WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 3, 254-275. Review Article ISSN 2277– 7105

PHARMACOGENOMICS: CONCEPT AND BENEFIT

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Article Received on
28 Dec. 2019,

Revised on 18 Jan. 2020,
Accepted on 08 Feb. 2020,

DOI: 10.20959/wjpr20203-16680

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ABSTRACT

Pharmacogenomics is the concept which involve the analysis of how genes are responsible for variable action of drug in concerns to Individual. The emerging new field deals the knowledge and facts of pharmacology combine with genomics. Genomic which deals with the systemic form, function and interaction of the gene. When drug administered to individual the variable effect if observed is due to individual genetic makeup. Research on Pharmacogenomic will help Physician to prescribe more specific drug and dose as per the genetic orientation of the Individual which aims to minimize adverse drug events.

KEYWORDS: Genomic which deals with the systemic form, function and interaction of the gene.

INTRODUCTION

Pharmacogenomics is a science that examines the inherited variations in genes that dictate drug response and explores the ways these variations can be used to predict whether a patient will have a good response to a drug, a bad response to a drug, or no response at all.

- It is the study of how an individual's genetic inheritance affects the body's response to drugs. The term comes from the words pharmacology and genomics and is thus the intersection of pharmaceuticals and genetics.
- Researchers in the field are working on applying human genome knowledge to pharmaceuticals by identifying genes that account for varying drug reactions in different people. Eventually, they hope to be able to customize drug therapies for specific patient populations or even individuals.
- Pharmacogenomics holds the promise that drugs might one day be tailor-made for

individuals and adapted to each person's own genetic makeup. Environment, diet, age, lifestyle, and state of health all can influence a person's response to medicines, but understanding an “individual's genetic makeup” is thought to be the key to creating “personalized drug “therapies.

Currently, much of the research in the field of pharmacogenomics is focused on genes encoding either metabolic enzymes that can alter a drug's activity or defective structural proteins that result in increased susceptibility to disease.

Cause of ADR

Each of us responds differently to our environment, to the foods we eat, and to the drugs we take. The way we respond to drugs may mean that a drug that is effective for one person may be less effective for another, or that a drug that is safe for one person may be dangerous for another person—even at the same dosage.

Many drugs are altered by the body by metabolizing them using enzymes. In some cases, an active drug is made inactive or less active through metabolism.

In other cases, an inactive or less active drug is made more active through metabolism. The challenge in drug therapy is to make sure that the active form of a drug stays around long enough to do its job.

However, some of us have enzymes that are a little different than the “normal” so we may metabolize the drug too quickly or too slowly or not at all — meaning that the drug may be gone before it has its intended effect, or hangs around too long and may build up beyond safe level.

ONE SIZE FITS ALL?

Currently, there is no simple way to determine whether people will respond well, badly, or not at all to a medication; therefore, pharmaceutical companies are limited to developing drugs using a "one size fits all" system. This system allows for the development of drugs to which the "average" patient will respond. But, as the statistics above show, one size does “NOT” fit all, sometimes with devastating results. Today, nearly 3 million prescriptions out of the approximately 3.5 billion written annually are wrong. While most of those errors are minor, numerous studies have identified a rising incidence of adverse drug reactions in patients. At the core of the issue is that traditional drugs cannot differentiate among different

types of patients. In one measure, there are high responders, those who demonstrate high-drug efficacy; poor responders, those who demonstrate incomplete drug-efficacy; and non-responders, those who demonstrate no drug response. This latter group may have a hightened risk of ADR's.

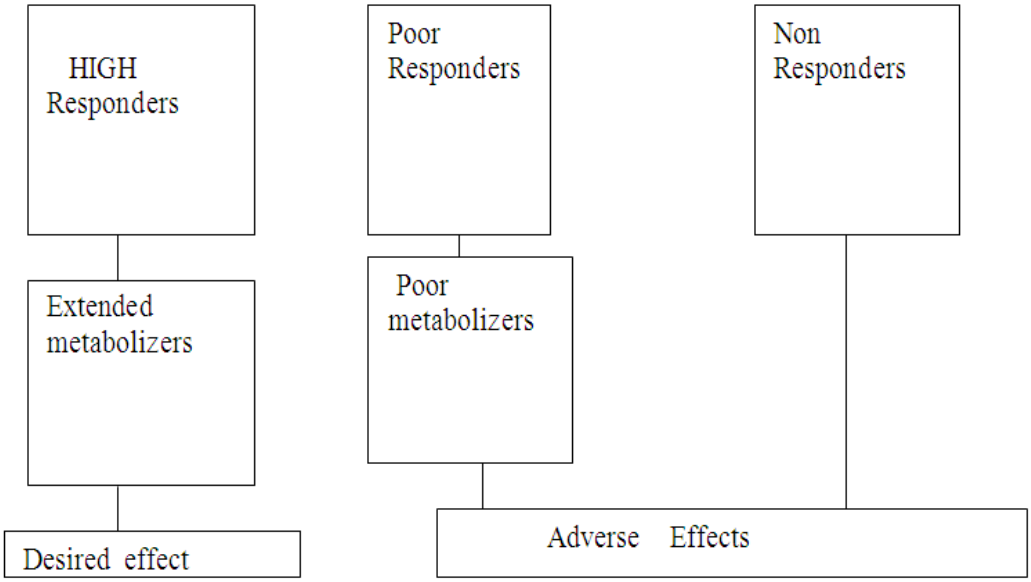


Fig: Factors determining an individual's drug reaction.

Thus Today's world is engulfed in a "rational drug design" in which drugs are created with the intention of aiding the population as a whole. However, these one-size-fits-all drugs only work for about 60 percent of the population at best. And the other 40 percent of the population increase their risks of adverse drug reactions.

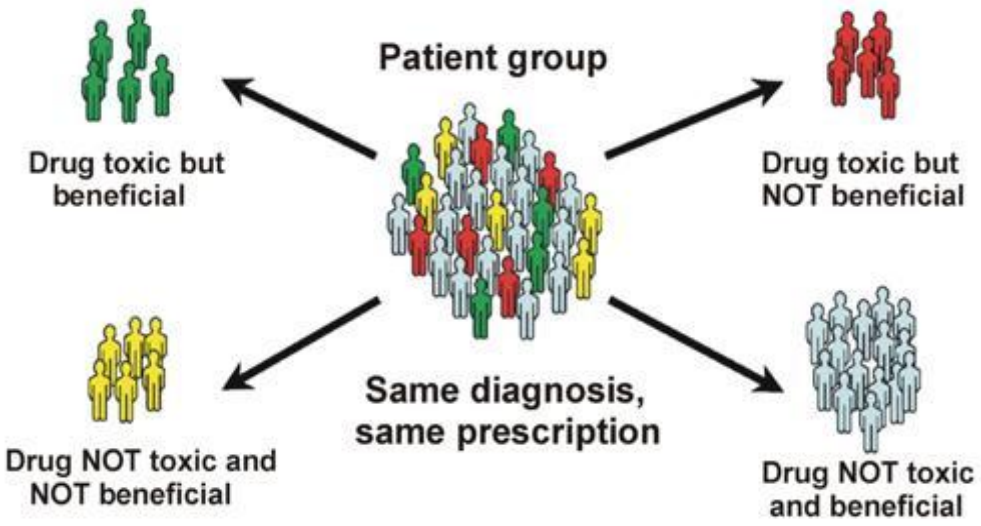


Fig: Disadvantages of the "one size fits all" system.

However many of these deaths due to ADR's, could be avoided if the physician had prior knowledge of patients genetic profile of drug metabolizing enzymes and receptors which determine drug responses. This is the wherein the study of "PHARMACOGENOMICS" comes into play.

VARIOUS METABOLIC ENZYMES WHICH AFFECTS BODY's RESPONSE TO DRUGS

There are two issues involved in giving a drug: how well it works and what side effects it causes. How you metabolize a drug will affect both of those.

There are a number of types of enzymes in the liver that metabolize medications. Some of these enzymes include:

- The Cytochrome P450 family
- N-acetyltransferase
- Thiopurine methyltransferase (TPMT
- UDP-glucuronosyltransferase

Due to variation of the se enzyme in human physiology, Many drus show variable effect in different individual.

Cause of Genomic variation

Scientists estimate that the genomes of non-related people—any two people plucked at random off the street—differ at about 1 in every 1,200 to 1,500 DNA bases, or "letters." There are more than three million differences between your genome and anyone else's. On the other hand, we are all 99.9 percent the same, DNA-wise.

- Most genome variations are relatively small and simple, involving only a few bases—an A substituted for a T here, a G left out there, a short sequence such as CT added somewhere else, for example. Your genome probably doesn't contain long stretches of DNA that someone else's lacks.
- If the genome were a book, every person's book would contain the same paragraphs and chapters, arranged in the same order. Each book would tell more or less the same story. But my book might contain a typo on page 303 that yours lacks, and your book might use a British spelling on page 135 "colour" where mine uses the American spelling "color"
- Every human genome is different because of variations -"mistakes" that occur occasionally in a DNA sequence. When a cell divides in two, it makes a copy of its

genome, then parcels out one copy to each of the two new cells. Theoretically, the entire genome sequence is copied exactly, but in practice a wrong base is incorporated into the DNA sequence every once in a while, or a base or two might be left out or added. These mistakes-"changes" might be a more accurate word, because they are not always bad news-are called variations.

- When a mutation occurs in a sex cell-a sperm or an egg-it can be passed along to the next generation of people. Your genome contains about 100 "new" variations- changes that occurred as your parents' bodies made the egg and spermcells that became you. These genome variations are uniquely yours. Other variations in your genome arose many generations ago and have been passed down from parent to child over the years, until they ended up in you.

Location and kind of Genome Variation

- Variations are found all throughout the genome, on every one of the 46 human chromosomes. But this variation is by no means distributed evenly: It's not as if there is one difference every 1,000 bases as regular as rain. Instead, some parts of the genome are "hot spots" of variability, with hundreds of possible variations of a sequence. Other parts of the genome, meanwhile, don't vary much at all between individuals - in scientific parlance, they are said to be "stable."
- The majority of variations are found outside of genes, in the "extra" or "junk" DNA that does not affect a person's characteristics. Mutations in these parts of the genome are never harmful, so variations can accumulate without causing any problems. Genes, by contrast, tend to be stable because mutations that occur in genes are often harmful to an individual, and thus less likely to be passed on.
- Genome variations include mutations and polymorphisms. Technically, a polymorphism (a term that comes from the Greek words "poly," or "many," and "morphe," or "form") is a DNA variation in which each possible sequence is present in at least 1 percent of people.
- For example, a place in the genome where 93 percent of people have a T and the remaining 7 percent have an A is a polymorphism. If one of the possible sequences is present in less than 1 percent of people (99.9 percent of people have a G and 0.1 percent have a C), then the variation is called a mutation.

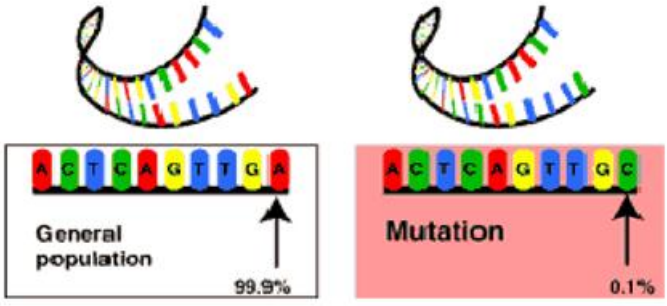
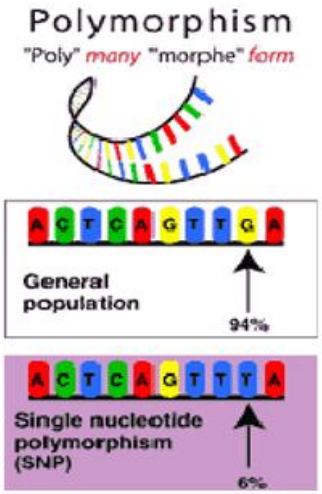


Fig: Example of mutations.

- Informally, the term mutation is often used to refer to a harmful genome variation that is associated with a specific human disease, while the word polymorphism implies a variation that is neither harmful nor beneficial.



- However, scientists are now learning that many polymorphisms actually do affect a person's characteristics, though in more complex and sometimes unexpected ways. There is a great deal of inter-individual variability at the DNA level. Single nucleotide polymorphisms (SNPs) account for over 90% of genetic variation in the human genome. The remainder of the variation is caused by insertions and deletions (indels), tandem repeats and microsatellites.
- With the completion of the human genome project and first phase of the HapMap, a wealth of polymorphism information is now readily accessible via publicly available databases.

SINGLE NUCLEOTIDE POLYMORPHISM

About 90 percent of human genome variation comes in the form of single nucleotide polymorphisms, or SNPs (pronounced "snips"). As their name implies, these are variations

that involve just one nucleotide, or base. Any one of the four DNA bases may be substituted for any other—an A instead of a T, a T instead of a C, a G instead of an A, and so on.

- Theoretically, a SNP could have four possible forms, or alleles, since there are four types of bases in DNA. But in reality, most SNPs have only two alleles. For example, if some people have a T at a certain place in their genome while everyone else has a G, that place in the genome is a SNP with a T allele and a G allele.

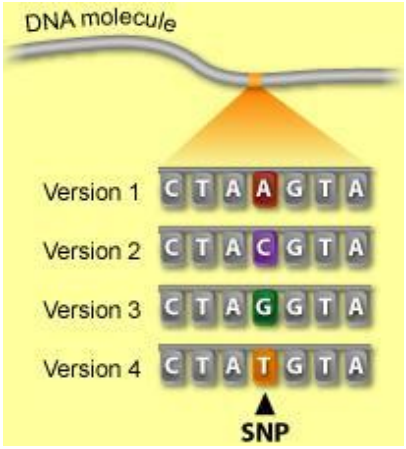


Fig: A Snp and its distribution in a population might look like this.

There are different types of SNPs

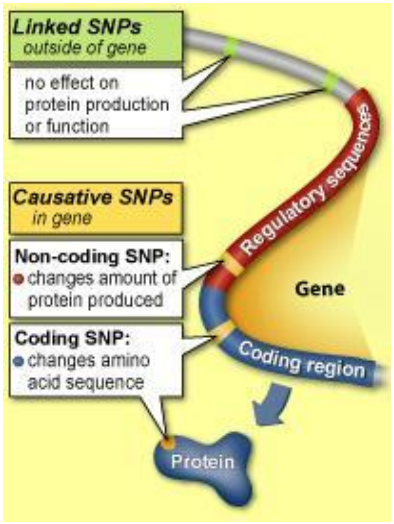


Fig: Different types of SNPs.

SNPs are divided into two main categories

1. Linked SNPs: (also called as indicative SNPs) do not reside within genes and do not affect protein function. Nevertheless, they do correspond to a particular drug response or to the risk of getting certain disease.

2. Causative SNPs: they affect the way a protein functions, correlating with a disease or influencing a persons response to a medication. Causative SNPs come in two forms:

3. CodingSNPs: these are located within the coding area of a gene, change the amino acid sequence of the gene's protein products.

4. Non-codingSNPs: these are located within the gene's regulatory sequences, chane the level of gene expression and therefore, how much rna and protein is produced.

The following examples show how important SNPs are in relation to medical practice. The effects of these sequence variations can be divided into two categories that are of relevance to medicine:

- On the one hand, interference with the action of drugs, or, to be more precise, with the way in which the body deals with drugs;
- On the other hand, involvement in the development and progression of diseases.
- Variations of the first category may help explain why drugs work more or less well in some people and why they may cause undesirable side effects only in certain people. This is the main area of study in the field of pharmacogenomics.
- Variations of the second category are important reasons why individuals differ in terms of their susceptibility to certain diseases.

Importance of SNPs in Pharmacogenomics

Pharmacogenomic studies investigate genes and their effects on the pharmacodynamics or pharmacokinetics of drugs.

- 'Pharmacokinetics' describes the metabolism of drugs, i.e. their uptake, conversion and breakdown in the body.
- In some people, for example, a drug fails even before it reaches its site of action. Their body takes up the molecule very slowly or sometimes not at all. In other individuals, conversion of the drug (for example to remove a protective molecular cap) proceeds sluggishly. And a third group of patients breaks the drug down too quickly or too slowly.
- Thus if a drug is broken down too rapidly, taken up too slowly or converted too slowly, its effects will not be felt. Conversely, if a drug is broken down or excreted too slowly, its effects may be magnified. It then remains too long in the body, and the risk of side effects increases sharply.
- These differences are due not only to environmental factors and diet but also to people's genetic makeup.

- This is because specific proteins in our body are responsible for metabolizing drugs. And the blueprint for those proteins resides in our genes. Hence, small differences in the genomes of patients can result in pharmacokinetic differences.
- 'Pharmacodynamics', by contrast, describes the interaction between drugs and their molecular targets. In the classic case this relates to the etiology of a disease, i.e. its underlying molecular causes.
- Usually the activity of an endogenous protein is impaired. The shape of such proteins is genetically determined. Small differences in our genome can therefore significantly alter the structure of these proteins. And since drug are usually highly sensitive to such differences –after all, a drug is supposed to act on a very specific target molecule so as to have as few side effects as possible – they may become ineffective if the target molecule is altered.
- Thus for pharmacogenomics to be effective, markers must be found that indicate the connection between drug response(pharmacokinetics and pharmacodynamics) and genetic makeup. The markers that companies are pursuing most diligently are known as single-nucleotide polymorphisms, or SNPs.
- SNPs, are thought to determine our individual genetic differences to a large degree. Depending on the position of a SNP within a gene, the corresponding gene product is more or less strongly affected.
- An enzyme, for example, may be impaired, destroyed or improved – with corresponding implications for drugs that interact with that enzyme.
- If specific SNPs are repeatedly associated with a disease or with specific side effects or drug failures.

It can thus be assumed that the genes concerned have something to do with the observed disturbance.

- Thus by collecting and analyzing the DNA of a diverse group of many individuals, researchers are working toward identifying SNPs that are relevant markers of drug response and disease susceptibility, an endeavor they hope will ultimately yield diagnostic tests and targeted drugs based on genotype.
- However SNPs tend to occur in patterns or blocks called haplotypes. Thus Haplotypes are inherited groups of SNPs that occur within a defined region of the chromosome, and some of them may influence drug response more than individual SNPs do.

- Some experts believe that identifying haplotypes of interest will yield more useful biomarkers of response by accounting for genomic variation in the multiple genes often involved in drug response.

Techonologies used for the detection of Genomic Variation

Breakthrough technologies such as polymerase chain reactions (pcr), high thoroughput robotic sequencing, DNA microassay as well as simultaneous advances in bioinformatics have enabled great leaps forward in the ability to quantify and analyze genetic variations.

1. Polymerase chain reaction (PCR)

Vanishingly small amounts of DNA can be rendered visible by means of the polymerase chain reaction (PCR).With the aid of the DNA-extending enzyme polymerase, a single DNA molecule can be copied in a chain reaction (‘amplified’) as many times as desired and thus made available for investigation., PCR can be used to identify the specific variant of this target molecule present in a patient and then select the most appropriate drug.

PCR plays a key role in identifying genes with SNPs responsible for variations in the metabolizing enzymes and proteins.

2. DNA chips (DNA microarrays)

One of the most important DNA chip technologies was developed by the Californian company Affymetrix. The name of this company’s best-known product, GeneChip, is often used synonymously with the term DNA chip to refer to any such product.

GeneChips uses the principle of photolithograpzhy, just as in the manufacture of computer chips. In this technique a light source, special masks and photosensitive protector molecules are used to deposit billions of oligonucleotides with (at present) up to 700,000 different base sequences alongside each other intiny cells (spots) on a chip. Such a GeneChip is then incubated with a solution containing the DNA of interest, which has previously been labelled with a fluorescent dye. Whether given oligonucleotides on the chip have hybridised with DNA in the solution is apparent from the positions on the chip at which fluorescent dye is present at the end of the experiment. For this purpose the individual positions on the chip are read with a scanner. The readings are analysed by computer with the aid of specially developed programs.

Use of DNA chips in identifying SNPs

Our genetic predisposition has considerable influence on the efficacy and tolerability of medicines. This is due mostly to small differences in our genome known as 'single nucleotide polymorphisms', or SNPs (pronounced 'snips')

DNA chips can be used to detect these differences rapidly and reliably, and in this way can provide doctors with crucial information to assist them in choosing the most appropriate treatment for a particular patient. Also, it is only with the aid of such techniques that novel medicines that take account of individual differences in the way our body reacts to drugs can be developed.

DNA chips are therefore set to play a major role in the development of personalised medicine.

The Amplichip cyp450

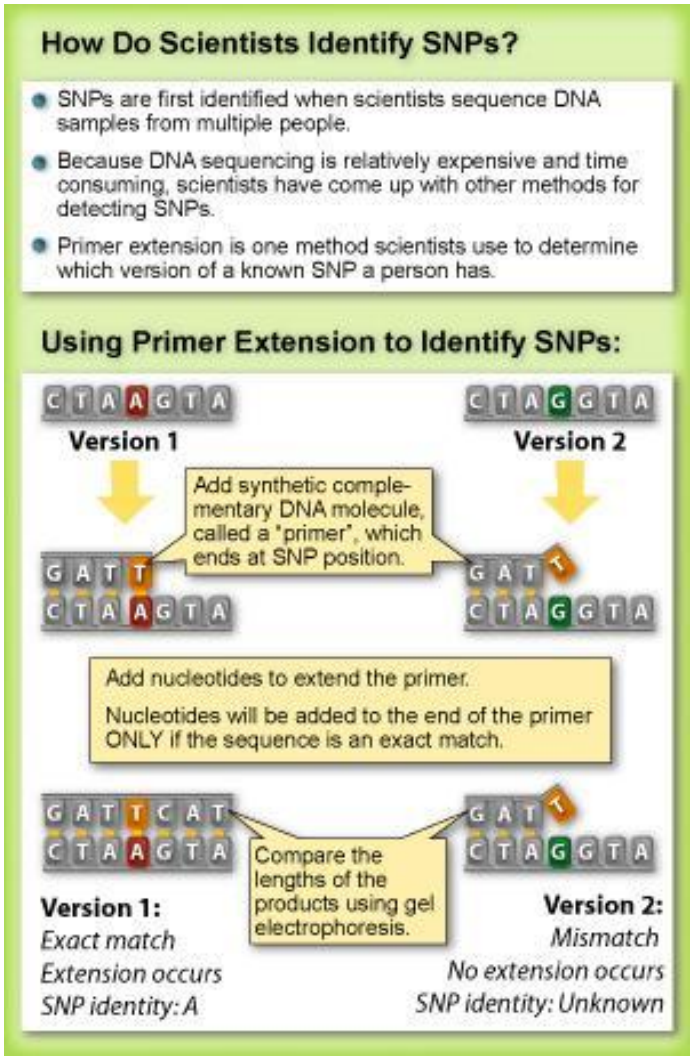
The AmpliChip CYP 450 arrived on the market in 2003. The scientific basis of this chip is formed by pharmacogenomic data on the influence of the cytochrome P450 gene family on the efficacy and tolerability of drugs.

The Ampli Chip CYP450 is able to identify the most important variants of two important members of this group of genes concerned and of the molecular basis of disease, such chips will in future contribute to earlier detection, more effective treatment and possibly even prevention of diseases.

Fig: Amplichip cyp 450.

3. Primer extensions to identify SNPs

The test would examine your DNA sequence in the area of the genome that contains the gene for the specific drug-binding protein. It would look for one or more SNPs. Reliable SNPs could serve as predictive markers that inform our decisions about numerous aspects of medical care, including specific diseases, effectiveness of various drugs and adverse reactions to specific drugs.



A group called the SNP Consortium-a partnership of pharmaceutical and technology companies, academic research centers, and the Wellcome Trust--is working to publish a high-density SNP map of the human genome to map 300,000 SNPs

- Sequenom, based in San Diego, uses mass spectrometric methods to study SNPs. "The advantage of using a mass spectrometer as a detector is that the mass spectrometer is a self-validating instrument.
- Genaissance Pharmaceuticals in New Haven, and Variagenics in Cambridge, Mass., look

for SNPs that travel in groups, known as haplotypes, and work together to cause a particular drug response.

- Variagenics uses a technology called NuCleave, which incorporates mass spectrometry as the detection method, for looking at haplotypes. A small region of the DNA around a SNP is amplified, the DNA is then fragmented and the mass of the fragments produced are measured. In this way the sequence around the SNP is determined.

INSILICO RESEARCH

For a long time now, the work that researchers do in their computers has been at least as important as the work they do in their laboratories. Modern experiments, especially if automated, yield an unimaginable amount of data that could not possibly be analysed without the aid of powerful computers and specially developed computer programs. Thus the insilico research of the drugs has gained prominence in the study of pharmacogenomics.

Fig: Pharmacogenomics relies on high-throughput genetic analysis.

BIOINFORMATICS

The application of modern information technology to biological research, is an independent scientific tool in aiding the sudy of pharmacogenomics.

Bioinformatics derives knowledge from computer analysis of biological data. These can consist of the information stored in the genetic code, but also experimental results from various sources, patient statistics, and scientific literature. Research in bioinformatics includes method development for storage, retrieval, and analysis of the data. Bioinformatics is a rapidly developing branch of biology and is highly interdisciplinary, using techniques and concepts from informatics, statistics, mathematics, chemistry, biochemistry, physics, and linguistics. It has many practical applications in different areas of biology and medicine.

Roughly, bioinformatics describes any use of computers to handle biological information. In practice the definition used by most people is narrower; bioinformatics to them is a synonym for "computational molecular biology"- the use of computers to characterize the molecular components of living things.

EXAMPLES OF PHARMACOGENOMIC DRUGS USED PRESENTLY

THE RIGHT DRUG - FOR CANCER

- Pharmacogenomics is used in targeted therapy for cancer to identify the best drug regimen for a particular tumor. Even tumors of the same type (such as lung, breast, or liver) vary at the genetic level. Cancer is fundamentally a genetic disease, but most of the genetic differences between cancer cells and normal cells are not inherited—they accumulate as the cancer develops. Analyzing specific genes in a patient's tumor helps doctors identify the drug combination to which the tumor will most likely respond.

1. Herceptin, which is used in the treatment of breast cancer is the first example of a genetically specific drug. Herceptin is only effective in women with a genetic defect which results in the overproduction of a molecule known as the HER2 receptor. When present in excessive numbers on the surface of certain breast cells, these receptors promote cellular growth, leading to tumours. Herceptin is directed against the receptor; it therefore only helps women who have an increased number of copies of the relevant gene. In all other women this highly specific drug is much less effective. Herceptin can therefore be used only in conjunction with a suitable genetic test.

- Three such tests are currently available:
- First, the receptors can be visualised on the surface of tumour cells with the help of specific antibodies linked to a dye.
- Second, there is a gene test known as FISH which directly detects the genetic change in question.
- Recently a third test based on the polymerase chain reaction has become available – at least for research purposes. Using this technique investigators can copy the relevant DNA section in the laboratory, thus revealing if the dangerous genetic change is present.

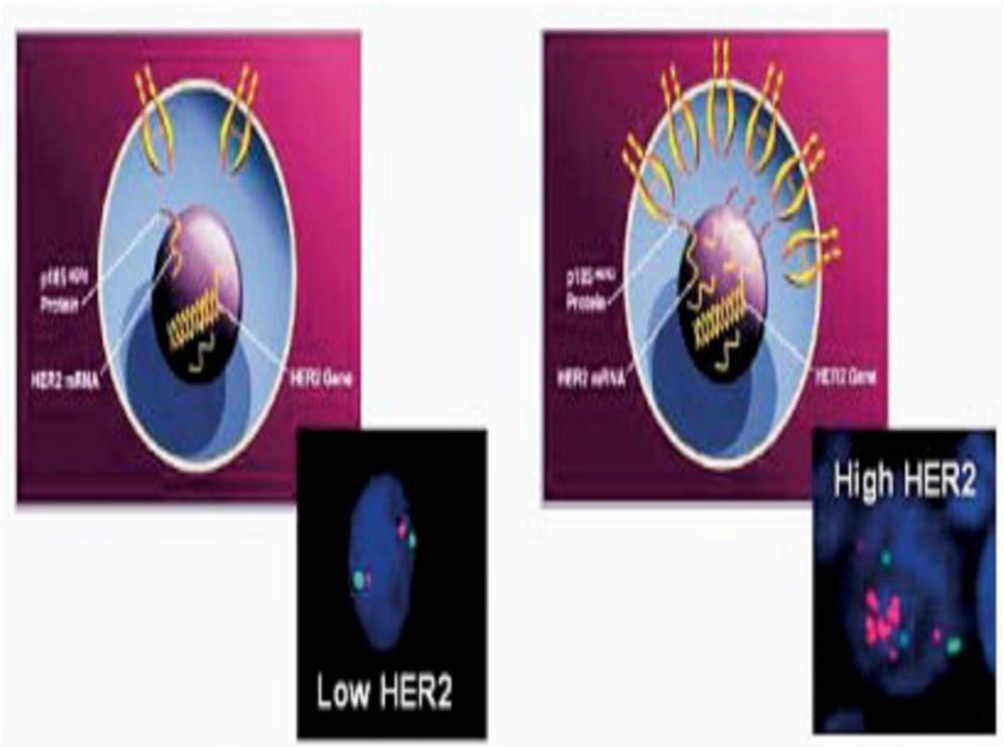


Fig: Normal and Overexpression of HER2.

2. There is now a commercially available diagnostic test measuring a patient's ability to produce the metabolic enzyme thiopurine S-methyltransferase (TPMT), which is essential for the metabolism of thiopurine medications used to treat acute lymphoblastic leukemia (ALL), the most common form of childhood cancer.

- Genetic testing gives clinicians the ability to classify" ALL" patients according to their TPMT genotype, which allows optimized dosing. Doses in patients with alleles rendering them deficient in TPMT (who are thus less tolerant of thiopurine medications) are reduced by as much as 95%. This means TPMT-deficient patients can tolerate the drug, yet enough is still metabolized to retain efficacy.

3. In patients with Chronic myeloid leukemia (Cml), an abnormal protein directs the body not only to overproduce white blood cell but to alter the cell's make up so that they live longer than normal cells do .Approximately 4500 new cases of Cml are reported in the united states each year, with an estimated 2400 americans dying from the disease annually.

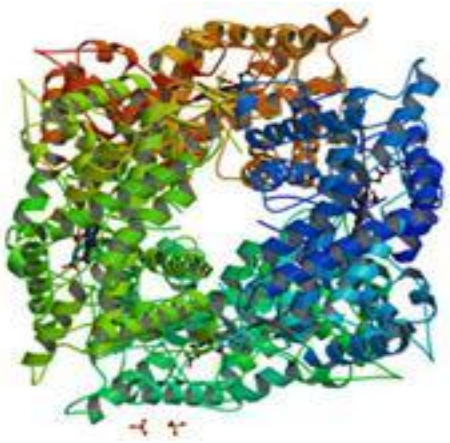
- This small subset of leukemia patients carries a distinct biomarkers: an abnormal chromosome 22, or the Philadelphia chromosome. the reciprocal translocation between 9 and 22 that creates the Philadelphia chromosome also directs the production of Bcr-Abl

tyrosine kinase, the abnormal protein that causes Cml.

In may 2001, a brand name version of the compound imatinib mesylate, designed to block the abnormal protein was approved in the USA. The drug reduces the number of WBC's to normal levels and relieves the symptoms associated with Cml. The drug is indicated for the treatment of newly diagnosed adult patients with Philadelphia chromosome- positive (Ph+) Cml in chronic phase.

THE RIGHT DRUG – FOR HIV

- For patients with a bacterial or viral infection, analyzing the genes of the infectious agent can reveal the most suitable drug treatment. For example, the Food and Drug Administration (FDA) has approved a genotyping kit that detects genetic variations in HIV that make the virus resistant to some antiretroviral drugs. If drug resistance is discovered, doctors can prescribe other medications.



THE RIGHT DRUG – FOR DEPRESSION

- This computer-generated image shows the molecular skeleton of a liver enzyme called Cytochrome P450 2D6, which helps people process a wide range of medicines. Because the enzyme comes in several varieties, it is of great interest to pharmacogenomics researchers.

Depression can be treated with a variety of different medicines, and it is often time-consuming and difficult to find the drug(s) that works best for each person. In the future, genomic testing may take some of the guesswork out of choosing a drug regimen. These tests are likely to involve analyzing a person's liver enzymes, especially those in the cytochrome P450 family, which are largely responsible for processing antidepressants.

- Other tests that may prove useful to psychiatrists will detect differences in the molecules targeted by antidepressants, such as the serotonin transporters targeted by a large class of antidepressants called selective serotonin reuptake inhibitors (SSRIs). Scientists have uncovered evidence for a link between a person's response to SSRIs and variations in serotonin transporters and other biological molecules that act on serotonin.
- Several companies now offer CYP450 genotyping tests to the pharmaceutical industry for clinical trial subject inclusion/exclusion based upon metabolic profile, and now such tests are making their way into the clinical diagnostic marketplace. Gentris, for example, soon expects to market five kits to physicians for pharmacogenomic testing of their patients. Genelex Corporation of Seattle, Washington, has taken the concept one step further, marketing tests directly to the public for three of the major CYP450 pathways--CYP2D6, CYP2C9, and CYP2C19. Once a consumer has placed an order for the test, Genelex sends them a blood collection kit, and the consumer either sees their own doctor or Genelex will refer them to a phlebotomist in their area.

THE RIGHT DRUG - FOR CARDIOVASCULAR DISEASE

Statins, the most widely prescribed drugs worldwide, help prevent cardiovascular disease by reducing the level of "bad" cholesterol in the bloodstream. While statins work well for many patients, responses are highly variable and doctors must adjust the dosage for each person.

- Researchers have discovered that variants in a number of molecules—including those that break down or transport statins, as well as the statins' molecular target in the cholesterol production pathway—contribute to the variable response among individuals. Using results of genomic tests, doctors may one day be able to prescribe the right dose from the start and more quickly reduce their patients' risk of dangerous cardiovascular events such as heart attack and stroke. Pharmacogenomic tests for cardiovascular diseases appear to be just over the horizon.
- In March 2003, at the 52nd Annual Scientific Session of the American College of Cardiology, Genaissance presented results from its STRENGTH (Statin Response Examined by Genetic Haplotype Markers) prospective clinical study, which showed that haplotype variations are associated with response to treatment with the statin class of cholesterol-lowering drugs. The associations discovered in the study were strongly predictive of efficacy. Genaissance plans to eventually develop the information into a point-of-care diagnostic test that will help physicians choose the safest and most effective drug for individual patients, maximizing the prevention of cardiovascular disease

afforded by the statins.

BENEFITS OF PHARMACOGENOMICS

- **More Powerful Medicines**

Pharmaceutical companies will be able to create drugs based on the proteins, enzymes, and RNA molecules associated with genes and diseases. This will facilitate drug discovery and allow drug makers to produce a therapy more targeted to specific diseases. This accuracy not only will maximize therapeutic effects but also decrease damage to nearby healthy cells.

- **Better, Safer Drugs the First Time**

Instead of the standard trial-and-error method of matching patients with the right drugs, doctors will be able to analyze a patient's genetic profile and prescribe the best available drug therapy from the beginning. Not only will this take the guesswork out of finding the right drug, it will speed recovery time and increase safety as the likelihood of adverse reactions is eliminated. Pharmacogenomics has the potential to dramatically reduce the the estimated 100,000 deaths and 2 million hospitalizations that occur each year in the United States as the result of adverse drug response.

- **More Accurate Methods of Determining Appropriate Drug Dosages**

Current methods of basing dosages on weight and age will be replaced with dosages based on a person's genetics --how well the body processes the medicine and the time it takes to metabolize it. This will maximize the therapy's value and decrease the likelihood of overdose.

- **Advanced Screening for Disease**

Knowing one's genetic code will allow a person to make adequate lifestyle and environmental changes at an early age so as to avoid or lessen the severity of a genetic disease. Likewise, advance knowledge of a particular disease susceptibility will allow careful monitoring, and treatments can be introduced at the most appropriate stage to maximize their therapy.

- **Better Vaccines**

Vaccines made of genetic material, either DNA or RNA, promise all the benefits of existing vaccines without all the risks. They will activate the immune system but will be unable to cause infections. They will be inexpensive, stable, easy to store, and capable of being engineered to carry several strains of a pathogen at once.

- **Improvements in the Drug Discovery and Approval Process**

Pharmaceutical companies will be able to discover potential therapies more easily using genome targets. Previously failed drug candidates may be revived as they are matched with the niche population they serve. The drug approval process should be facilitated as trials are targeted for specific genetic population groups --providing greater degrees of success. The cost and risk of clinical trials will be reduced by targeting only those persons capable of responding to a drug.

- **Decrease in the Overall Cost of Health Care**

Decreases in the number of adverse drug reactions, the number of failed drug trials, the time it takes to get a drug approved, the length of time patients are on medication, the number of medications patients must take to find an effective therapy, the effects of a disease on the body (through early detection), and an increase in the range of possible drug targets will promote a net decrease in the cost of health care.

- **More accurate methods of determining appropriate drug dosages**

Current methods of basing dosages on weight and age will be replaced with dosages based on a person's genetics --how well the body processes the medicine and the time it takes to metabolize it.

- **Economic issues from molecule to marketplace**

Pharmacogenomics eventually can lead to an overall decrease in the cost of healthcare because of decreases in:

- the number of adverse drug reactions
- the number of failed drug trials
- the time it takes to get a drug approved
- the length of time patients are on medication.

Future of Pharmacogenomic

The promise of Personalised Medecine

Imagine being able to walk into your doctor's office and present a "smart card" encoded either with the sequence of your genome itself or with an access code granting permission to log on to a secure database containing your genomic information.

Armed with a complete and accurate understanding of your unique genome, your physician would be able to prescribe the "right drug in the right dosage at the right time" to effectively treat your condition, with little or no concern that the therapy won't work or that you will suffer adverse side effects.

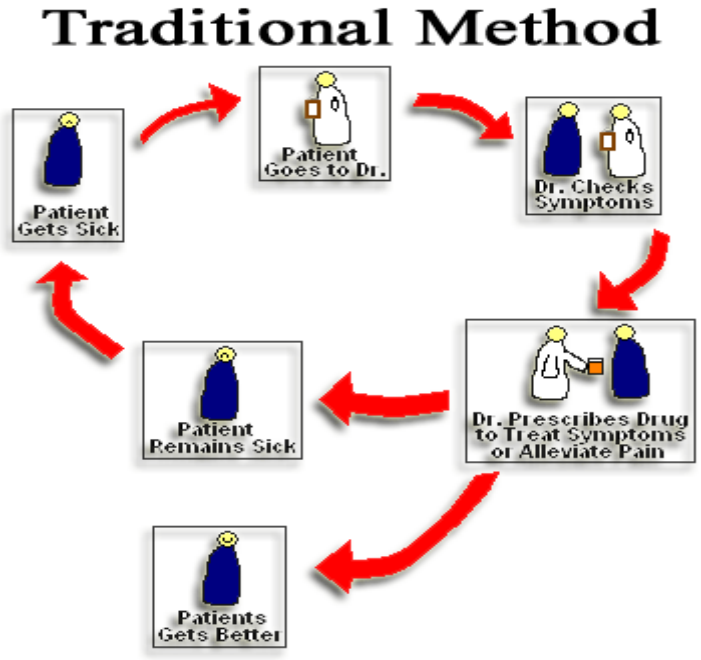
That day of truly personalized medicine is still just a gleam in the eyes of the scientists engaged in pharmacogenomics, but they are unanimous in their belief that it is achievable and that it will arrive.

In the future, pharmacogenomics will increasingly enable doctors to prescribe the right dose of the right medicine the first time for everyone. This would mean that patients will receive medicines that are safer and more effective, leading to better health care overall.

Also, if scientists could identify the genetic basis for certain toxic side effects, drugs could be prescribed only to those who are not genetically at risk for these effects. This could maintain the availability of potentially lifesaving medications that might otherwise be taken off the market.

Pharmacogenomic knowledge will enable pharmaceutical companies to design, develop and market drugs for people with specific genetic profiles. Testing a drug only in those likely to benefit from it could streamline its development and maximize its therapeutic benefit.

THE PAST, THE PRESENT AND THE FUTURE



In the past, doctors prescribed drugs based on "guesses" made from the observation of the patient's visible symptoms (i.e. rashes, swelling, joint pains, muscle pains, etc). However, these "guesses" were not always accurate and some patients remained sick after taking their full prescription.

CONCLUSION

Today, doctors prescribed drugs based on facts and test results that determine the patient's disease. However, there are some flaws in the system. Only 30-60% of drug prescriptions are effective for patients, while the rest of the population experiences no effect or raise their changes of adverse drug reactions.

With the development and application of pharmacogenomics, individuals hope that in the future, not only will doctors be able to accurately determine the cause of Pharmacogenomics

will help physicians and their patients by enabling pharmaceutical companies to bring more drugs to market that are targeted at those who are most likely to benefit from them Ultimately, the goal of pharmacogenomic testing is to help medicine and pharmacotherapy become less uncertain disciplines and more capable of improving the quality of an individual's life through a more "personalized approach to drug therapy.

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