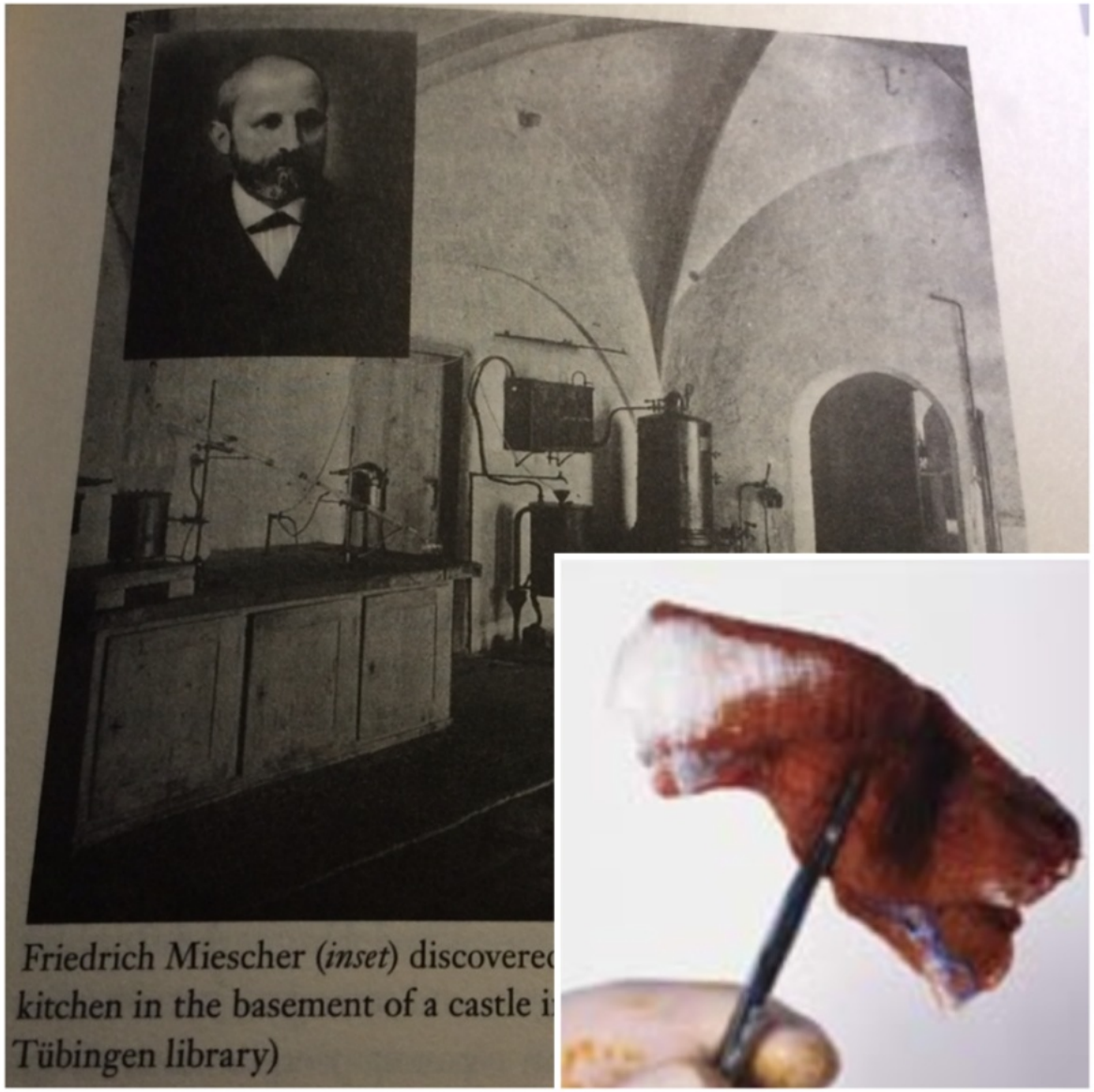
The nucleus

A specific part was identified as the nucleus and it has specific chemical and physical characteristics.



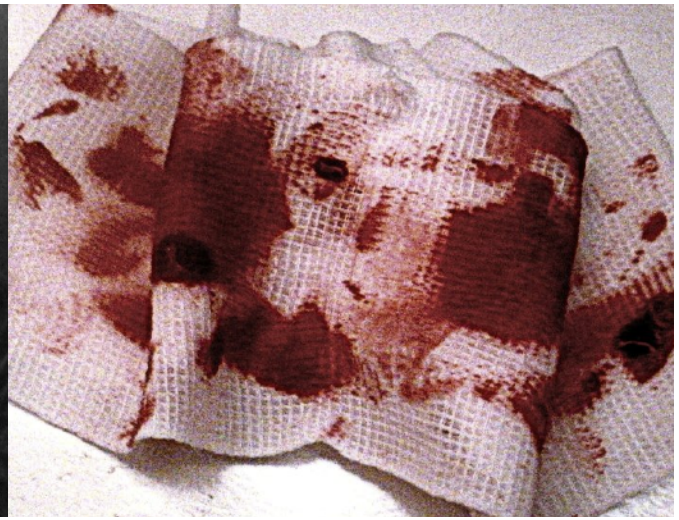


Nuclein



Friedrich Miescher (*inset*) discovered
kitchen in the basement of a castle i
Tübingen library)

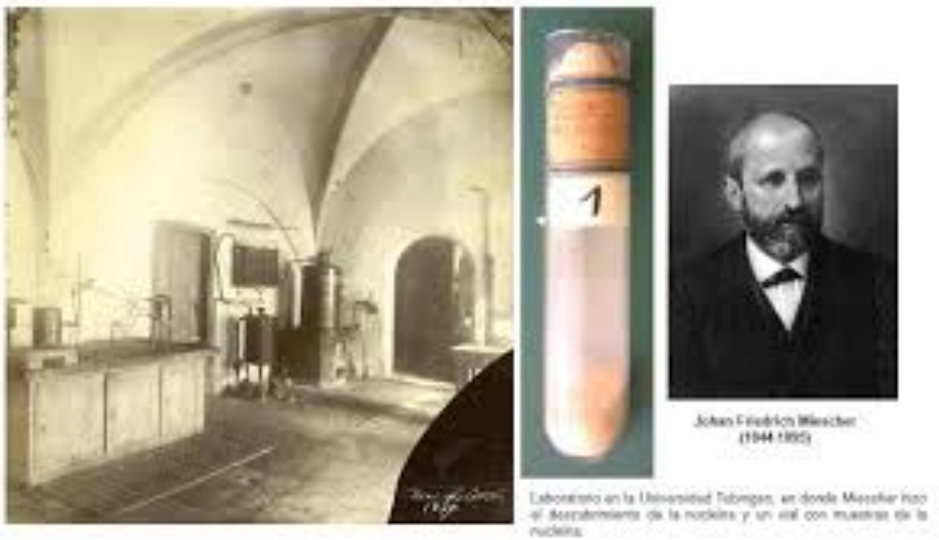
Nuclein



Fredrick Miescher
bloody bandages
(1869)

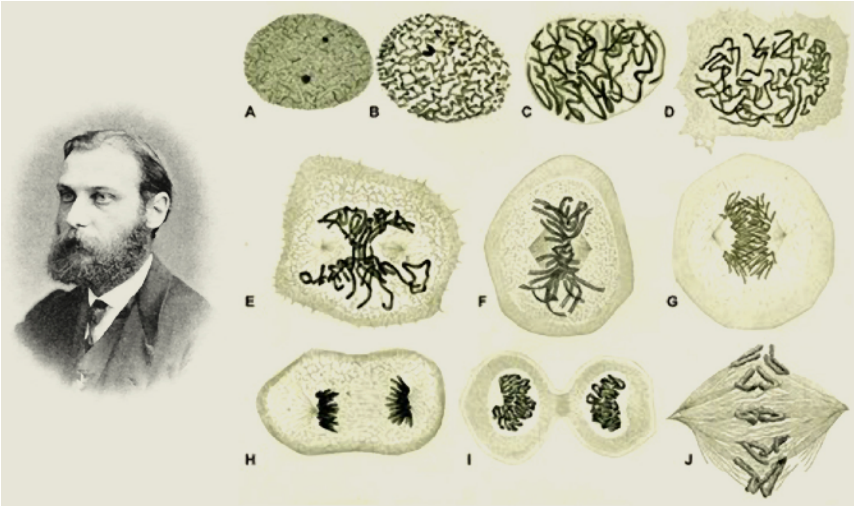
- Bloody bandages as a source of cells.
- When added HCl, got pure nuclei (singular = nucleus).
- When adding a base then an acid to the nuclei, got a gray precipitate.

Nuclein



- The molecule is different than other molecules (contain C, O, N, H, and P – not known to be in proteins).
- Since the molecule came from nucleus, he called it **Nuclein (today called DNA)**.

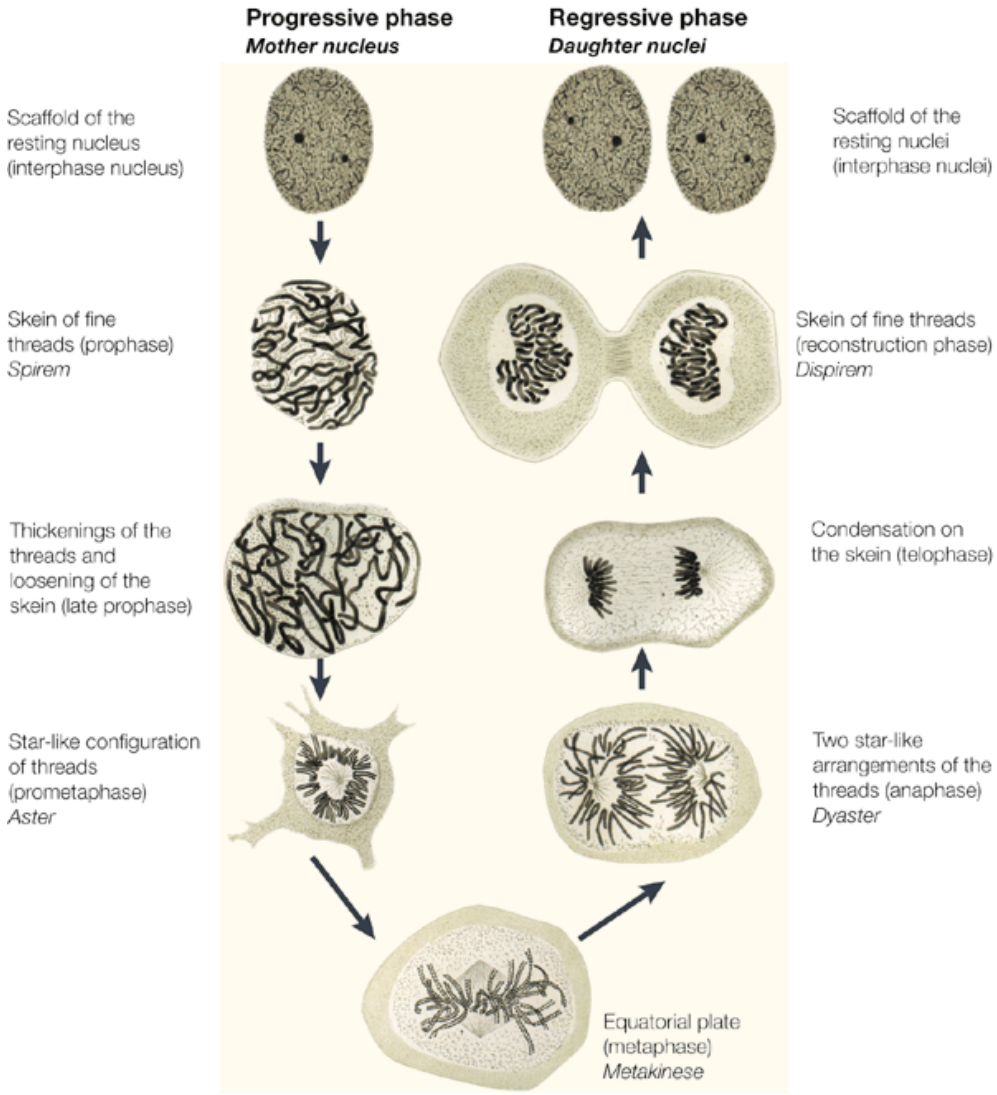
Chromatin



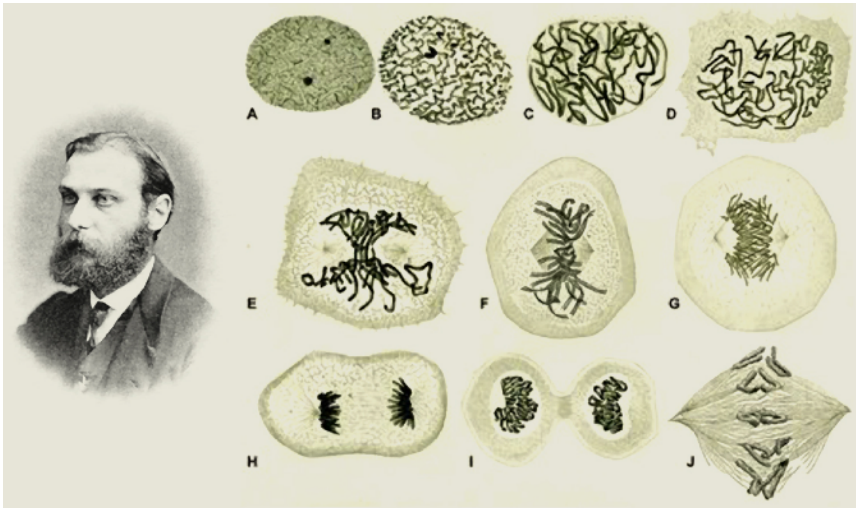
Walther Flemming band structure in dividing cells (1879)

- Used cells of salamanders and staining techniques to study cell division (he called it mitosis).
- The intensely stained parts of the nucleus he called **chromatin** (chroma is Greek for color).

Chromatin


Progressive phase
Mother nucleus
Regressive phase
Daughter nuclei
Scaffold of the resting nucleus (interphase nucleus)
Skein of fine threads (prophase) Spirem
Thickenings of the threads and loosening of the skein (late prophase)
Star-like configuration of threads (prometaphase) Aster
Equatorial plate (metaphase) Metakinese
Two star-like arrangements of the threads (anaphase) Dyaster
Condensation on the skein (telophase)
Skein of fine threads (reconstruction phase) Dispirem
Scaffold of the resting nuclei (interphase nuclei)
Nature Reviews | Molecular Cell Biology

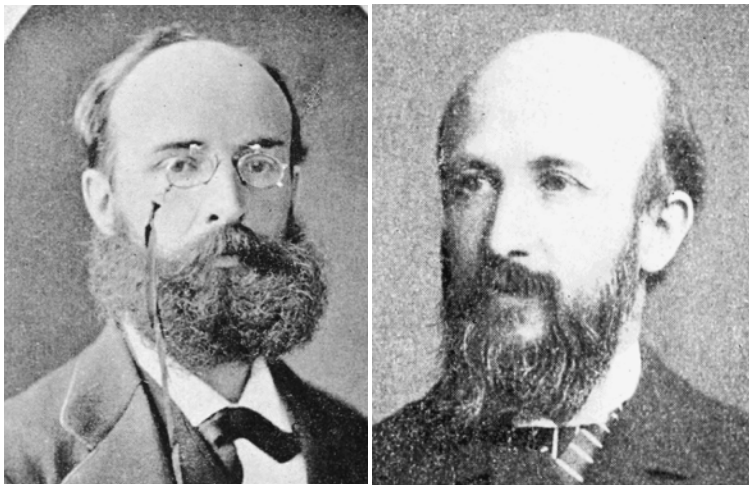
Chromatin



Walther Flemming band structure in dividing cells (1879)

- When a base then an acid added to chromatin, the same gray precipitate is found.
- Conclusion: Miescher's nuclien and chromatin are the same.

Chromosomes



Hermann Fol and Oscar Hertwig (1870-1880)

- Observed fertilization and fusion of the eggs and sperms nuclei.
- Chromatin is called **chromosomes**.

Chromosomes

- **The study of fertilization using light microscopy led to:**
  - Eggs and sperms have equal number of chromosomes.
  - Chromosomes get passed to future generations.
  - By 1890 almost everybody agreed that nuclien = chromatin = chromosomes are the basis of heredity.

Chromosomes and heredity

- Chromosomes are proteins and nucleic acid.

Which one is the genetic molecule?

- Many suspected proteins to be the hereditary molecule because of the high capacity to store info (20 amino acids – now 22) compared to 4 nucleotides in DNA.

Characteristics of genetic material

- **What should the hereditary molecule have?**
  - Contain the information in a stable form.
  - Able to self replicate and pass to future generations.
  - Can be changed (allowing for adaptation and evolution).

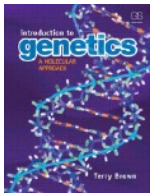
The hereditary molecule

Proteins or DNA?

Need some cool experiments

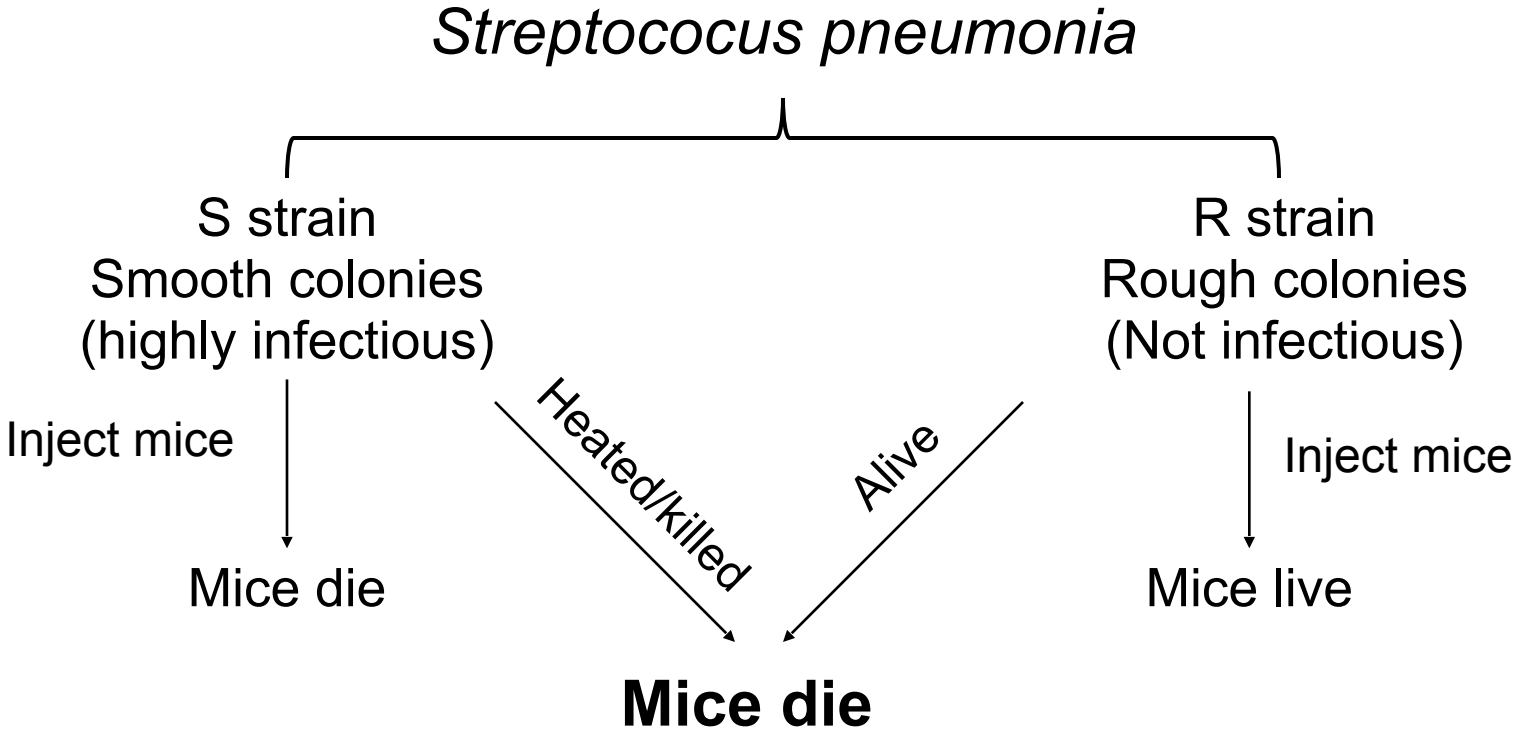
RESEARCH BRIEFING 2.2 GENES ARE MADE OF DNA

- At first it was thought that genes might be made of **protein**.
- **Two experiments** suggested that genes might be made of DNA.
- The double helix convinced biologists that genes are made of DNA.
- It was not proved that human genes are made of DNA until cloning was invented.



Griffith's transformation experiment

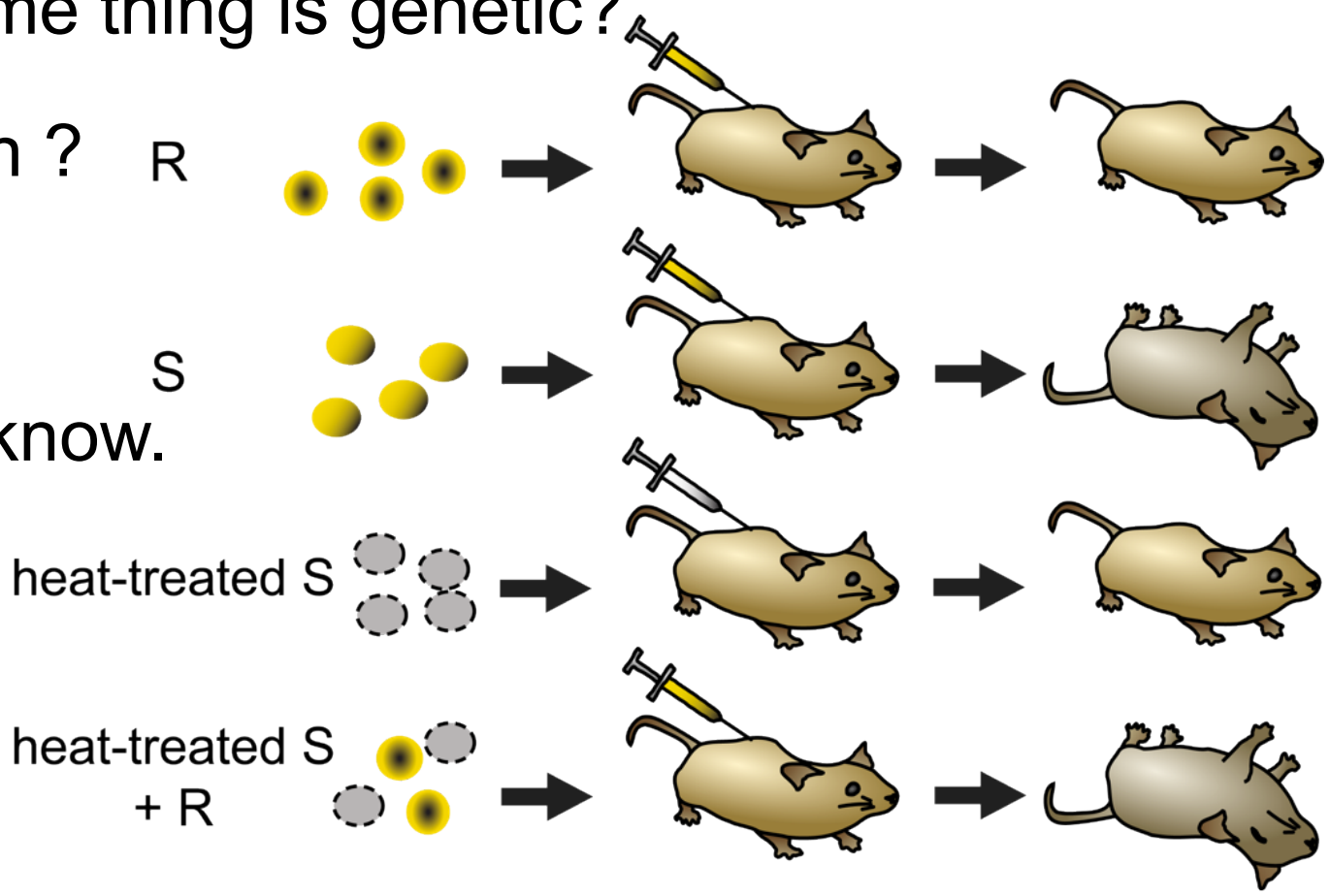
• Fredrick Griffith used *Streptococus pneumonia* (causes lung disease – pneumonia).



So R living cells were transformed by interacting with molecules of dead S starin

Griffith's transformation experiment

- He called the molecule (the transforming principle).
- So some thing is genetic?
- Protein ?
- DNA ?
- Don't know.



Griffith's transformation experiment

- He called the molecule (the transforming principle).
- So something is genetic?
- Is it Protein ?
- Is it DNA ?
- Don't know.

What is the chemical identity of the genetic material?

Avery's transformation experiment

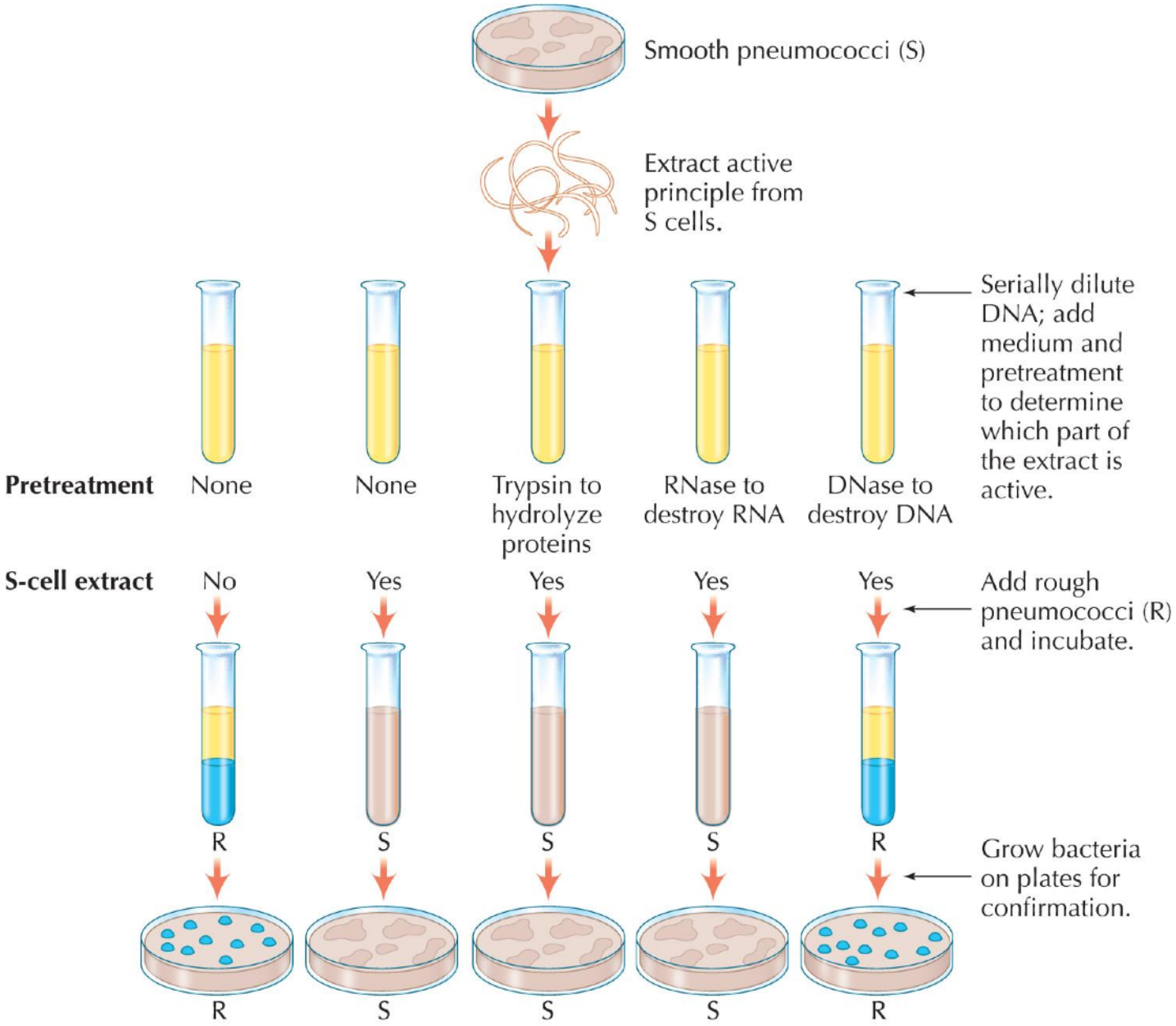
- Avery is asking the question: which component of the S cells is the transforming principle (genetic material)?
- Rerun Griffith's experiment with some modifications.
- lysed cells contain:
  - Proteins
  - Polysaccharides
  - RNA
  - DNA

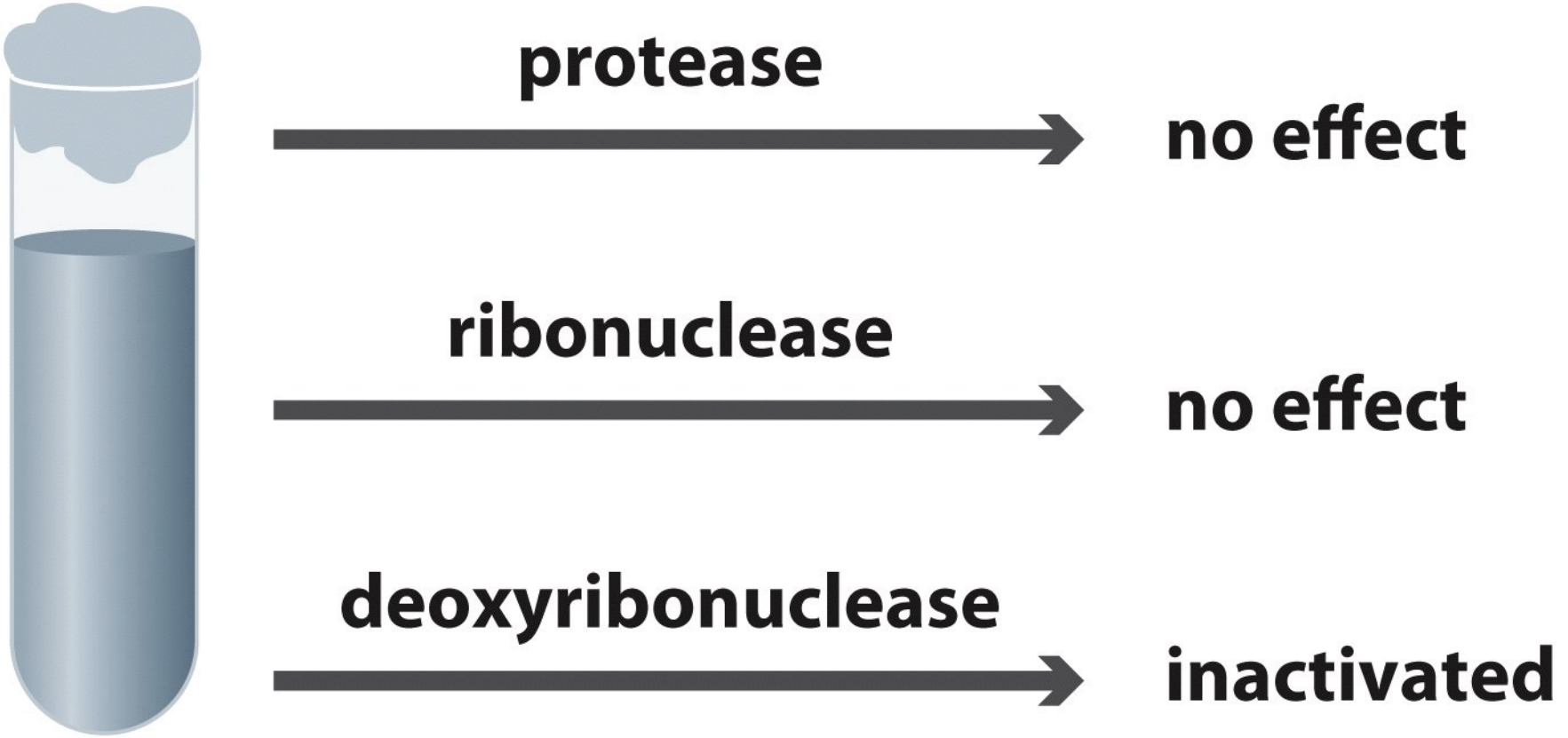
One of these molecules must be the genetic material

Avery's transformation experiment

- He used enzymes to degrade a specific class of molecules at a time then study the transformed cells.
- When DNA was degraded with DNase, no transformation occurred.
- Thus, DNA is the transformation principle!
- Clever right?
- Not good enough and convincing for some scientists. Why?
- Because the degrading enzymes were not pure!

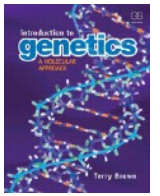
Avery's transformation experiment





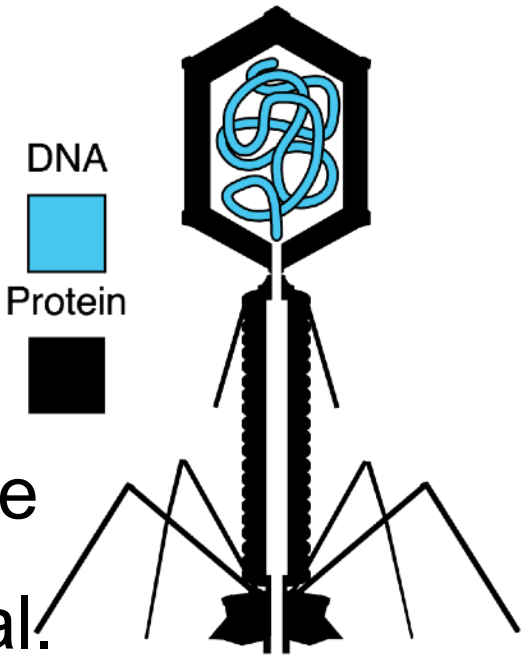
Research Briefing 2.2 Figure 1 Introduction to Genetics (© Garland Science 2012)

Chapter2



Hershey and Chase experiment

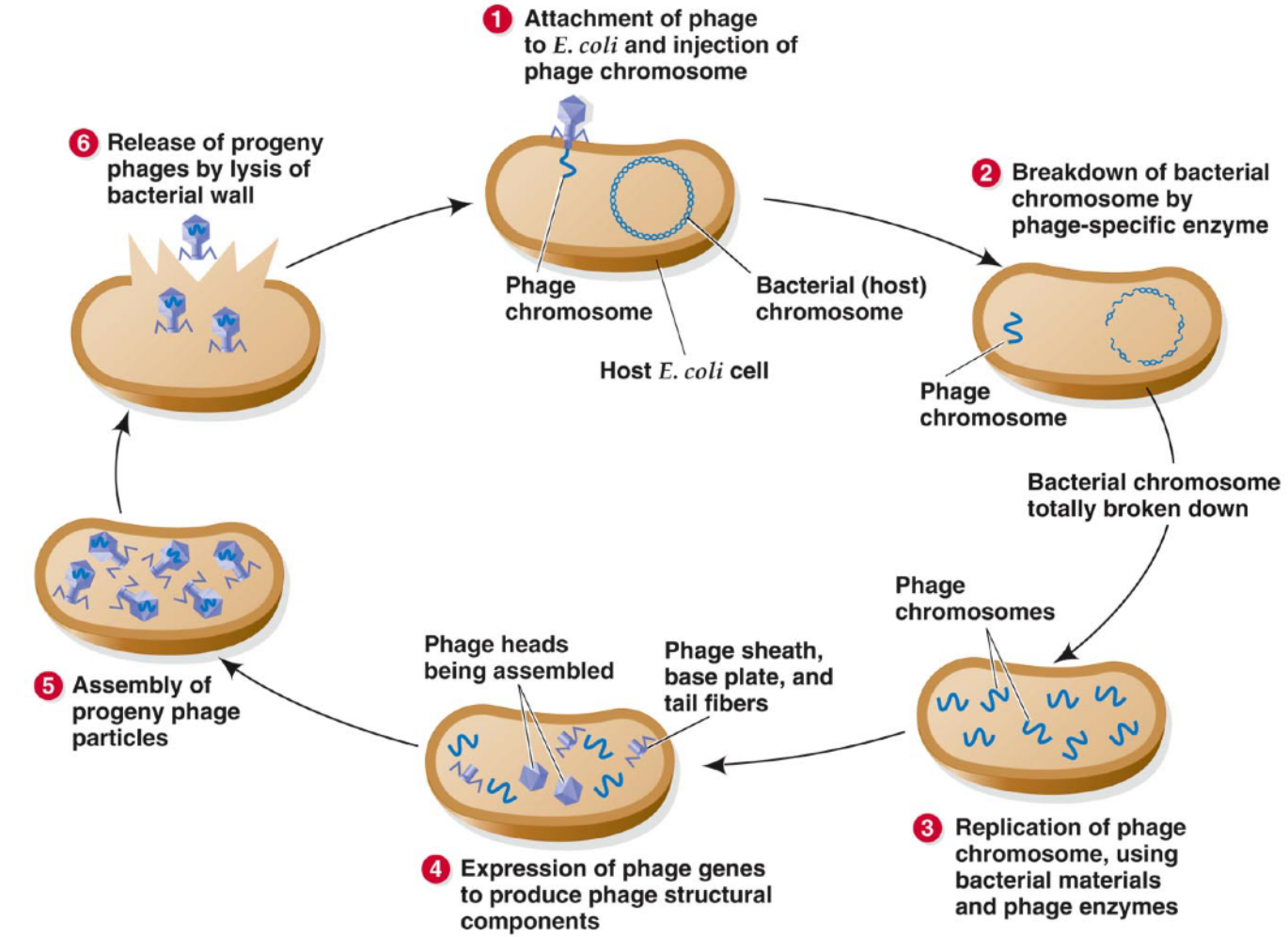
- Need more evidence that DNA is the genetic material.
- Hershey and Chase used a bacterial parasite (virus) to study the genetic material.
- Bacteriophage (phage):
  - Protein body.
  - DNA inside.



- Use the knowledge about the life cycle to study the genetic material.
- What is phage's life cycle?

Hershey and Chase experiment

Phage's life cycle



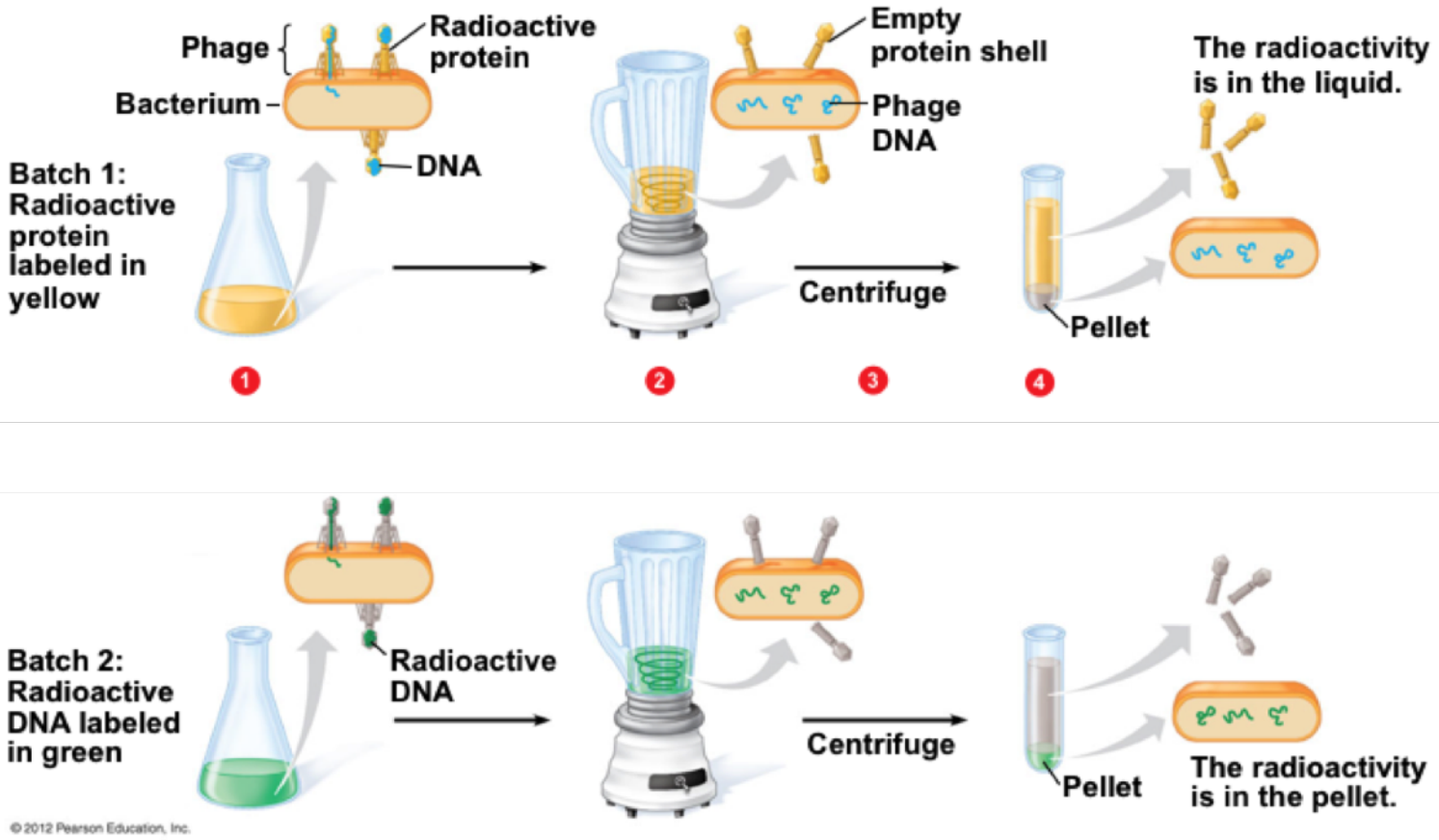
Hershey and Chase experiment

Track where the radioactive material go!

- Labeled proteins with radioactive S^{35}.
- Labeled DNA with radioactive P^{32}.
- The molecule that would enter the cell is the hereditary molecule.
- Study where the molecule go (in pellet or in supernatant)?

Hershey and Chase experiment

Track where the radioactive material go!

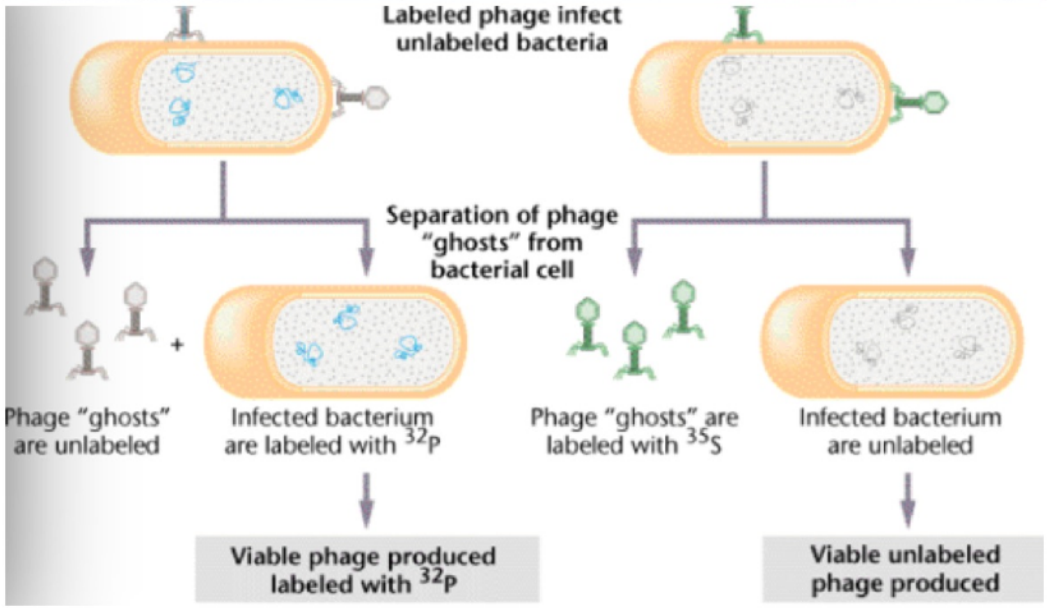


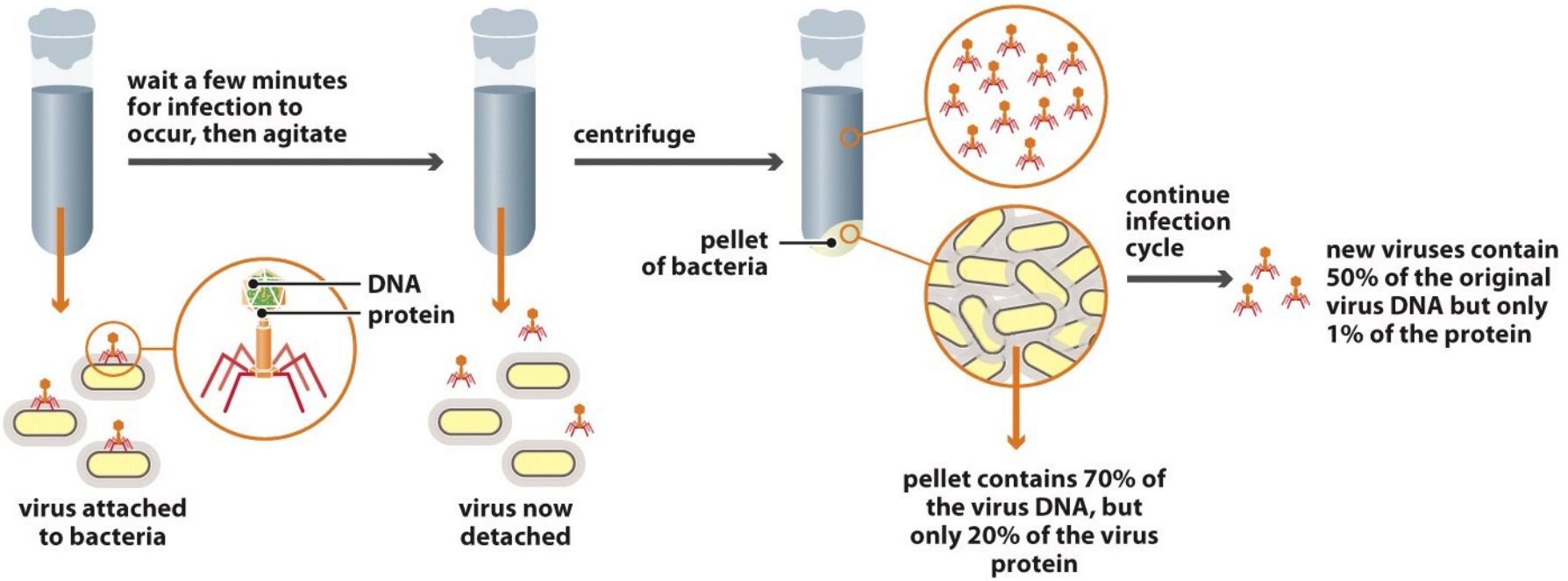
DNA is the genetic material!!!

Hershey and Chase experiment

Track where the radioactive material go!

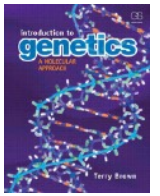
However, in 1952, Hershey and his colleague Martha Chase made use of another technology from physics, radioactive labelling, to reveal what the templates were made of. They took advantage of the fact that the proteins which made up the phage's coat contained sulphur but no phosphorus, while the DNA contained phosphorus but no sulphur. They labelled some phage with radioactive isotopes of each chemical and then infected bacteria with their labelled phage. Their analysis showed that the protein coat remained outside the bacterium, while all the DNA in fact entered the cell. The





Research Briefing 2.2 Figure 2 Introduction to Genetics (© Garland Science 2012)

Chapter2



To study

Griffith's transformation experiment

Transforming principle

Phage

Radioactive S

S Strain

Avery's transformation experiment

Phage life cycle

Hershey and Chase experiment

R Strain

Radioactive P

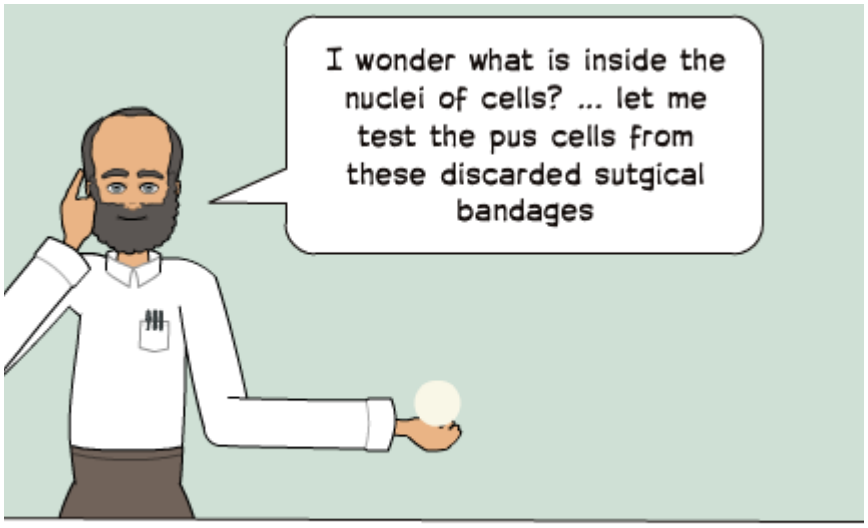
Nuclien

Bacteriophage

Expectations

- Know the experiments that lead to the conclusion that DNA is the genetic material.
- Know what each experiment added to the previous knowledge.
- You know a bit of the story to tell your friends and family.

For a smile



1868 ... in the lab of Friedrich Miescher