

Introduction to Biochemical Genetics

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Field that links DNA sequence information to the biochemical functions of the gene products (proteins, RNAs, metabolites).

1. Core Concepts

Concept	Definition	Relevance to Biochemistry
Gene	A DNA segment that encodes a functional product (protein or functional RNA).	Determines the primary structure of enzymes, structural proteins, and regulatory RNAs.
Allele	Alternative forms of a gene that differ in nucleotide sequence.	Can cause quantitative or qualitative changes in enzyme activity, stability, or regulation.
Expression	Process by which genetic information is converted into a functional product (transcription ? translation).	Controls the amount and timing of enzyme synthesis, influencing metabolic pathways.
Mutation	Permanent change in the DNA sequence.	May alter amino?acid sequence, affect catalytic sites, change substrate specificity, or disrupt regulation.
Metabolic Pathway	Series of enzymatic reactions converting substrates into final products.	Each step is encoded by a specific gene; mutations in any gene can modify flux through the pathway.

2. From Gene to Enzyme: The Molecular Flow

1. DNA ? RNA

- *Transcription*: RNA polymerase reads a gene's template strand, producing a pre? mRNA (or a functional RNA for non?coding genes).
- *RNA processing*: Capping, splicing, poly?A tail addition (eukaryotes) generate mature mRNA.

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2. RNA → Protein

- *Translation*: Ribosome reads codons, recruiting tRNAs loaded with amino acids.
- *Co-translational modifications*: Signal peptide cleavage, N-terminal acetylation.

3. Protein → Functional Enzyme

- *Folding*: Assisted by chaperones; determines active-site geometry.
- *Post-translational modifications*: Phosphorylation, glycosylation, proteolysis can regulate activity, localization, or stability.

4. Enzyme → Metabolic Effect

- Catalyzes substrate conversion, influencing metabolite concentrations, energy balance, and cellular signaling.

3. Types of Genetic Variation and Their Biochemical Impact

Variation	Molecular Change	Typical Biochemical Consequence
Missense mutation	Single nucleotide change → different amino acid	Altered enzyme kinetics (K_m , V_{max}), loss/gain of function, altered regulation.
Nonsense mutation	Premature stop codon	Truncated protein; often loss of activity, possible degradation via nonsense-mediated decay.
Frameshift	Insertions/deletions not in multiples of three	Disrupts downstream reading frame → aberrant protein, usually nonfunctional.
Splice-site mutation	Alters intron-exon boundaries	Exon skipping or intron retention → abnormal protein isoforms.
Regulatory region mutation	Changes in promoters/enhancers	Modified transcription rate → altered enzyme levels.
Copy-number variation	Gene duplication/deletion	Over-expression or haploinsufficiency; can change pathway flux dramatically.

4. Classical Biochemical Genetics Approaches

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Method

Principle

What It Reveals

Complementation test

Cross two mutants;
observe phenotype of
diploid.

Whether mutations affect the same gene (non?
complementation) or different genes
(complementation).

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