Aim: How was the DNA code deciphered?

What is the "one-gene, one-polypeptide" hypothesis?

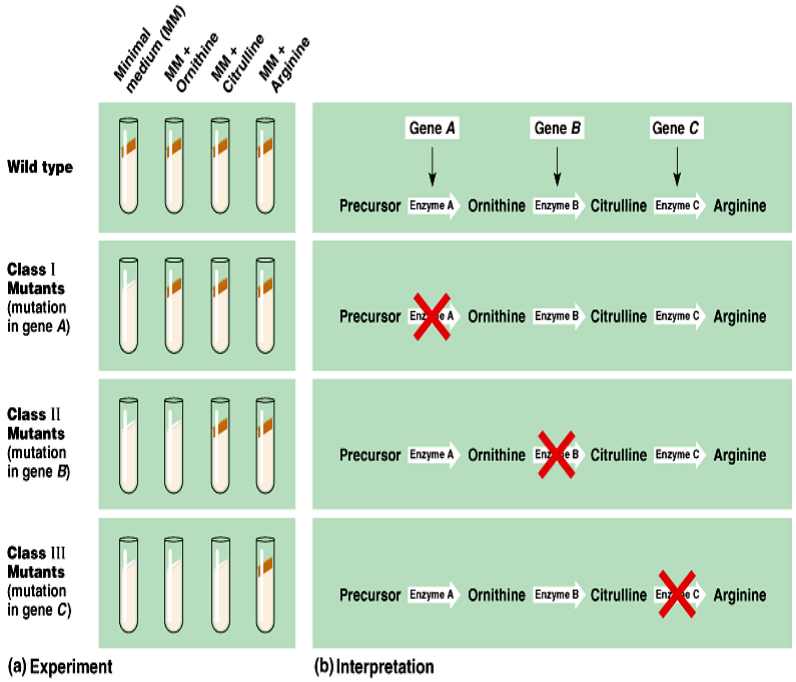
- 1909 – A Garrod, British physician, suggested that gene create enzymes that determine phenotype. To him:
- Inherited disease= inability to create a particular enzyme
- Example: alkaptonuria (black urine) – inability to make the enzyme that hydrolyzes alkaptons, a black chemical in urine

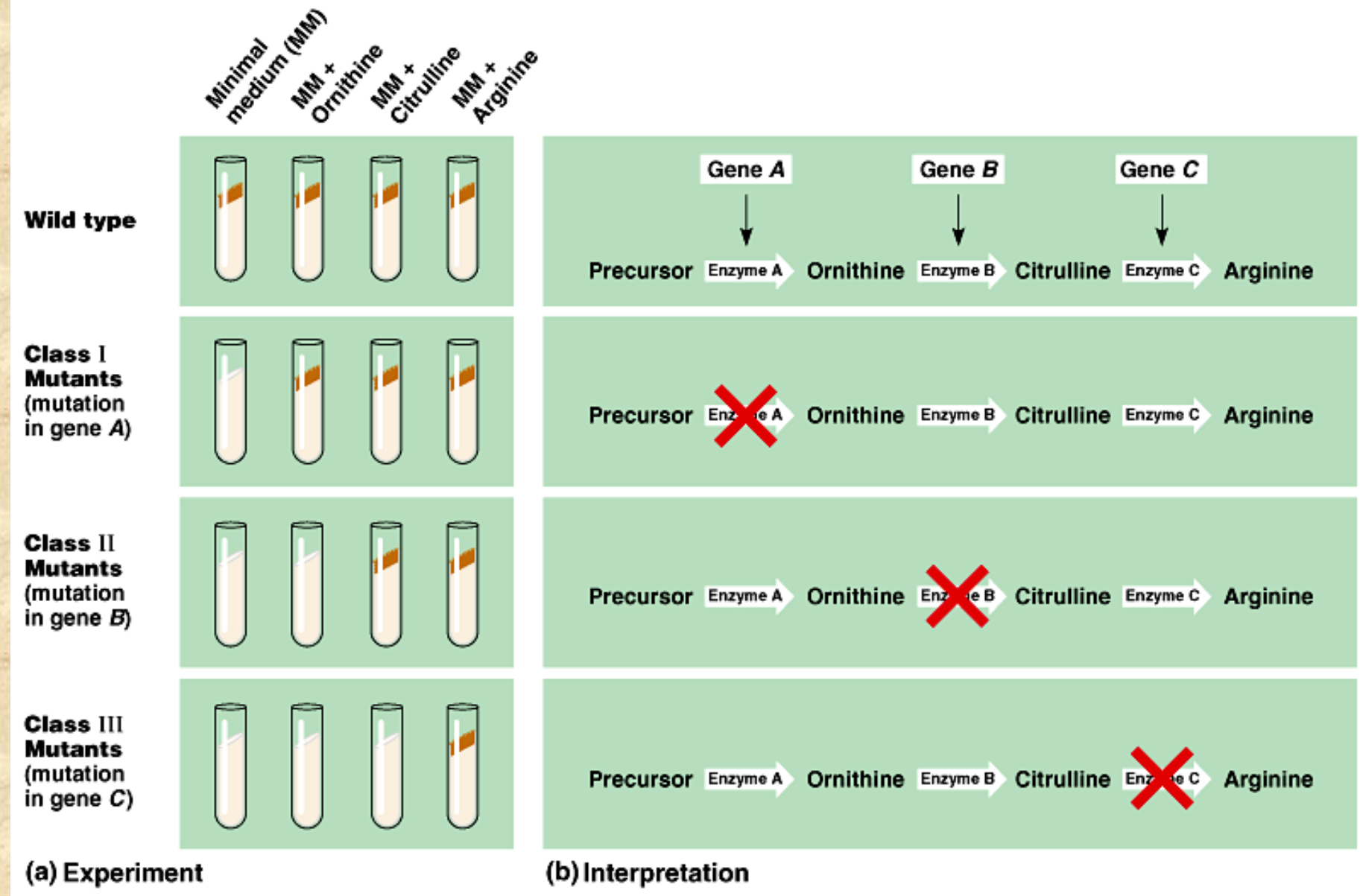
What is the “one-gene, one-polypeptide hypothesis? (2)

- 1930’s – George Beadle and Edward Tatum – worked with bread mold – *Neurospora Crassa*
- 1) wild type Neurospora survive on minimal media, a basic nutrient containing sugar, agar protein, salt, and biotin vitamin.
- 2) auxotrophs – mutants (created by X-ray) that cannot survive on minimal media and must be given supplements of amino acids.

What is the "one-gene, one-polypeptide hypothesis? (3)

- Results:
- Wild type makes all three enzymes.
- Class 1 mutants cannot make enzyme A and need to be given ornithine. Then they can make citrulline and arginine.
- *One gene makes one enzyme.*




Minimal medium (MM)
MM + Ornithine
MM + Citrulline
MM + Arginine
Wild type
Class I Mutants (mutation in gene A)
Class II Mutants (mutation in gene B)
Class III Mutants (mutation in gene C)
Gene A
Gene B
Gene C
Precursor
Enzyme A
Ornithine
Enzyme B
Citrulline
Enzyme C
Arginine
(a) Experiment
(b) Interpretation

What is the “one-gene, one-polypeptide hypothesis? (4)

- But not all proteins are enzymes. Examples of non-enzyme proteins include keratin, insulin, hemoglobin, collagen.
- Therefore, one gene makes one polypeptide !!

What is translation?

- Translation = process by which the genetic code stored in mRNA is translated into polypeptides.
- Genetic code is found in the arrangement of nitrogen bases on the mRNA.
- Genetic code is universal and is used by all organisms with few variations.
- The universality of the genetic code allows scientists to use bacteria to synthesize human proteins (genetic engineering or recombination).

How was the genetic code deciphered?

- Crick said that it takes 3 nitrogen bases to produce a *codon*.
- A codon controls the placement of one amino acid on a growing polypeptide chain.
- Codons are found on mRNA and are read in a 5’ to 3’ direction.

Crick's experiment:

1) He used varying concentrations of acridine enzyme to delete nitrogen bases from DNA.
2) When 3 consecutive nucleotides were deleted, a functional protein could be synthesized.
3) This was not the case when one or two nucleotides were removed.

An analogy of Crick's experiment

- THE BIG RED ANT ATE ONE FAT BUG.
- 1 deletion:
- THB IGR EDA NTA TEO NEF ATB UG
- 2 deletions:
- THI GRE DAN TAT EON EFA TBU G
- 3 deletions:
- THE RED ANT ATE ONE FAT BUG
- *Crick' s conclusion: Three nitrogen bases on mRNA create one codon.*

Nirenberg and Matthaei (National Institute of Health) and Severo Ochoa (NYU) --- Early 1960's

- Created synthetic RNA:
- A) polyuracil (UUU…) made phenyalanine chains
- B) polyadenine (AAA…) made lysine chains
- C) polycytosine (CCC…) made proline chains
- D) polyguanine (GGG…) made glycine chains

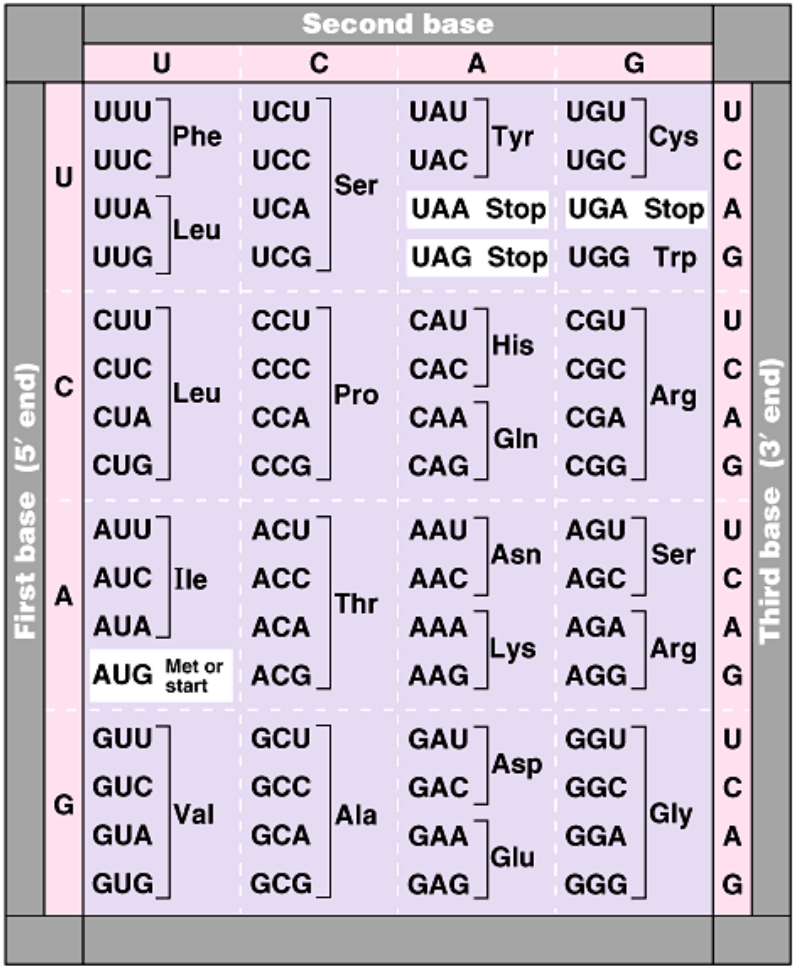
Nirenberg and Philip Leder - 1964

- Developed a technique for getting ribosomes to bind to RNA trinucleotides.
- Specific amino acids were found to go with specific codons.
- Found 64 possible triplets = genetic code

H.G. Khorana (University of Wisconsin)

- Developed a technique for making repeating units of mRNA.
- Found that usually the first 2 bases of a 3-base codon specify a specific amino acid. The third base can vary.
- Example: UCU, UCC, UCA, UCG all code for serine.

H.G. Khorana (University of Wisconsin)



First base (5′ end)	Second base: U	Second base: C	Second base: A	Second base: G	Third base (3′ end)
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
	UUA Leu	UCA Ser	UAA Stop	UGA Stop	A
	UUG Leu	UCG Ser	UAG Stop	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC Leu	CCC Pro	CAC His	CGC Arg	C
	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
	AUG Met or start	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

- This redundancy helps prevent many dangerous mutations in the DNA template.
- You could change the third nitrogen base of most codons and have no effect on the amino acid added.