

Unit-4

Pharmacogenomics-

Pharmacogenomics is the study of how a person's genes affect their response to medicines, helping to choose the right drug and dose for each individual.

Everyone's body is different because of their genes.

Some people respond well to a drug, while others may have side effects or no effect.

Pharmacogenomics helps doctors choose the right drug and dose for each person, based on their DNA.

Why is it Important?

To make medicine safer and more effective.

To avoid side effects.

To choose the best drug for the individual.

To guide personalized medicine (custom treatment based on genes).

Example:

A gene called CYP2C19 affects how people process the drug clopidogrel (used for heart problems).

Some people can't activate the drug properly due to their gene type.

Gene Mapping

Gene mapping is the process of finding the exact location of a gene on a chromosome.

It helps scientists know where a gene is and what it might do.

Purpose:-

To locate genes responsible for diseases.

Steps (Simple):

Collect DNA samples from affected families.

Use genetic markers to find regions linked to the disease.

Narrow down to a small region on a chromosome.

Identify the disease gene.

Types of Gene Mapping -

1. Linkage Mapping:

Uses genetic markers (known DNA sequences) to find how close they are to a disease gene.

Based on how genes are inherited together.

2. Physical Mapping:

Shows the actual physical location of genes using DNA sequences.

More precise than linkage mapping.

Cloning a disease gene

Cloning a disease gene means copying the gene that causes a disease, so scientists can study it in detail.

Why Clone a Disease Gene?

- To understand how the gene causes disease
- To develop treatments or gene therapy
- To make genetic tests

Simple Steps of Disease Gene Cloning:

Identify the gene

→ Using gene mapping, scientists find the location of the disease gene.

Isolate the gene

→ The DNA containing the gene is carefully cut out using special enzymes.

Insert into a vector

→ The gene is placed into a plasmid (a small circular DNA used as a carrier).

Transfer into bacteria

→ The plasmid is put into bacteria, which will make many copies of the gene.

DEPTH OF BIOLOGY

Grow bacteria in lab

→ As bacteria multiply, they also copy the gene—this is cloning.

Study the gene

→ Scientists analyze the cloned gene to understand its role in the disease.

Genetic variation and it's role in health/pharmacology

Genetic variation means differences in DNA between people.

It can happen in the form of:

SNPs (Single Nucleotide Polymorphisms) – a change in one base (letter) of DNA

Insertions/Deletions – small bits of DNA added or missing

Gene duplications or mutations

Role in Health:-

1. Disease Risk:

Some variations increase risk for diseases like diabetes, cancer, or heart disease.

Others may offer protection from certain conditions.

2. Inherited Disorders:

Caused by specific gene mutations (e.g., sickle cell anemia, cystic fibrosis).

3. Different Traits:

Variations affect things like height, eye color, metabolism, etc.

Role in Pharmacology (Pharmacogenomics):-

Drug Response:

People with different gene variants may respond differently to the same drug.

Example: Some may need a higher or lower dose.

Side Effects:

Genetic variation can cause severe side effects in some individuals.

Personalized Medicine:

Helps doctors choose the best drug and dose based on a person's genes.

Polymorphism Polymorphism affecting drug metabolism

Polymorphism means a small change in a gene (like a different DNA letter) that is common in the population.

How It Affects Drug Metabolism:-

Your body uses enzymes to break down (metabolize) drugs.

Some of these enzymes are made by genes that can have polymorphisms.

This can change how fast or slow a person processes a drug.

Types of Drug Metabolism Based on Polymorphism:

1. Poor Metabolizers

Enzyme works too slowly

Drug stays longer in the body → may cause side effects

2. Ultra-Rapid Metabolizers

Enzyme works too fast

Drug is removed quickly → not enough effect

3. Intermediate Metabolizers

Enzyme activity is reduced

May need lower doses

4. Extensive (Normal) Metabolizers

Enzyme works normally → expected drug response

Example: CYP2D6 Gene-

Controls an enzyme that breaks down many drugs (e.g., codeine, antidepressants)

Polymorphisms in CYP2D6 can cause different drug reactions:

Some people turn codeine into morphine too fast → risk of overdose

Others do it too slowly → drug doesn't work

Genetic variation in drug transporter

Drug transporter-

Drug transporters are proteins that help move drugs into or out of cells.

They are found in organs like the intestines, liver, kidneys, and brain.

Examples of drug transporters:

P-glycoprotein (P-gp / ABCB1)

OATP1B1 (SLCO1B1)

What Is Genetic Variation in Transporters?

Some people have gene variations (polymorphisms) in the transporter genes.

These changes can affect:

How well the transporter works

How much drug gets absorbed or removed

The effectiveness or toxicity of the drug

Effects of Genetic Variation:

Increased Transporter Activity

- Drug is removed too fast
- Low drug levels → less effect

Decreased Transporter Activity

- Drug stays longer in the body
- High drug levels → more side effects

Example: ABCB1 (P-gp)

Helps pump drugs out of cells (e.g., in the brain or intestines)

A variation in ABCB1 can affect drugs like:-

Digoxin (heart medicine)

Anticancer drugs

HIV drugs

Genetic variation in GPCR

GPCRs (G-Protein Coupled Receptors) are proteins found on cell surfaces.

They help the body respond to signals like hormones, neurotransmitters, and drugs.

Many medicines work by binding to GPCRs to trigger or block a response.

Genetic variation– (polymorphism or mutation) means a change in the DNA of GPCR genes. This can change the structure or function of the receptor.

How It Affects Drug Response:-

Reduced receptor function

→ The drug may not work well (less effect)

Increased sensitivity

→ The drug may have a stronger effect or cause side effects

No response

→ Receptor may not work at all → drug is useless for that person

Examples:

Beta-2 Adrenergic Receptor (ADRB2 gene):

Affects response to asthma drugs like salbutamol

Some people have poor response due to gene variation

Dopamine Receptors (DRD2 gene):

Variations affect response to antipsychotic drugs

Can influence side effects or drug effectiveness

Opioid Receptors (OPRM1 gene):

Variations affect how people respond to painkillers like morphine

Applications of Proteomics Science -

Proteomics is the study of all proteins in a cell, tissue, or organism – their functions, structures, and interactions.

Applications of Proteomics in Science:

1. Medical Research

Understand how proteins change in diseases like cancer, diabetes, and Alzheimer's.

Identify biomarkers for early detection and better diagnosis.

2. Drug Discovery

Find new protein targets for drugs.

Study how drugs affect protein expression and interactions.

3. Personalized Medicine

Analyze proteins in individuals to give custom treatments.

Predict who will respond better to a certain drug.

4. Vaccine Development

Identify proteins on viruses or bacteria to create effective vaccines.

5. Agricultural Science

Study plant proteins to improve growth, nutrition, and stress resistance.

Detect disease-resistant or high-yield crops.

6. Microbial and Environmental Science

Understand proteins in bacteria for bioremediation or waste treatment.

Study proteins affected by pollution or environmental changes.

7. Food Industry

Detect food contamination or spoilage by protein analysis.

Improve food quality and safety.

Genomics–

Genomics is the study of the entire DNA (genome) of an organism, including all of its genes and how they work together.

It helps us understand:

How genes control the body

How genes are related to diseases

How organisms are related to each other

Applications of Genomics:

Human health – find disease genes, develop treatments.

Personalized medicine – tailor drugs to a person's genes.

Agriculture – improve crops and livestock.

Forensics – identify people using DNA.

Evolution – compare genomes to study species history.

Metabolomics–

Metabolomics is the study of all small molecules (metabolites) in a cell, tissue, or organism.

These molecules are the end products of chemical reactions in the body, like:

Sugars

Amino acids

Fats

Hormones

Why Is It Important?

Metabolomics helps us understand:

How the body's metabolism is working

What's happening during disease

How the body responds to drugs or diet

Applications of Metabolomics:

Disease Diagnosis

Detects changes in metabolites linked to diseases (e.g., diabetes, cancer).

Drug Testing

Checks how drugs affect metabolism.

Nutrition Studies

Understands how different diets affect health.

Personalized Medicine

Tailors treatment based on a person's unique metabolism.

Environmental Science

Studies how pollutants affect organisms.

Functiononomics

Functiononomics is the study of the functions of genes and proteins in a living organism.

It focuses on what each gene or protein does and how it affects the body's processes.

Why is Functiononomics Important?

Helps understand diseases by knowing which genes/proteins cause problems

Supports drug discovery by identifying key protein functions

Aids gene therapy by knowing which genes to fix

Helps in biotechnology (e.g., engineering better crops or enzymes)

Nutrigenomics–

Nutrigenomics is the study of how your food (nutrition) interacts with your genes.

It helps understand:

How different people respond differently to the same food

How genes affect nutrition and health

Why is Nutrigenomics Important?

Helps make personalized diets based on your genes

Can prevent diseases like obesity, diabetes, or heart disease

Improves understanding of food allergies or sensitivities

Aids in designing functional foods (foods that boost health)

Example:

Some people have a gene that makes them process caffeine slowly → they should drink less coffee.

Others may have a gene that affects how they absorb vitamins like folate.

Immunotherapeutics

Immunotherapeutics are treatments that use the immune system to fight diseases, especially cancer, infections, and autoimmune disorders.

They are part of a broader field called immunotherapy.

Types of Immunotherapeutics:

1. Monoclonal Antibodies

Lab-made antibodies that target specific antigens on cancer cells or viruses.

2. Immune Checkpoint Inhibitors

Help remove the "brakes" on immune cells, so they can attack cancer better.

3. Cancer Vaccines

Stimulate the immune system to recognize and destroy cancer cells.

4. Cytokine Therapy

Uses proteins (like interleukins or interferons) to boost immune responses.

5. CAR-T Cell Therapy

A patient's T-cells are modified in the lab to better attack cancer cells.

6. Immune Modulators

Drugs that stimulate or suppress parts of the immune system.

Applications of Immunotherapeutics:

Cancer treatment (e.g. lung cancer, melanoma)

Chronic infections (e.g. HIV, hepatitis)

Autoimmune diseases (e.g. rheumatoid arthritis, multiple sclerosis)

Allergies and inflammation

Humanisation antibody therapy

Antibody therapy- uses antibodies (proteins made by the immune system) to target and destroy disease-causing cells, like cancer or viruses.

What is Humanization of Antibodies?

Sometimes, antibodies are made in animals (like mice) for treatment.

But when given to humans, the body may see them as foreign and attack them.

Humanization means modifying the animal antibody so it becomes more like a human antibody, reducing the chance of rejection.

Why Humanize Antibodies?

To reduce immune reactions

To make the therapy safer and more effective

To allow repeated doses without side effects

Types of Antibodies Used in Therapy:

Murine (mouse) antibodies – 100% mouse;
high risk of reaction

Chimeric antibodies – ~65% human

Humanized antibodies – ~90–95% human

Fully human antibodies – 100% human (best tolerated)

Examples of Humanized Antibody Therapies:

Trastuzumab (Herceptin) – for breast cancer

Bevacizumab (Avastin) – for colon and lung cancer

Omalizumab (Xolair) – for asthma and allergies

Immunotherapeutics in Clinical Practice

Immunotherapeutics are treatments that use the immune system to fight diseases.

In clinical practice, doctors use them to treat cancer, autoimmune diseases, infections, and allergies.

Immunotherapeutics in Clinical Practice...

1. Monoclonal Antibodies–

Target specific proteins on cancer or disease cells.

Example: Trastuzumab for breast cancer.

2. Immune Checkpoint Inhibitors

Remove brakes on immune cells to fight cancer better.

Example: Pembrolizumab for melanoma.

3. CAR-T Cell Therapy

Patient's immune cells are modified to attack cancer.
Used for some blood cancers.

4. Cytokine Therapy

Uses immune signaling proteins to boost immune response.

Example: Interleukin-2 in kidney cancer.

5. Cancer Vaccines

Teach immune system to recognize cancer cells.

Example: HPV vaccine to prevent cervical cancer.

6. Immune Modulators

Adjust immune system activity up or down.

Used in autoimmune diseases like rheumatoid arthritis.

7. Applications

Cancer treatment

Autoimmune disease management

Allergy treatment

Fighting infections