- Pharmacogenomics
- Dr. Naser Ashraf
- Learning objectives
- Define Pharmacogenomics
- Discuss drug polymorphism
- Explain the clinical relevance of Pharmacogenomics

- **Pharmacogenetics VS. Pharmacogenomics Definitions**
- _Pharmacogenetics:_ Study of inherited variation in drug metabolism and response determined by single genes.

- *Pharmacogenomics:* General study of many different genes that determine drug behaviour

- Gene
- *Genes* are the fundamental units of heredity
- They consist of ordered sequences of nucleotides located in particular positions in a particular DNA strand
- Variations in genes
- Monogenic: due to variation at a single gene
- Polygenic: due to variations at two or more genes

- Polymorphic: frequently occurring monogenic variants occurring at a frequency   >1% population
- Single nucleotide polymorphism (SNP) most common type of genetic variation

- **Single nucleotide polymorphisms (SNPs)**
  ➢ Single base mutation which substitutes one nucleotide for another
    --Single nucleotide polymorphisms (SNPs)

- For example a SNP might change the DNA sequence
- AAGCTTAC
  to ATGCTTAC

- Drug polymorphism
- Variations in enzymes of drug metabolism
- Cytochrome Oxidase P450 Enzymes
- 57 Different active genes
- Different families 1,2,3
- CYP1, CYP2 and CYP3 are primarily involved in drug metabolism.
- CYP2A6, CYP2B6, CYP2C9 ,CYP2C19, CYP2D6, CYP2E1 and CYP3A4 are responsible for metabolizing most clinically important drugs
- Effect of Metabolic Rate on Drug Dosage
- Metabolism of 6-MP

- Pharmacogenetics: A Case Study
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- A genetically polymorphic phase II enzyme, N-acetyltransferase 2 (NAT2), catalyzes the acetylation of isoniazid.
- Variations in the enzymatic hydrolysis of the short-acting muscle relaxant

succinylcholine by the enzyme butyrylcholinesterase (BChE)
- Codeine converted by CYP2D6* to morphine
- Warfarin Levels Depend on Enzyme – CYP2C9

- Clinical relevance of Pharmacogenomics
- Knowing the frequency of pharmacogenomic variants in a given population can be helpful in prescribing
- Can reduce the rate of treatment failure

- Decrease the incidence of adverse effects
- Correct dose of a drug can be given depending on genotype
- Drug therapy can be individualized
- Polymorphism (Variation) in drug targets
- Identification of pharmacogenetic variants

- IMAGINE
- Patient will be entering into the clinic with "Data card" encoded with the sequence of it's genome.

- On the basis of patient's genetic information doctor will be prescribing the right drug in right dosage at the right time to effectively treat the condition.
- {Making the patient and the doctor free from the fear whether the treatment will work effectively or not.}