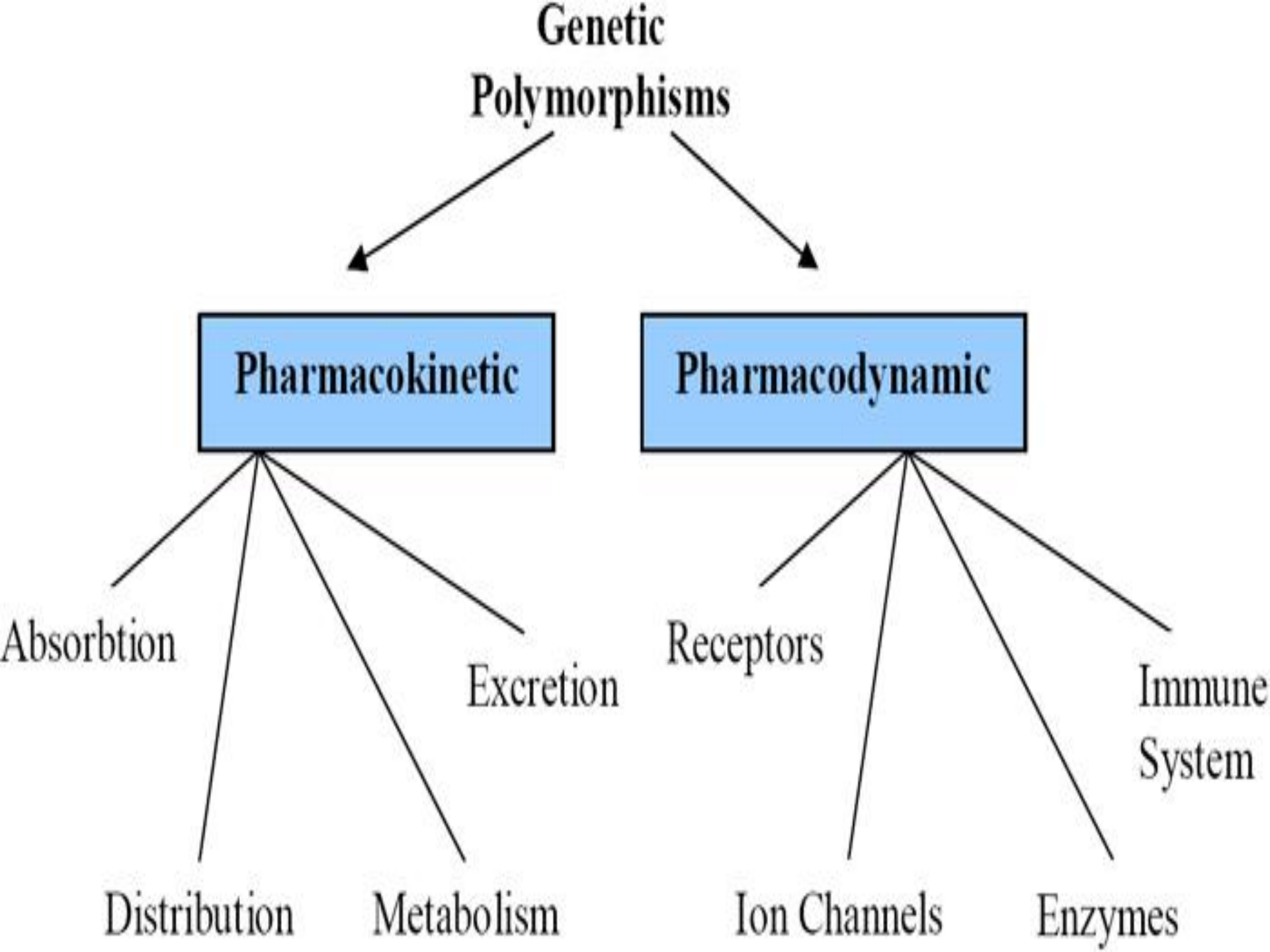
PHARMACOGENOMICS

PERSONALIZED MEDICINE

BY:
P.SANDHYA RANI

DEFINITION:

- The study of how an individual genetic makeup responds to medication.
- This term was introduced by Vogel in 1957.
- Intersection of pharmaceuticals and genetics.


Genetic
Polymorphisms
Pharmacokinetic
Pharmacodynamic
Absorbtion
Distribution
Metabolism
Excretion
Receptors
Ion Channels
Enzymes
Immune
System

BASIS OF PHARMACOGENOMICS

- Mutations-less than 1% population.
- Polymorphism-more than 1% population.
- Mostly SNPs.

➢ Where are SNPs located?

TYPES OF SNPs

- rSNPs (random SNPs).
- gSNPs (gene associated SNPs).
- cSNPs (coding SNPs).
- pSNPs (phenotype relevant SNPs).


PERSONALIZED
MEDICINE

PERSONALISED MEDICINE

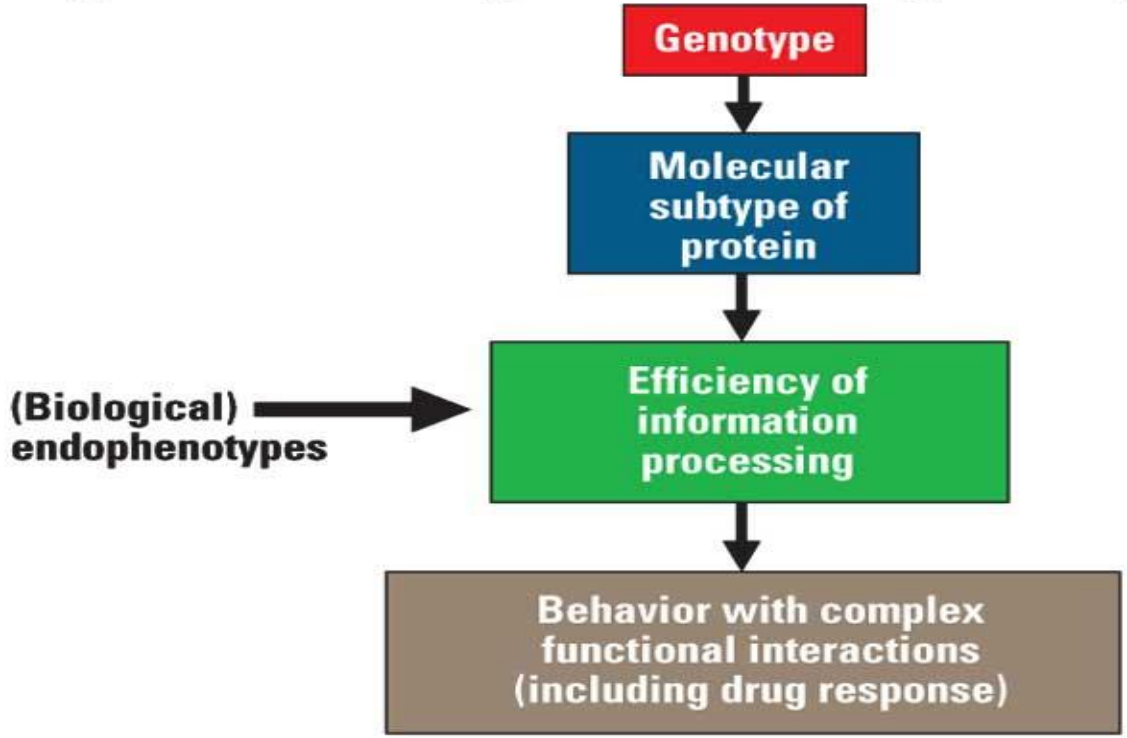
- **Personalized medicine** is the use of information from a patient's genotype to:
- initiate a preventive measure against the development of a disease or condition, or
- select the most appropriate therapy for a disease or condition that is particularly suited to that patient.

FACTORS CONTRIBUTING TO VARIABILITY IN DRUG ACTION

- Age
- Race
- Weight
- Gender
- Previous history of diseases
- Effect of drugs
- Environmental factors
- Genetics

FIGURE 1.[3]

Pharmacogenetics: how relevant are your genes to your drug response?



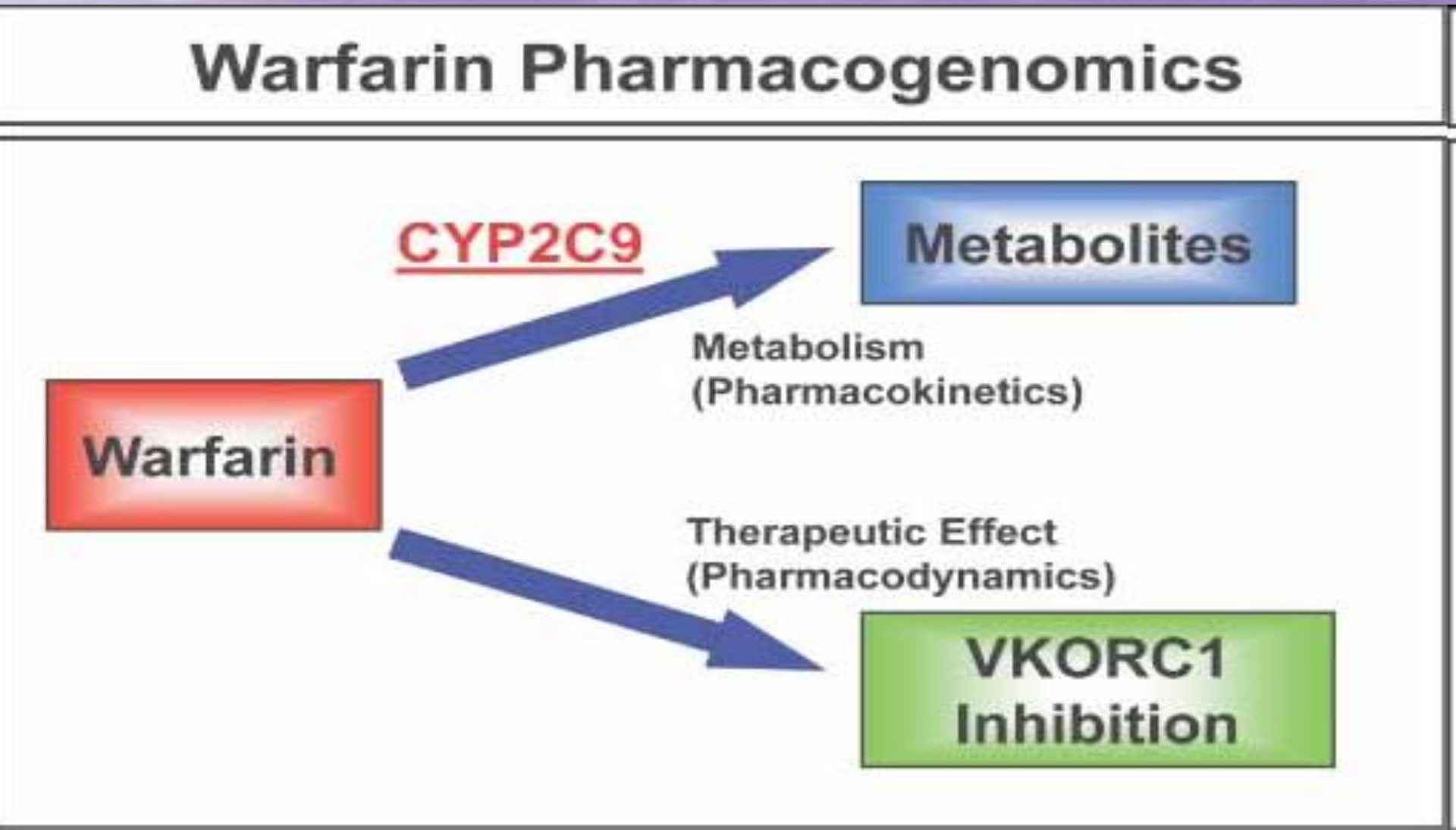
Stahl SM. *Essential Psychopharmacology*. 3rd ed. New York, NY: Cambridge University Press. In press. Reproduced with permission. Copyright Neuroscience Education Institute.

Stahl SM. *CNS Spectr*. Vol 13, No 2. 2008.

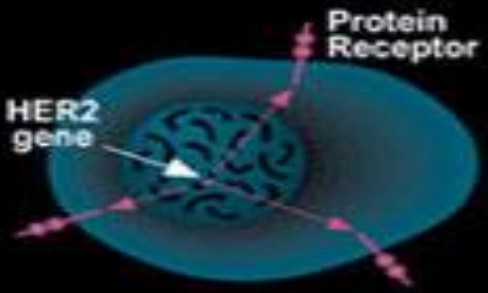
Examples of SNPs Linked to Drug Response

Gene Symbol	Description	SNPs	Clinical Phenotype
CYP2C9	Cytochrome P450 2C9	multiple	variable metabolism of CYP substrates in the liver
TPMT	thiopurine methyl transferase	multiple	hematopoietic thiopurine toxicity
UGTIAI	UDP-glcyosyl transferase IAI	multiple, in promoter & encoding regions	UGTIAI*28 variants associated with increased irinotecan toxicity
VKORC1	vitamin K epoxide reductase complex I	multiple, i.e. 1639G>A in promoter	variable anticoagulant effect of warfarin
t(9,22) translocation	t(9,22) BCR-ABL translocation	translocation	Gleevee (imatinib) effective againist chronic myeloid leukemia with translocation
ERBB2	ERBB2, HER/Neu	overexpression of protein	Herceptin for breast cancer with ERBB2 overexpression
EGFR	epidermal growth factor receptor	exon 18-21 mutations	human lung cancers with mutations response better for Iressa (gefitinib)

EXAMPLES


Warfarin Pharmacogenomics
CYP2C9
Metabolites
Metabolism
(Pharmacokinetics)
Warfarin
Therapeutic Effect
(Pharmacodynamics)
VKORC1
Inhibition

HERCEPTIN

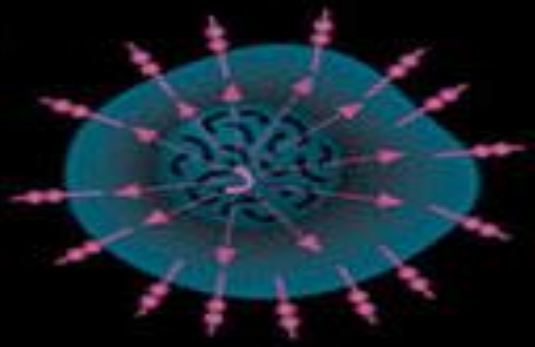


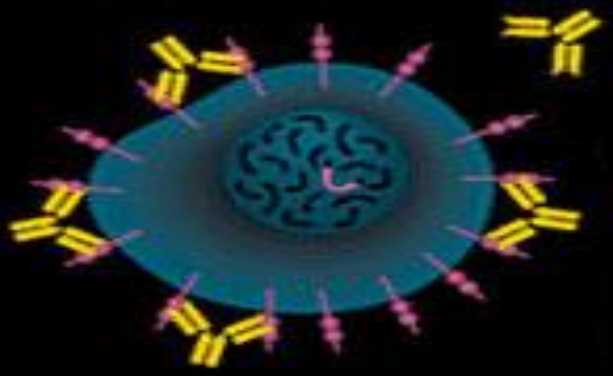
Normal Cell

In normal breast tissue cells, the HER2 gene produces a protein receptor on the cell surface. These growth factor-like receptors are thought to play a role in normal cell growth by signaling the cell to divide and multiply.

HER2 Overexpressing Cancer Cell

Cancerous breast tissue cells that overexpress (or overproduce) the HER2 gene produce extra protein receptors on the cell surface which triggers the cell to divide and multiply at an accelerated rate thus contributing to tumor growth.





Herceptin ®
(Trastuzumab)

Herceptin (a Her2 antibody) binds to numerous HER2 receptor sites found on the cell surface, blocking the receptor sites and possibly preventing further growth by interrupting the growth signal. As a result, the HER2 antibody may slow progression of the disease.

IMPORTANCE

- Novel target for drug development.
- Genetic inheritance influences variability response to drug.
- Reduces occurrence of unwanted effects of individual.

BENEFITS

- More powerful medicine.
- Better and safer drugs for the first time.
- More accurate methods of determining appropriate drug dosage.
- Advance screening for disease.
- Better vaccines.
- Improvement in drug discovery and approval process.
- Decrease the cost of health care


FEAR
MY GENES


Thank You!
shawnliv.com