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Review Article

Roll of Pharmacogenomics in Personalized Medicine

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ABSTRACT

The topic of pharmacogenomics is about the systematic identification of human genes, their Intra- and inter-individual variability, as well as products as well as in terms of expression and function. Additionally, customized treatment the goal of precision medicine, sometimes referred to as precision medicine, is to treat patients with Medicines given in accordance with their genetic makeup, lifestyle, environmental, and other aspects. This method Represents a shift away from the “one drug fits all” approach and towards therapy that is tailored to the individual. Pharmacokinetics and Pharmacodynamics are essential in pharmacogenomics. The manufacture of pharmaceuticals. Although DNA-based technology is quicker, has not completely looked at the relationship between the genotype and phenotype of several genetic variants. Between Understanding individual variability is necessary for effective medication responses. Cancer treatment, because genetic variations might influence how well the medicine works. Impacting both toxicity and efficacy. Artificial metabolism. Intelligence (AI) is crucial in enabling. By fostering and promoting the healthcare sector Pharmacogenomics applications and machine learning (ML) Integrates deep learning to build artificial neural networks (ANNs) that affect the DNA-related phases of the pharmacogenomics procedure. Pharmacists have a special position in this process. Well-suited to advocate individualized medicine as a therapeutic approach due to their knowledge, proficiency, and competence in Clinical, pharmacodynamics, and pharmacokinetics Pharmacology. In this review, we have gathered a body of pharmacological data. Pieces on a wide range of topics in pharmacogenomics. Genetic differences are among them, as well as pharmacogenomics. Drug development, phenotype, and genotype The challenges, introduction, and indicators of pharmacogenomics The function of pharmacists and the application of artificial intelligence in pharmacogenomics.

INTRODUCTION

The scientific field of pharmacogenomics focuses on the methodical identification of all human

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Genes, their products, and variations both between and within individuals. In words and. When A gene mutation is associated with a patient's specific response to a medication, it may be Possible to make treatment choices based on genetics, such as in the case of a patient's specificResponse to a medication. Like modifying the dosage or choosing a different drug. Researchers Use methods similar to those used to evaluate gene variations associated with disease to identify Genetic loci related to known drug responses, and they then test individuals based on how they React to the drug. To evaluate gene variations that influence a person's reaction to the medicine. Two cuttingedge methods used in medicine development are whole-genome single nucleotide Polymorphism (SNP) profiling and multi-gene analysis.[1] Pharmacogenomics, which will lead to safer and more effective medication treatment, assist Enhance medication therapy adherence, lower hospitalizations, and improve overall health Care. [19]The lack of taste The first example of inherited variation in response to external Chemicals or xenobiotics was phenylthiocarbamide. When patients with a glucose-6-phosphate Dehydrogenase deficiency were given the antimalarial medicine primaquine in the 1950s, they Suffered significant hemolysis. Primaquine is a traditional pharmacogenetic trait that modifies Amino acids. After the administration of succinylcholine, the sequence resulted in extendedParalysis and peripheral neuropathy in individuals who were also receiving isoniazid. The Scientific field of pharmacogenetics, which examines heredity and medication response, was Established as a result of these initial findings. The term "pharmacogenomics" first appeared In the medical the end of the 1990s literature.[1] Personalized medicine:

Personalized medicine occurs when a disease becomes predictable and preventable based on Genotypes. When the genetic diagnosis of a condition and the availability of prospectively Validated molecular-targeted treatments lead to safer and more efficient treatments, it Happens. The clinician's function then changes and switches from trial-error assignments To logical assignments based on well-defined molecular alterations and effective drugs. [7]The genetic revolution, which includes genomics, transcriptomics, proteomics, metabolomics, And other "omics," has produced a plethora of novel biological data, the majority of which is Focused on individual genetic diversity. Thus, the personalized, directed medicine of today Provides previously unattainable opportunities for more successfully targeting the treatment of Diseases like cancer. The aim of medicine has always been to offer the best possible care, Taking into account the best available data and evidence-based facts. Some aspects of this are now achievable through Methods that were previously unavailable. The term "pharmacogenomics," "pharmacogenetics," or "genomic medicine" refers to the research on How the genome affects how drugs work. It combines genomics and pharmacology, as seen by Its name (pharmaco- + genomics). Pharmacogenomics studies how a person's genetic Makeup influences how they react to medications. By comparing gene expression or single-nucleotide polymorphisms with pharmacokinetics (drug absorption, distribution, etc.), it explores how genetic variation affects how patients Respond to drugs. Pharmacodynamics (effects mediated via a drug's biological targets) and Metabolism, and elimination).[2]

Fundamental of pharmacogenomics:



Copy number variations (CNVs) have been highlighted as a significant factor in the study of gene expression, single nucleotide polymorphisms (SNPs), and insertions/deletions (InDels) [21,23,27,28]. a novel and important source of genetic polymorphism that accounts for phenotypic variety, such as virulence, in several fungal species .[12]Indeed, several fungal investigations, including those on yeast, have demonstrated the impact of CNVs on population genetic and phenotypic diversity. The wheat pathogen *Zymoseptoria tritici* (Ascomycota, Dothideomycetes) [32], the human fungal pathogen *Cryptococcus deuterogattii* (Basidiomycota, Tremellomycetes) [33], and *Saccharomyces cerevisiae* (Ascomycota, Saccharomycetes) [30,31] are all examples of pathogens[3]

The clinical implimentation of pharmacogenomics:

Pharmacogenomics, which is a part of personalized and precision medicine, utilizes a person's Genetic data, along with other clinical variables, to guide choices regarding medicationTherapy and dosage. The aim of pharmacogenomics is to increase effectiveness and decrease Negative effects by reducing the trial and error involved with drug prescription. The clinical Use of pharmacogenomics has accelerated over the past ten years, primarily as a result Of the creation of evidence-based clinical practice recommendations that Offer advice on how To turn pharmacogenomic test findings into actionable prescribing choices for specific drugs.Pharmacogenomics is implemented in a wide range of environments (inpatient and outpatient) And facilities (academic health centers, community health systems.[4]

Electronic health record:

A key element of precision medicine is pharmacogenomics. Despite persistent challenges to Implementation, the usefulness of pharmacogenomics-oriented electronic health record (HER) Informatics is becoming more and more apparent, using electronic health records to stay Informed about pharmacogenomic outcomes and help with medicine selection and dosage. In Particular, clinical decision support (CDS) has been recognized as an essential Instrument for integrating pharmacogenomics into regular patient treatment.The sheer amount, ever-changing, and longlasting character of Pharmacogenomic information that has to be used during a patient interaction makes it Difficult to integrate pharmacogenomics into regular treatment.[5]

The drug efficiency and toxicity verification:

A therapeutic drug's usefulness in treating a specific illness is determined by its effectiveness and safety. The drug's interaction with on-target and off-target molecules determines its effectiveness and safety profile. In addition, the availability of the medication to its targets will be unavoidably impacted by how it is metabolized in the body, which is made up of the following processes: A number of essential procedures, including absorption, distribution, metabolism, and excretion (ADME).[6]

Benefits of pharmacogenomics:

Enhanced Medication Effectiveness: Pharmacogenomics has been shown to Improve drug efficacy in a number of studies.Greatly improves the effectiveness of drugs by making sure that patients are given Treatments that are specifically suited to their needs.Their genetic profiles. For instance, genetic testing is used in oncology to Find mutations.Which forecast a positive reaction to targeted therapies, such as the use of EGFR inhibitorsFor individuals suffering



from non-small cell lung cancer (Lynch et al., 2004). Individualized strategies Have resulted in greater survival rates and less dependence on traditional methods Chemotherapy.

Fewer Negative Drug Responses (ADRs): Among the main advantages of The possibility of lowering ADRs, a significant contributor to illness, is the Basis of pharmacogenomics and mortality. For example, pharmacogenomic testing Can pinpoint individuals who are at risk of dying from their condition. Significant adverse drug reactions, such as those caused by warfarin Clopidogrel. Studies like those of Rieder et al.(2005) demonstrated that variations in the genes of enzymes like CYP2C9 affect the Action of warfarin. Metabolism, which makes individualized dosing possible and lowers the chance of Bleeding episodes.

Optimal Dosing: Pharmacogenomics enables more accurate drug administration. Decreasing both underdosing and overdosing. For instance, people with various genetic profiles may experience different reactions to the Same drug dosage. Different individuals may metabolize drugs at different rates. The dosage can be adjusted According to genetic profiles. The traditional trial-and-error method has been proven to be less efficient than using markers. Is especially helpful in medications with a limited therapeutic window, such as Anticoagulants and chemotherapeutic drugs.

Improved Management of Complex Diseases: The use of pharmacogenomic Techniques has been especially helpful in treating complicated illnesses Like cardiovascular disease and cancer. psychiatric illnesses, and diseases. Targeted treatments.[7]

Ethical and Privacy Issues:

The use of genetic data in clinical settings raises ethical and Privacy concerns. serious ethical issues

pertaining to data security and Privacy. Worries about genetics. the possibility of discrimination by insurers or employers, as Well as The illegal use of genetic data continues to be a persistent problem in the Implementation process of pharmacogenomics (Hudson et al., 2008). In addition, The inclusion of genetic Testing into routine care can be contentious, especially when it comes To informed consent. as well as the possibility of stigmata arising from Inherited predispositions. The Complexity of Genetic Interactions: Although some genetic variants have well-Documented effects, others are more complicated. the entire complexity of genetic links to drug Metabolism and reaction has been established. Little is known about how these drugs interact. Pharmacogenomic

Responses may be impacted. Through the interaction of several genes in a manner that is still not fully understood.

Ethical Issues Ralated to personalized medicine:

Ethics of personalized medicine become an issue when a healthy person has been reported to Have a risk of breast or ovarian cancer. Also associated with the use and storage of genetics Information of an individual. Protection of privacy of genetics data of an individual from the Government or insurance companies.[8]

Pharmacogenomics Biomarkers:

It includes genetic or somatic gene variant changes in expression level , functional Irregularities and chromosomal abnormalities used for diagnosis of disease or assessment of Therapeutic efficacy. pharmacogenomics biomarkers is used for rescribing The drug or its dose Based on the level of biomarkers and presence or absent of its variants.



Her_2/neu receptors: select hercepting
trastuzumab for breast cancer

BRCA1/2: Breast and ovarian cancer inherited risk
prophylactic tamoxifen And surgery

VKOR/CYP2C9: dosing of warfarin
Transcriptional profile _21 genes: avoid use of
chemotherapy in breast Cancer patient with low
risk of recurrence

CYP2D6/CYP2D19: guide prescribing adjust
dose of 25% of commonly used Drug's [9]

Epigenetics and other elements:

Epigenetic factors like age, gender, liver and kidney function, lifestyle, prior illnesses, and The therapeutic response of a medicine is also determined by adverse reactions. Due to a low rate of physiology and metabolism, elderly patients are at risk of experiencing negative side effects. Physiological variations unique to women, such as pregnancy and breastfeeding, have an impact on The outcome of treatment with medications. There is a degree of variation in the harms suffered by men and women, which may result in a. Males and females react differently to various medications. By drug, environment chemicals, natural compounds, and medications can alter the drug's effectiveness. A drug-herb or drug-drug interaction. Personalized medicine has several benefits, including: Predict disease susceptibility. Make a prescription for a better drug. Refrain from prescribing drugs that have known side effects. Lower the duration, expense, and failure rate of clinical studies for pharmaceuticals. The advent of customized medicine: Personalized medication treatment. Pharmacogenetics. Choose the drug treatment plan. [10]

The effect of pharmacogenomics on tailored medicine:

Cancer

Neurodegenerative condition Thrombo

Cardiovascular illnesses Anesthesia

Diabetes type 2 Depression Cancer therapy:

Karger published the book "Pharmacogenomics of Human Drug Transporters." In 2008. Since drug transporters are necessary for the Accumulation of chemotherapeutic drugs in malignant cells. Multidrug therapy is often the reason for treatment's limited effectiveness. Categorization of human transporters includes ATP-binding cassettes, SLCO, and resistance. LR RC, SLC15A, SLC16A, SLC22A, SLC28A, and SLC29A. (Cystic Fibrosis Transmembrane Conductance Regulator) and its impact on how Well cancer reacts. The initiation of chemotherapy for patients is detailed in the monograph. The monograph 'Pharmacogenomics of Human Drug Transporters' was published by Karger.

Cardiovascular illness:

Cardiovascular disease is the main cause of death in both wealthy and developing nations. A general improvement in public health care and has resulted in a 60% increase. The decrease in the death rate from cardiovascular illnesses in wealthy nations has improved the quality of life. The trend of steadily increasing life expectancy is accompanied by a rise in population. Who is responsible for treating cardiovascular diseases [17-23]. Particularly in wealthy countries, this is the case. Especially among populations, elderly individuals, and economies that are marginalized. In reality, It is believed that 40% of all fatalities worldwide will be caused by CAGD in thirty



years. With an increase in the number of people who have suffered a heart attack .[11]

The role of pharmacogenomics In adverse drug reactions:

Unwanted adverse reactions may result from the use of drugs. These can be treated when they occur. The term “adverse drug reactions” is preferable since it is directly related to a specific treatment course (ADRs). Morbidity and mortality are significantly influenced by genetic diversity and ADRs. Mortality. Significantly raises the likelihood of them occurring. Negative drug Type A (pharmacological) and Type B (idiosyncratic) are the two categories of responses. At the most basic level. The dose of pharmacological response determines its occurrence. Dependent and perhaps caused by a drug’s recognized targets, which should be accepted and possibly expected negative reaction to the well known process of action. Examples of high-penetrant risk include the CYP2D6 and opiate-induced alleles. Which are among the genes that code for drug-metabolizing enzymes, respiratory depression, and CYP2C9. And hemorrhage while taking warfarin, which demonstrates how warfarin functions. The pharmacokinetic processes impacted by genetic variation may be relevant to these ADRs. Uncommon and unexpected ADRs, on the other hand, are less frequent. Although the medicine has a well-known pharmacological profile, it may be fatal and result in serious negative effects. Many of these ADRs have been linked to immunological mechanisms and organ dysfunction. Harm. The majority of recommendations link them to polymorphisms in genes that are related to the immune system. The answer. Particularly the HLA system. These findings emphasize the possibility of creating ADR. Predictive systems that improve patient safety and resource usage. According to

estimates, That primary care patients are exposed to drugs with at least 65% of the time. Pharmacogenomics. Over a five-year period, indications that genomic data may be used (Kimpton et al., 2019). To lessen or avoid unwanted adverse effects from medications. These medicines are a bit overrepresented among individuals receiving standard care (Barbarino et al.). Pharmacogenomic variance may be the result of the combination of the two possibilities. Routinely recorded in a regular health record. [12]

Variations in genes:

The human genome is made up of around 20,500 genes, with 99.5% of them being identical. The remaining 0.5 percent is made up of variations that influence a person’s blood type, eye color, And other characteristics. Single nucleotide polymorphism (SNP), which is used to determine color, susceptibility to certain diseases, and other characteristics. The most common kind of DNA sequence variation seen in the Human genome. Deletions, Examples include insertions, tandem repeats, inversions, and copy number variations (CNV). A further class of variation is called structural variants (SV). There are several of them in the Human genome. Approximately 11 million SNPs, or one for every 1,300 base pairs. SNPs act as Biological markers. that foretell how someone may react to particular drugs and how susceptible they are to environmental factors the potential for contracting diseases and pollutants. [13]

Genotype and phenotype:

It may be possible to use diagnostic tests that directly assess the phenotype as opposed to a Genetic variation. More precise if there are multiple mutations that might cause similar ADR sensitivities. DNA-based technology, however, can be faster and only require one blood sample



from a The link between genotype and phenotype for many genetic variants has not yet been Established for the patient.has been extensively investigated. The doctor is interested in Learning about the phenotype, butRegrettably, the entire range of diseases may Not be accurately identified by the existing DNA-based diagnostic methods.Phenotypic variance. Consequently, creating reliable, affordable, high-throughput For firms creating DNA-based diagnostics, genotyping platforms present a significant Hurdle, andFinding comprehensive and therapeutically significant genotype-Phenotype links is a significant challenge.a challenge for pharmacogenomic science Acute lymphoblastic inflammatory bowel diseasePatients receiving organ transplants or Leukemia treatment are all given thiopurine drugs.Although these drugs are beneficial, they are also harmful, and Only a few dosages will result In the desired therapeutic effect.while not being harmful. Thiogurine's main toxicity has potenTo be fatal.A metabolic enzyme produced by a gene that is expressed by a thiopurine S-methyltransferase (TPMT) polymorphic gene that inhibits thiopurines. The TPMT*3C gene variant contains a Cytosine.While TPMT*3A is more prevalent in position 3, it is common among Asian Populations.There are two different SNPs in TPMT*3A that alter the encoded amino acids In different ways for Caucasians.methods. In their cells, individuals who are homozygous for This allele exhibit very little or no TPMT protein.since the gene product encoded by TPMT*3A Is quickly broken down in tissues.[14]

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