Nature, Structure, Replication of Genetic Material

1. *Genes are composed of nucleic acids, not proteins*
2. *Nucleic acids are polymers of nucleotides (A, T/U, G, C)*
3. *Nucleic acids differ in length and cellular function*
4. *DNA molecules are produced through replication*
5. *DNA molecules are organized into chromosomes*
6. *Chromosome regions differ in structure and function*

Genetic Material is Composed of Nucleic Acids

Genetic material located in nucleus of eukaryotes
Nucleus contains primarily DNA and protein
Proteins: *Stable, large, complex, initially favored*
DNA: *Initially viewed as small, simple, unstable;*
Consequence of crude isolation methods
Early "tetranucleotide" model of structure
Correct structure: Complex macromolecule;
Capable of replication, information storage

Evidence Favoring DNA as Genetic Material:

A. Bacterial Transformation:

Griffith (1920's) and Avery et al. (1940's)
Transforming Factor = Bacterial Gene = DNA (not protein)

***Griffith Experiments**:*

Bacterium (Diplococcus) that caused pneumonia in mice
2 strains that differed in single heritable trait

Virulent Strain (V)	*Lethal*	*Cells contain capsule*
Non-Virulent (NV)	*Not Lethal*	*Cells lack capsule*

[V + Heat] --- Inject --- Mice lived (control)
[(V + Heat) + NV] --- Inject --- Mice died --- Recover V cells

*NV cells **Transformed** into V cells*
Transformation: Integration of external DNA into genome

Avery et al. Experiments:

Extract from (V + Heat) Cells:

+ Proteases ----> mice died -----	*TF not protein*
+ RNases ------> mice died -----	*TF not RNA*
+ DNases -----> mice LIVED ---	*TF is DNA*

B. Hershey and Chase Experiment (1940's)

Phage: *Bacterial viruses composed of DNA and protein*
Phage genetic material injected into bacterial cell
Is phage DNA or protein or both injected?

Conclusion: Phage genes are composed of DNA (injected)

Experiment used radioactive isotopes (available in 1940s)

Element	Isotope	Protein	Nucleic Acid
Phosphorus	32-P	No	Yes
Sulfur	35-S	Yes	No
Hydrogen	3-H	Yes	Yes
Nitrogen	15-N	Yes	Yes

Label cells by adding isotope to growth medium
Label viruses by letting them infect labeled cells

Hershey and Chase Experiment:

Prepared 2 different stocks of labeled phage:

(a) 32-P DNA core; (b) 35-S Protein coat

Infected bacterial cells with labeled phage (32-P or 35-S)
Allowed phage genetic material to enter cells
Phage coats remained outside cells
Centrifuged tube to precipitate cells
32P label in precipitate and 35-S label in supernatant

Conclude: *Phage genes composed of DNA;*
Only 32-P entered bacterial cells

C. UV Mutagenesis Studies in Bacteria

UV light induces mutations; Efficiency depends on wavelength
Most effective = 260 nm (absorption max. for genes)

Proteins = 280 nm; DNA = 260 nm

D. DNA Content and Composition

[DNA] in diploid cells = 2 x [DNA] in haploid cells
Same relationship does not hold for protein concentration

Chargaff: ***Nucleotide (base) composition of DNA***

[A] = [T] and [G] = [C] in DNA
Suggested highly ordered DNA structure

E. DNA Structure: Watson and Crick (1953)

First correct model of DNA structure

Large macromolecule; Double Helix structure
Revealed through X-ray crystallography
Consistent with information storage and replication

F. Transfection Experiments

Purified DNA from phage - added to bacterial spheroplasts
Result: New phage produced
Isolated DNA sufficient to function as genetic material

G. Some Viral Genomes are Composed of RNA

Experiments with tobacco mosaic virus (TMV)
RNA core (not protein coat) functions as genetic material

H. Functional Genes can be Synthesized in the Lab

Direct chemical synthesis of DNA of known sequence
Enzymatic amplification of template DNA sequence

I. Functional Viral Genomes can be Synthesized

Recent example of complete synthesis of polio virus genome

Conclusions:

All Genes and Genomes are Composed of Nucleic Acids
Nucleic Acids Store Genetic Information