What if a single “typo” in your DNA could change the way a drug works in your body?
What if that same typo could make a life-saving medication either useless or dangerous?
That’s what mutations can do.

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SafePolyMed.eu

**Improving Safety in Polymedication by Managing Drug-Drug-Gene Interactions**

# Safety in Polypharmacy training 2026

## Session 3 - Video 2/3

## Drug-Gene & Drug-Drug-Gene Interactions

When Genes Mutate: Variations, Genomics & Ethical Frontiers

Rachel Giles, Olga Millán

LeukaNET Leukemia Advocates Network

Patvocates PATIENT ENGAGEMENT IS IN OUR DNA

Funded by the European Union

***AI Disclosure:*** *Avatars, voices, and some visual elements in this video were generated using HeyGen & Copilot. The educational content was created by humans and subsequently edited and summarised with AI assistance.*

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# Genetic Variations: Typos in Your Cookbook

Genetic variations are small changes in your DNA "recipes" Everyone has some, and they can affect how you respond to drugs

## Types of gene mutations

**1 Point Mutation**

single base-pair substitution




**a Silent**

amino acid unchanged




**b Missense**

amino acid changes
Sickle Cell example




**c Nonsense**

Premature STOP

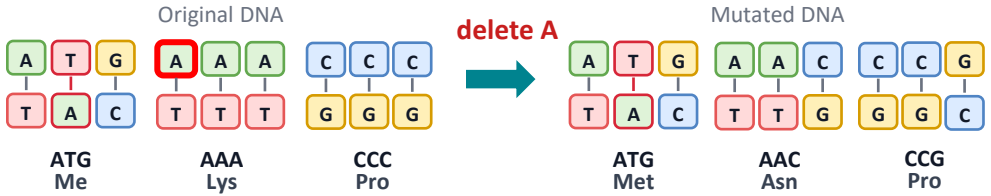


# Genetic Variations: Typos in Your Cookbook

Genetic variations are small changes in your DNA "recipes" Everyone has some, and they can affect how you respond to drugs

## Types of gene mutations

**2 Frameshift**
insertion/deletion
changes reading frame




Reading frame shifts

# Genetic Variations: Typos in Your Cookbook

Genetic variations are small changes in your DNA "recipes" Everyone has some, and they can affect how you respond to drugs

## Chromosome-level mutations

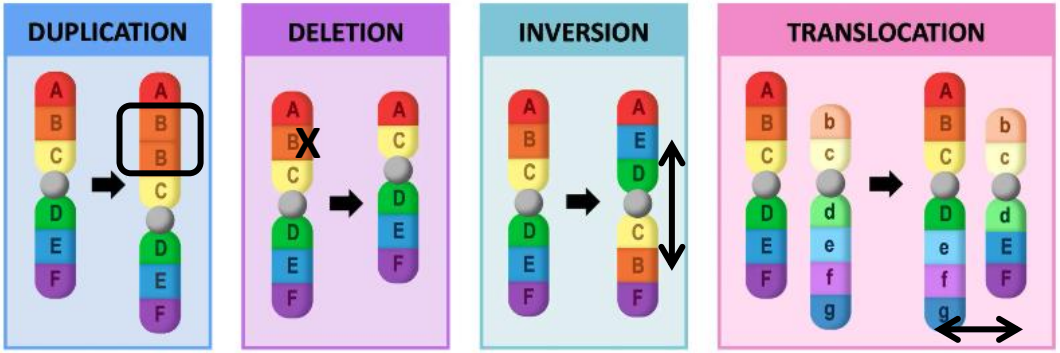
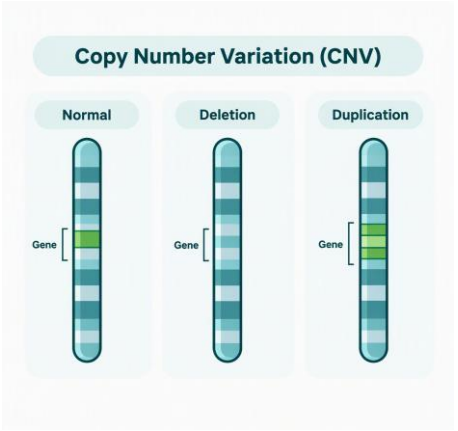



Image source: Adapted from Cornell, B. (2016). Types of Mutations. BioNinja. Available at: http://ib.bioninja.com.au/types-of-mutations/




**CNVs:** changes in gene copy number. Linked to autism and certain cancers.

💡 *Mutations can be harmless, beneficial, drive evolution, or cause disease. They arise spontaneously or from UV-radiation, chemicals, or viruses.*

*https://ib.bioninja.com.au/types-of-mutations/*
*https://geneticeducation.co.in/what-is-copy-number-variation-and-how-to-detect-it/*

# Epistasis: When One Gene Hides Another

One gene's effects can mask or modify the effects of another gene

## Sickle Cell Disease

A missense mutation in the HBB gene results in the production of HbS. Two inherited copies → red blood cells become crescent-shaped, get stuck in vessels, causing severe pain and organ damage.

***Inherit 2 copies of HBB mutation → Sickle Cell Disease develops***

## HPFH-Hereditary Persistence of Foetal Haemoglobin

People who also carry an HPFH mutation keep producing foetal haemoglobin (HbF) throughout life. This protects against the effects of the disease, leading to much milder symptoms.

***Basis for CRISPR gene therapy: to reactivate HbF in sickle cell patients***

https://microbenotes.com/epistasis-classes-types-examples-significances/
https://kidshealth.org/en/kids/sickle-cell.html

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# From Genetics to Genomics

Genomics is the study of entire genomes. Enabled by Next Generation Sequencing (NGS)



## Whole Genome Sequencing

All 20,000+ genes plus the regions between them, used to find mutations in unhealthy cells, e.g. cancer (genomic sequencing).



## Targeted Gene Sequencing

100–500 genes most likely relevant to a condition, used to find inherited mutations in healthy cells (genetic testing).

***Both are enabled by Next Generation Sequencing (NGS)***

Genetic testing is typically used to find inherited mutations in healthy cells, while genomic sequencing can be used to find mutations in unhealthy cells

*https://intermountainhealthcare.org/blogs/article/understand-the-difference-between-genetic-testing-and-genomic-sequencing*

# Incidental Findings and the Right to (Not) Know

What do you do when you are looking for one thing genetically and find something else entirely?

- **Consent & autonomy**
- **Harm vs. benefit**
- **Confidentiality (relatives)**

## Actionable finding

e.g. BRCA1 mutation raising breast-cancer risk. Preventive options exist and there is an ethical obligation to inform the patient.

## Non-actionable finding

e.g. Huntington's disease. No treatment available. Many patient communities support letting the patient choose whether to know or not.

Fully inform patients about the possibility of discovering incidental findings & Provide professional genetic counselling

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# Key Takeaways

- Mutations are "typos" in your DNA that affect drug response
- Epistasis can mask genetic effects, as seen with sickle cell and HPFH
- Genome sequencing reveals both answers and ethical dilemmas
- Genetic counseling helps patients navigate incidental findings

**Coming up next: Video 3 — pharmacogenomics, how gene editing is transforming medicine, and real-world drug-gene interaction cases.**

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# Credits & Attributions

## Authors

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## AI disclosure

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## Figures

- Chromosome-level mutation illustration adapted from Cornell, B. (2016). Types of Mutations. BioNinja. Available at: http://ib.bioninja.com.au/types-of-mutations/

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