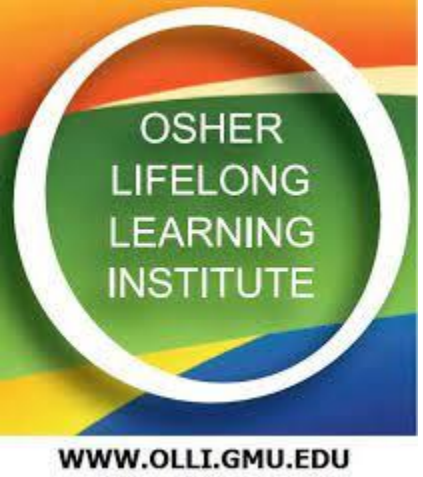

Discovery of DNA

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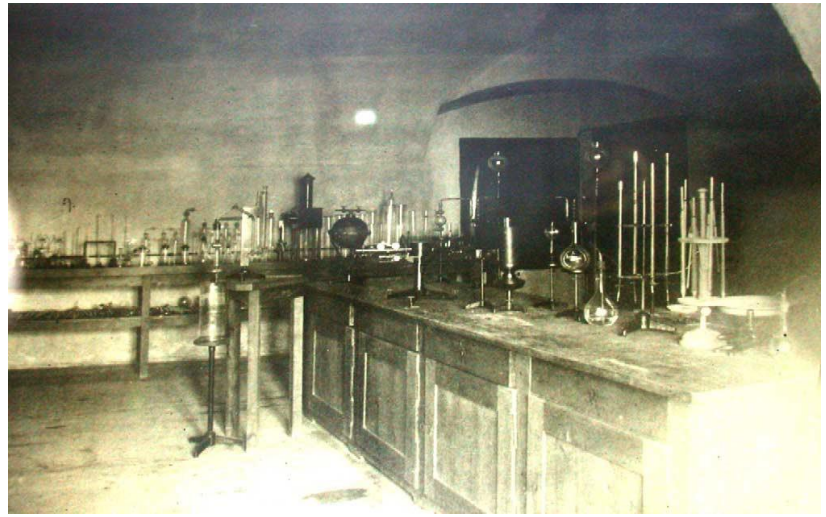
Discovery of DNA

- Friedrich Miescher, 1869, first isolates a substance from the nucleus of cells that he calls "**nuclein.**" His student, Richard Altmann, calls the substance "**nucleic acid**."
- Used leucocytes as his source material to study biochemistry of nucleus
  - Bandages with pus
- Yet during these tests, Miescher noticed that a substance precipitated from the solution when acid was added and dissolved again when alkali was added
- Studied salmon sperm
  - Large amount
- Miescher also noticed that nuclein was not well diffusible and concluded that it must be a molecule with a high molecular weight.



Miescher, F., 1869a. Letter I; to Wilhelm His; Tqbingen, February 26th, 1869. In: His, W., et al. (Eds.), Die Histochemischen und Physiologischen Arbeiten von Friedrich Miescher—Aus dem wissenschaftlichen Briefwechsel von F. Miescher, vol. 1. F.C.W. Vogel, Leipzig, pp. 33– 38.

Miescher, F., 1869b. Letter IV; to Miescher's parents; Tqbingen, August 21st 1869. In: His, W., et al. (Eds.), Die Histochemischen und Physiologischen Arbeiten von Friedrich Miescher—Aus dem wissenschaftlichen Briefwechsel von F. Miescher, vol. 1. F.C.W. Vogel, Leipzig, p. 39.

Miescher, F., 1869c. Letter V; to Wilhelm His; Leipzig, December 20th 1869. In: His, W., et al. (Eds.), Die Histochemischen und Physiologischen Arbeiten von Friedrich Miescher—Aus dem wissenschaftlichen Briefwechsel von F. Miescher, vol. 1. F.C.W. Vogel, Leipzig, pp. 39– 41.

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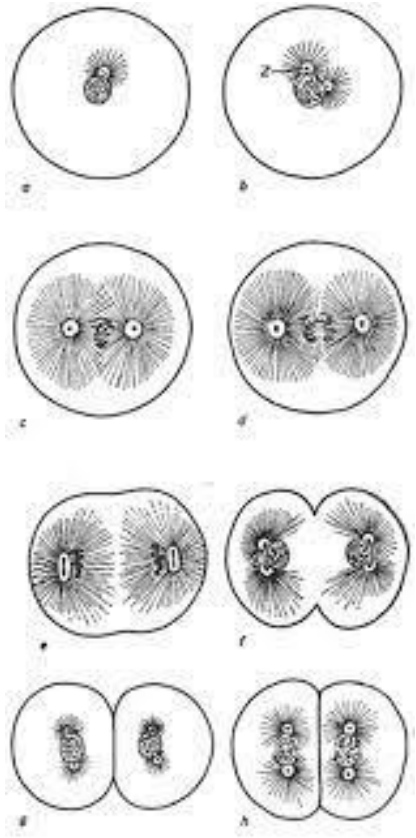
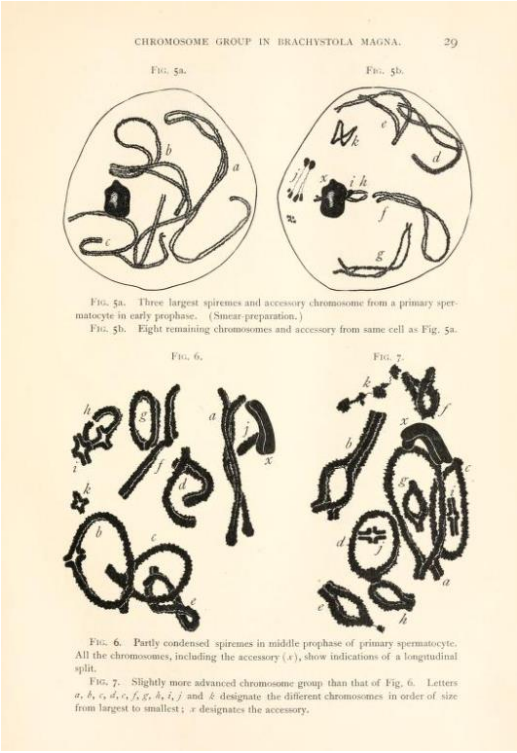
Chromosome Theory

- 1902
- Inheritance from each parent
  - Two copies
    - One copy from each parent
    - Body cells 2 copies
    - Gamete one copy
  - The chromosome theory of inheritance arose out of Sutton and Boveri's careful observations of meiosis. It states that chromosomes are composed of Mendel's hereditary determinants, or what we now call genes.





CHROMOSOME GROUP IN BRACHYSTOLA MAGNA. 29

FIG. 5a. FIG. 5b.

FIG. 5a. Three largest spiremes and accessory chromosome from a primary spermatocyte in early prophase. (Smear-preparation.)

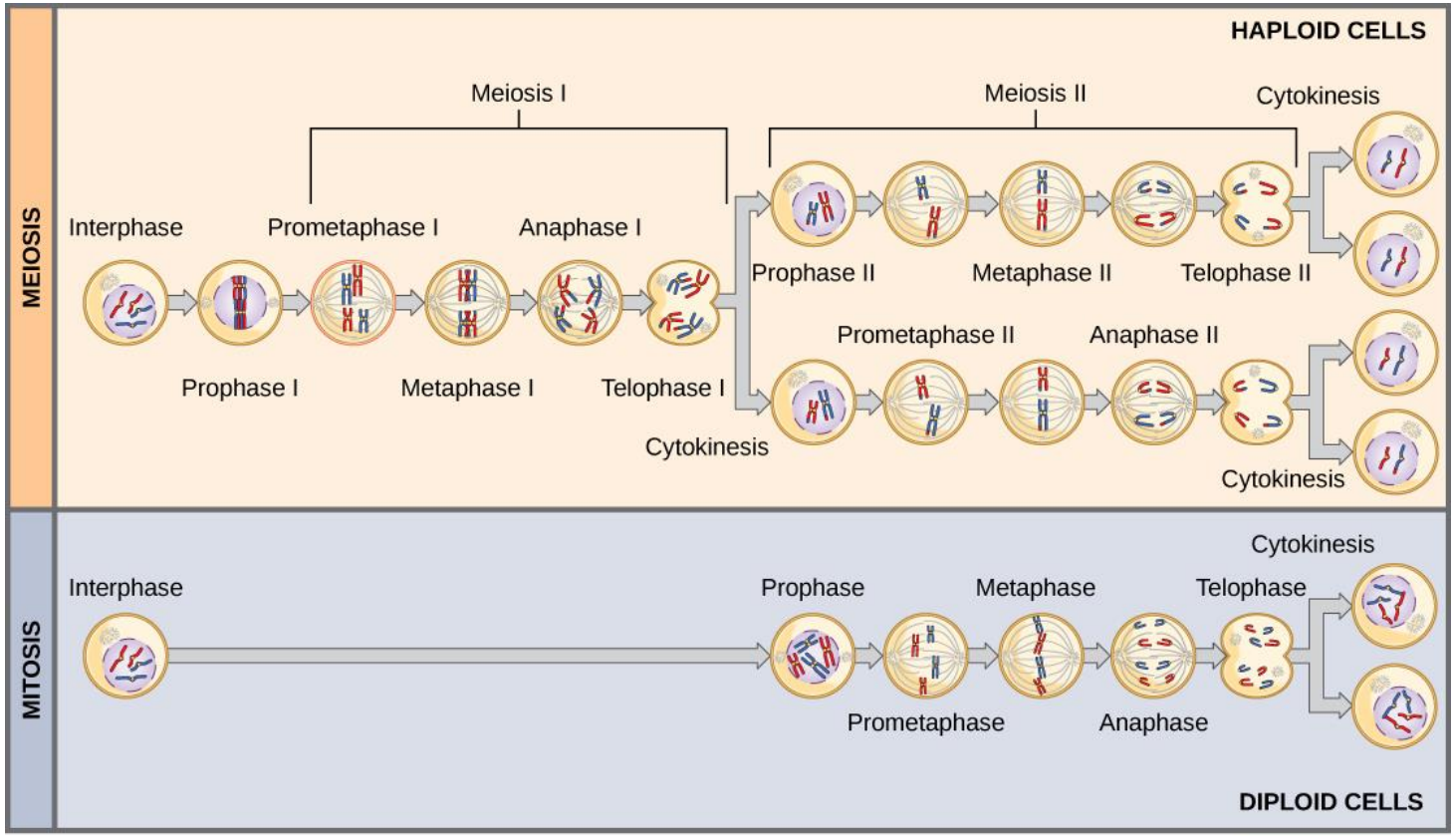
FIG. 5b. Eight remaining chromosomes and accessory from same cell as Fig. 5a.

FIG. 6. FIG. 7.

FIG. 6. Partly condensed spiremes in middle prophase of primary spermatocyte. All the chromosomes, including the accessory (x), show indications of a longitudinal split.

FIG. 7. Slightly more advanced chromosome group than that of Fig. 6. Letters a, b, c, d, e, f, g, h, i, j and k designate the different chromosomes in order of size from largest to smallest; x designates the accessory.

Sutton, Walter. "On the Morphology of the Chromosome Group in Brachystola magna." *The* Biological Bulletin 4 (1902): 24–39



						OUTCOME
PROCESS	DNA synthesis	Synapsis of homologous chromosomes	Crossover	Homologous chromosomes line up at metaphase plate	Sister chromatids line up at metaphase plate	Number and genetic composition of daughter cells
MEIOSIS	Occurs in S phase of interphase	During prophase I	During prophase I	During metaphase I	During metaphase II	Four haploid cells at the end of meiosis II
MITOSIS	Occurs in S phase of interphase	Does not occur in mitosis	Does not occur in mitosis	Does not occur in mitosis	During metaphase	Two diploid cells at the end of mitosis

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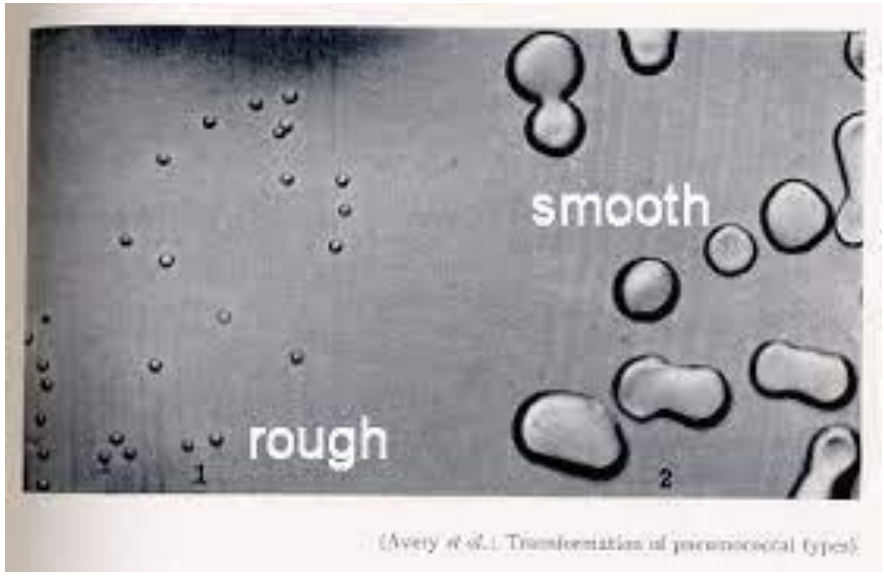
Griffith's

- In 1928 Frederick Griffith published a paper on his attempts to develop a vaccine for bacterial pneumonia
  - Pneumonia was leading cause of death in the 1918-1919 flu pandemic
- Griffith worked with two strains of a bacterium, one pathogenic and one harmless
  - Rough non-virulent strain
  - Smooth virulent

- When he mixed heat-killed remains of the pathogenic strain with living cells of the harmless strain, some living cells became pathogenic
- He called this phenomenon **transformation**, now defined as a change in genotype and phenotype due to assimilation of foreign DNA
- Transforming material is genetic material



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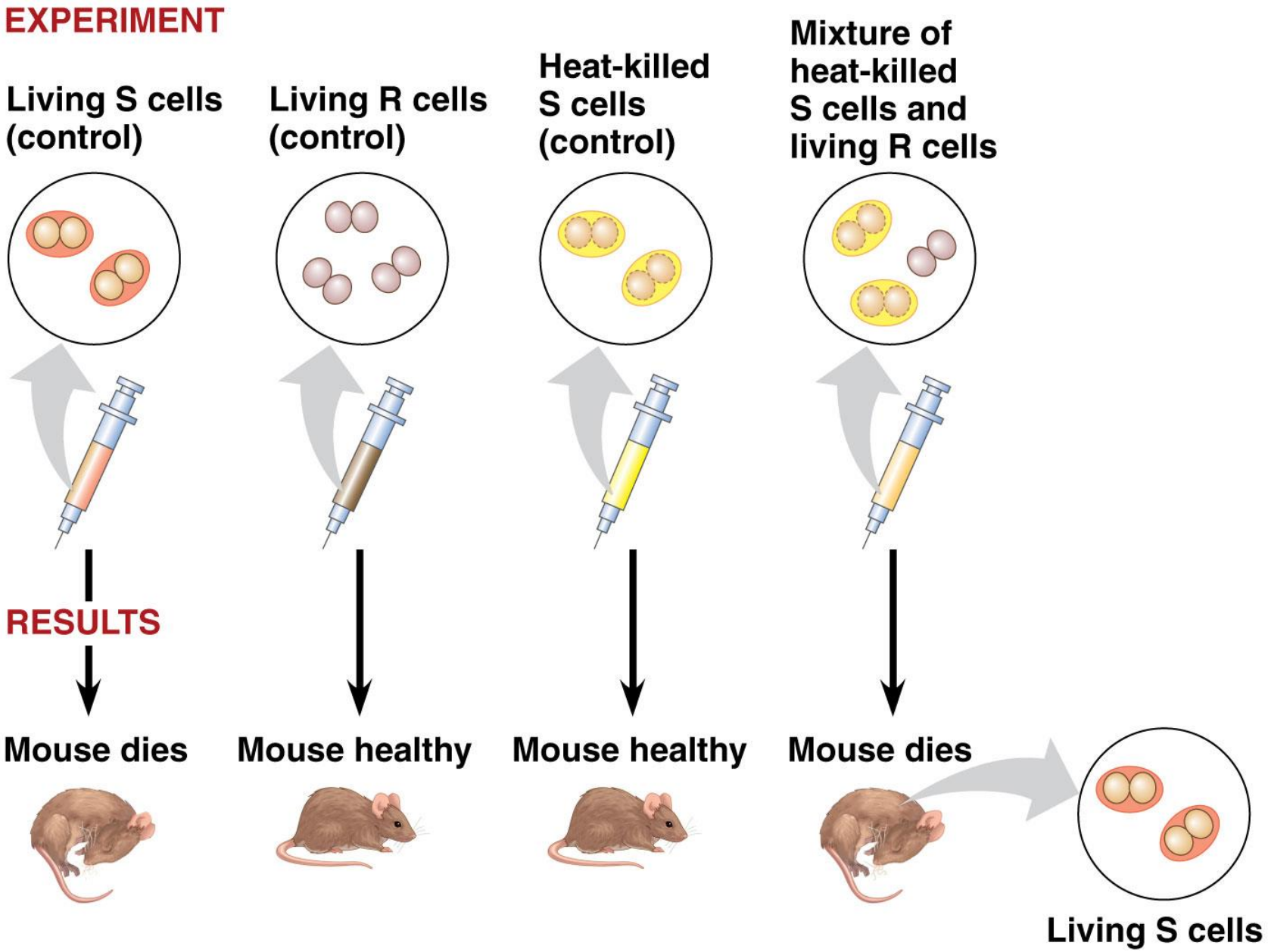


Oswald Avery: Transforming Material is DNA

- Griffith wanted to develop a vaccine and did not pursue transforming material
- Oswald Avery realized that the transforming material must be the genetic material and could experimentally determine what molecule coded for genes
  - Protein vs. DNA
- **In February 1944, *Journal of Experimental Medicine*, entitled "Studies on the Chemical Nature of the Substance Inducing Transformation of Pneumococcal Types: Induction of Transformation by a Deoxyribonucleic Acid Fraction Isolated from Pneumococcus Type III".**

- Used two approaches
  - Isolate pure molecules and test
    - DNA
    - Protein
    - RNA
    - Lipids
  - Remove molecules by digestive enzymes

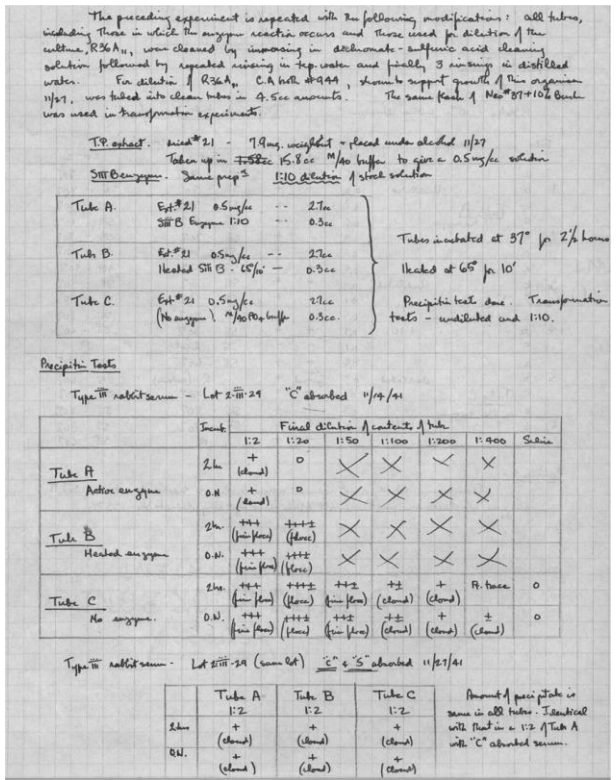


TABLE IV

Titration of Transforming Activity of Preparation 44

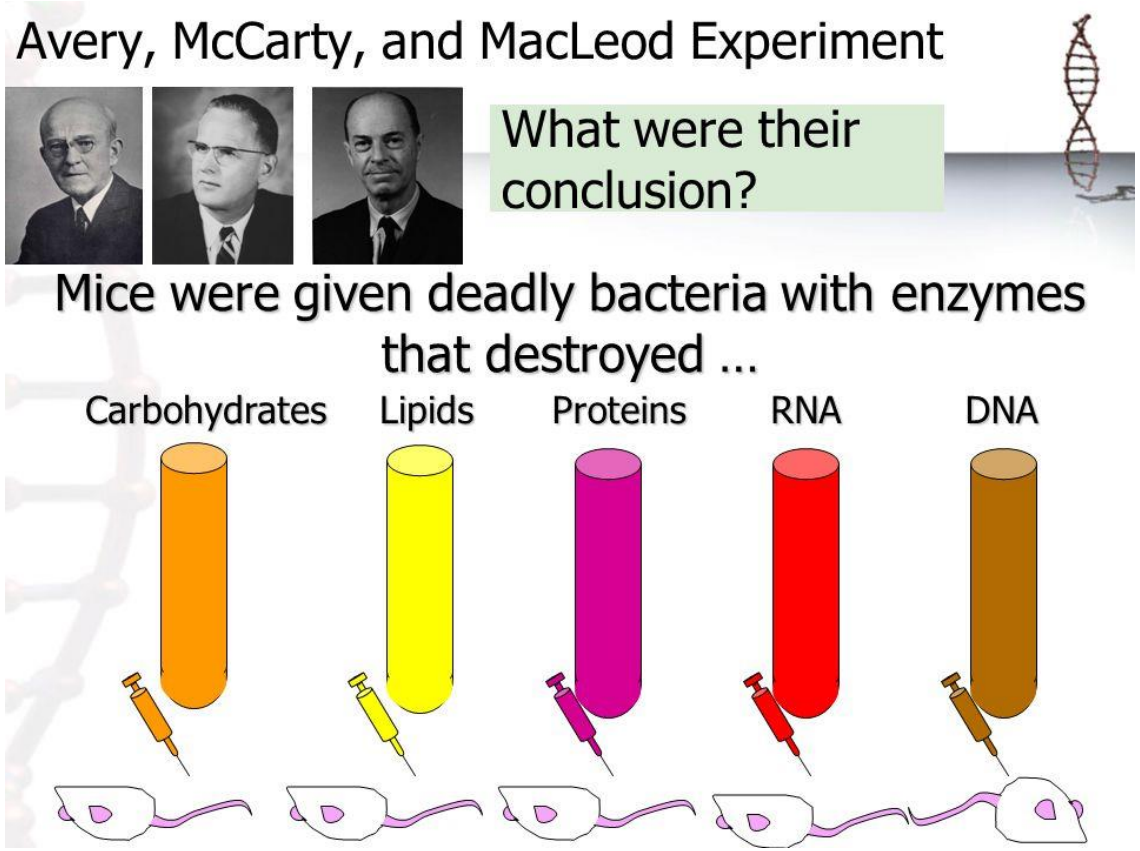
Transforming principle Preparation 44*		Quadruplicate tests							
		1		2		3		4	
Dilution	Amount added	Diffuse growth	Colony form	Diffuse growth	Colony form	Diffuse growth	Colony form	Diffuse growth	Colony form
	μg.								
10^{-2}	1.0	+	SIII	+	SIII	+	SIII	+	SIII
$10^{-2.5}$	0.3	+	SIII	+	SIII	+	SIII	+	SIII
10^{-3}	0.1	+	SIII	+	SIII	+	SIII	+	SIII
$10^{-3.5}$	0.03	+	SIII	+	SIII	+	SIII	+	SIII
10^{-4}	0.01	+	SIII	+	SIII	+	SIII	+	SIII
$10^{-4.5}$	0.003	−	R only	+	SIII	−	R only	+	SIII
10^{-5}	0.001	−	R "	−	R only	−	R "	−	R only
Control	None	−	R "	−	R "	−	R "	−	R "

* Solution from which dilutions were made contained 0.5 mg. per cc. of purified material. 0.2 cc. of each dilution added to quadruplicate tubes containing 2.0 cc. of standard serum broth. 0.05 cc. of a 10^{-4} dilution of a blood broth culture of R36A is added to each tube.

ratio of 1.58, exhibited high transforming activity. Titration of the activity of this preparation is given in Table IV.

A solution containing 0.5 mg. per cc. was serially diluted as shown in the protocol. 0.2 cc. of each of these dilutions was added to quadruplicate tubes containing 2.0 cc. of standard serum broth. All tubes were then inoculated with 0.05 cc. of a 10^{-4} dilution of a 5 to 8 hour blood broth culture of R36A. Transforming activity was determined by the procedure described under Method of titration.

The data presented in Table IV show that on the basis of dry weight 0.003 μg. of the active material brought about transformation. Since the reaction system containing the 0.003 μg. has a volume of 2.25 cc., this represents a final concentration of the purified substance of 1 part in 600,000,000.



STUDIES ON THE CHEMICAL NATURE OF THE SUBSTANCE INDUCING TRANSFORMATION OF PNEUMOCOCCAL TYPES INDUCTION OF TRANS]~ORMATION BY A DESOXYRIBONUCLEIC ACID FRACTION ISOLATED I~RO~¢ 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)

IDENTIFICATION OF DNA AS THE GENETIC MATERIAL

- To fulfill its role, the genetic material must meet several criteria
  - 1. Information: It must contain the information necessary to make an entire organism
  - 2. Transmission: It must be passed from parent to offspring
  - 3. Replication: It must be copied
    - In order to be passed from parent to offspring
  - 4. Variation: It must be capable of changes
    - To account for the known phenotypic variation in each species