



## A REVIEW ON PHARMACOGENOMICS AND ITS IMPACT IN THE DEVELOPMENT OF HEALTHCARE SYSTEM

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### ABSTRACT

Pharmacogenomics is the study of genomics/genetics and proteomics. It is the field of science which can make the goal of personalised medicine possible. This review article briefly explains about various genes associated with therapeutic activity of various Anti-cancer and Anti-retroviral drugs in humans. The need to perform PGx test to find the ADR's of these drugs and narrowing of these drugs which are used for the treatment of these diseases especially during their lethal stages. This is an critical review on why same drugs in same doses have different effects in different persons and how this field has been used in various health care systems over the period of time was described. This presentation also emphasizes the scope of pharmacogenomics in improving health care system.

**KEYWORDS** :-Pharmacogenomics, Pharmacogenomic test (PGx test), Biomarkers of Anti-cancer and Anti-retroviral drugs, Personalised medicine, Genetic polymorphism

### INTRODUCTION

#### WHAT IS PHARMACOGENETICS AND PHARMACOGENOMICS ?

The term pharmacogenetics is associated with inheritance. Study of role of inheritance in inter-individual specific genetic variation related to drug response is known as pharmacogenetics. Study of genomics and proteomics information for identification of new drugs targets and their mechanisms of action is known as pharmacogenomics. Together pharmacogenetics and pharmacogenomics are represented as PGx<sup>1</sup>.

The advancements in these field makes the development of personalized medicine or individualized medicine possible. Due to the introduction of highly sophisticated methods in genetic testing, diagnosis of the disease and identification of adverse drug reactions caused due to unidentified gene-drug variations made this approach to be used for various drugs which are having potent action. Apart from this It is also useful in identification of various genetic disorders in hereditary. By performing a genomic test known as PGx test. By using this test we can identify the potent action of various drugs on humans and identify the right drug in right dose for the right person at right time without any ADR's and narrowing of drug therapy can also be done by PGx test<sup>2,3</sup>.

#### A BRIEF HISTORY

All of this has been started in the year 1990 when a Project has been initiated to identify all the genes present within the human body and this project was known as human genome project (HGP) and It was completed in the year 2003. Its Primary goal is to identify all the genes present in the human body and to demonstrate why the effect of same drug in same dose is different from one individual to other individual even though there is similarity was maintained in all the aspects while conducting trails<sup>4,5</sup>.

This was explained after the completion of human genome project as per this project scientists have identified about 10500 genes in human body. Among which most of the genes are similar in all the individuals but the differences in effect is due to the folds present in the genes. Each gene is found to have about 100-150 folds in it. And about all the known genes are having these folds and there is slight difference in these folds from one individual to another individual and due to this their enzyme activity varies. Based on this they have categorized humans into four subgroups due to the differences in their enzyme activity<sup>4,5</sup>.

1. Slow /poor metabolisers - they have reduced or no enzyme activity.
2. Intermediate metabolisers – they have reduced enzyme activity.
3. Extensive metabolisers – they have normal enzyme activity.



## 4. Ultrarapid metabolisers – they have high enzyme activity.

Due to these differences the activity of drugs varies from individual to individual even though same drug is given in similar doses. All of this is due to the success of human genome project and this knowledge of genomics has been used by various fields to identify better drug therapy for treatment, narrowing of drugs used for therapy and it is also to reduce many ADR's. Thus the usage of pharmacogenomics is not limited to a specific field and the following piechart representing various fields which are using pharmacogenomics in their therapy<sup>4</sup>.

### VARIOUS PHARMACOGENOMIC BIOMARKERS of ANTI-CANCER DRUGS AS PER FDA DRUG LABELING<sup>6,10,11,12,13</sup>

Disease	Biomarker	Therapy
BREAST CANCER	HER2	Trastuzumab, lapatinib, pertuzumab, ado-trastuzumab emtansine
BREAST CANCER	ESR1	Exemestane, letrozole, anastrozole, fulvestrant, tamoxifen
Colorectal	KRAS	Cetuximab, panitumumab
Colorectal	EGFR	Cetuximab, panitumumab
Colorectal	DPYD	5-Fluorouracil, capecitabine
Colorectal	UGT1A1	Irinotecan
Lung	ALK	Crizotinib, ceritinib
Lung	EGFR	Erlotinib, gefitinib, afatinib, osimertinib
Melanoma	BRAF	Vemurafenib, dabrafenib, trametinib
Acute promyelocytic leukemia	PML-RAR $\alpha$	Arsenic trioxide, tretinoin
Chronic myeloid leukemia	BCR-ABL	Imatinib, dasatinib, nilotinib, bosutinib, ponatinib, omacetaxine mepesuccinate
Chronic myeloid leukemia	UGT1A1	Nilotinib
Cutaneous T-cell lymphoma	CD-25/IL2RA	Denileukin diftitox
Chronic lymphocytic leukemia	(CLL) del(17p)	Ibrutinib
Chronic lymphocytic leukemia (CLL)	CD20/MS4A1	Obinutuzumab, rituximab
Acute lymphocytic leukemia	TPMT	6-Mercaptopurine, thioguanine

These are various biomarkers available for anti-cancer drugs. Each biomarker is unique and differs in function from other biomarkers in metabolizing various anti-cancer drugs. One or more biomarkers are available for same cancer type. These biomarkers are given by U.S. FDA and are helpful in narrowing of drug therapy for patients diagnosed with lethal stages of cancer. This method was also proven to be very effective in identification of effective therapy for the patient without causing any ADR's while performing PGx test for specified cancer<sup>12</sup>.



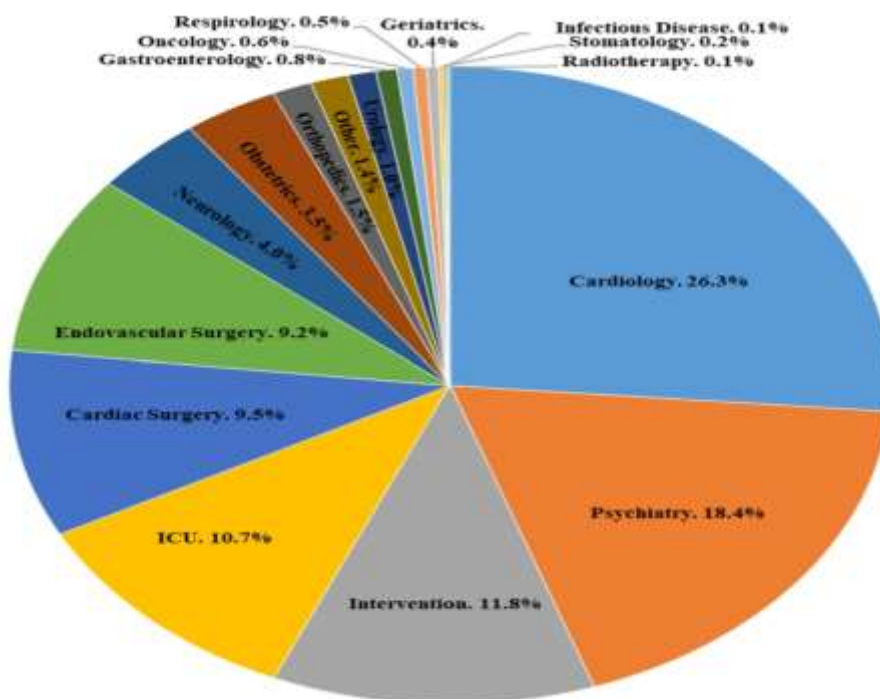
**BIOMARKERS OF ANTI-RETERO VIRAL DRUGS<sup>13</sup>**

BIOMARKERS	ANTI-RETERO VIRAL DRUGS
<b>IL-6</b>	Tenofovir,emtricitabine
	Abacavir,lamivudine
	Efavirenz
	Atazanavir
<b>hs-CRP</b>	Tenofovir,emtricitabine
	Efavirenz
	Abacavir,lamivudine
<b>sCD14</b>	Efavirenz
	Lopinavir/ritonavir
<b>IP10</b>	Atazanavir/ ritonavir
	Tenofovir,emtricitabine
<b>MIG</b>	Abacavir,lamivudine
	Lopinavir/ritonavir

Above mentioned are some of the biomarkers identified for the respective anti-reteroviral drugs. The identification of these biomarkers has helped to reduce the adverse drugs reactions the occurred during anti-reteroviral therapy. Performing of PGx test also helps in narrowing of drug therapy which will be a cost effective method in treating HIV patients when compared to other methods<sup>7,8</sup>.

Even though a vast number of biomarkers are present above mentioned biomarkers are having major influence on drug therapy and these are recognized by U.S FDA and certain guidelines have been issued to conduct PGx test<sup>13</sup>.

**VARIOUS FIELDS OF SCIENCE USING PHARMACOGENOMICS<sup>8</sup>**





## CONCLUSION

Pharmacogenomics is useful in development of personalized medicine for every individual and personalized medicine holds the promise that treatments will be one day tailored to your genetic makeup. Thus there is wide scope for the usage of pharmacogenomics in all the fields of life sciences for identification of a disease and also to minimize the adverse reactions which arises during their drug therapy .

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