OPEN ACCESS

Precision Medicine Communications

DOI: doi.org/10.55627/pmc.002.002.0210

In This Issue

Editor's Summaries of the Articles Published in This Issue of Precision Medicine Communications

Editorial Staff

In this issue, Anum and colleagues have reported evidence-based prioritization and scoring of genomic loci interacting with pioglitazone therapeutic response in diabetic patients; Hasan and colleagues designed a study to determine the association of CP2C19*2 loss of function polymorphism with acute coronary syndrome patients receiving Clopidogrel, Zaheer et al., reviewed escitalopram use in depression & the influence of genetic variations on its safety & efficacy, Ahmed and colleagues reviewed and discussed single nucleotide polymorphisms associated with the safety and efficacy of anti-gout medications, while Haroon et al., compiled, reviewed and discussed the studies showing the genetic influence on Losartan's antihypertensive and uricosuric actions.

Evidence-Based Prioritization and Scoring of Genomic Loci Interacting with Pioglitazone Therapeutic Response in Diabetic Patients

Anum and colleagues performed evidence-based semi-automated prioritization and scoring of candidate genes of pioglitazone in diabetic patients to overcome the inconsistency in pharmacogenetics and pharmacogenomics data. They developed a Python script and searched with MeSH terms of "Pioglitazone (PIO)" and synonyms," and (i) built a complete library of published data (22,532 publications), (ii) extracted sentences containing pioglitazone-gene pair by using Python 3.6, (iii) annotated each sentence for its relevance, (iv) developed evidence scoring algorithm based on pharmacogenomics relatedness, frequency, and consistency. They showed that the gene encoding peroxisome proliferator-activated receptor *gamma* and polymorphisms in genes affecting the pharmacokinetics, i.e., *Cyp2C8, Cyp3A4,* and *Cyp2C9,* and pharmacodynamics-protein tyrosine phosphokinase (*Ptprd*), Lipoprotein (*Lpl*), *Adiponectin receptor 2* (*Adipora2*), and PPARG coactivator 1 alpha (*Ppargc1*) were as strong predictor of the drugs response. Furthermore, drug-induced adverse drug reactions were associated with polymorphisms in the Solute carrier family 12 member 1 (*Scl12a1*) and Aquaporin 2 (Aqp2) genes. Their results showed PPAR-α receptors/ PPARG as one of the most robust evidence of therapeutic response to pioglitazone and highlighted other variants in different pathways.

Cytochrome P450 2C19*2 Genetic Polymorphism in Patients with Acute Coronary Syndrome

Hasan and colleagues designed a study to determine the association of *CP2C19*2* loss of function polymorphism with acute coronary syndrome patients receiving Clopidogrel. They determined *CYP2C19*2* genetic polymorphism by polymerase chain reaction followed by restriction fragment length polymorphism. The frequency of CP2C19*2 heterozygous GA was 38.3%, homozygous (wild type) GG was 58.7%, and

homozygous (mutant) AA was 3.4% in patients while in control subjects, the frequency of heterozygous GA was 29.5%, homozygous GG was 59.0%, and homozygous AA was 11.4% (p= 0.3513, OR 1.2927, 95% CI 0.75-2.21). Their result showed no statistical significance regarding the distribution of this genetic polymorphism between acute coronary syndrome patients and control individuals. The authors concluded that the CYP2C19*2 loss of function polymorphism is not associated with acute coronary syndrome in this Pakistani cohort.

Escitalopram Use in Depression & the Influence of Genetic Variations on Its Safety & Efficacy

Zaheer and colleagues compiled the studies on the genetic variations associated with escitalopram efficacy and adverse effects and reviewed them. They also briefly discussed the pathophysiology and currently available treatment options for major depressive disorder (MDD). MDD is a common debilitating mental illness marked by sad feelings, depressed mood, and lack of interest in routine chores that persists daily or for a minimum of two weeks. Serotonin-norepinephrine inhibitors, selective serotonin reuptake inhibitors, tricyclic antidepressants, monoamine oxidase inhibitors, and atypical antidepressants are some common classes of drugs used to treat MDD. Despite strenuous efforts by the researchers, hardly any new antidepressant agent has entered the market. Escitalopram, a highly selective serotonin reuptake inhibitor, is the drug of choice for treating MDD. However, although escitalopram is one of the most frequently prescribed antidepressant agents, a large percentage of MDD patients show variable remission and response to escitalopram. Scientists spent decades finding the underlying mechanism responsible for the significant variations in drug response and incidence of adverse effects. These inter-individual variations in therapeutic response serve as a foundation for the inception of the pharmacogenomic. Pharmacogenomics is a field of research that expounds on the impact of gene variation on altered clinical outcomes of drugs. There has been substantial hope and potential that pharmacogenomics will ameliorate the current therapies for MDD and aid in finding novel targets for new drug discoveries. The authors identified and discussed numerous candidate genes implicated in changing drug response, whether at the receptor, transporter, or drug-metabolizing enzyme.

Single Nucleotide Polymorphisms Associated with the Safety and Efficacy of Anti-Gout Medications

Ahmed and colleagues summarized the progression of gout disease, the complications of current gout therapy, and the relationship between genetic variations and therapeutic outcomes of certain drugs used to manage gout. Gout is inflammatory arthritis accompanied by sporadic pain, inflammation, and swelling within joints due to the accretion of monosodium urate crystals. The global incidence of gout has mounted in developed countries and has afflicted particular ethnic groups, for instance, South Pacific Island populations. Hyperuricemia, manifested by an amplified serum urate, is the key predictor of gout. The optimum serum urate concentration is less than 6.8 mg/dl, whereas individuals with hyperuricemia have a serum urate of over 6.8 mg/dl. The effective treatment of gout is relative to the type of gout. Nevertheless, controlling serum urate levels is central to effective gout management. Antiinflammatory drugs are available to mitigate acute flares and inhibit inflammation. Additionally, urate-lowering therapies are available to dissolve crystals and avert gout flares. The authors described that genomic and experimental data provide sufficient evidence that genetic variants linked to gout disease are of pharmacogenetic relevance.

Genetic Influence on the Antihypertensive and Uricosuric Actions of Losartan

Hypertension (HTN), a globally prevalent non-communicable chronic disease (NCCD), is an international health concern. HTN has multifaceted pathogenesis with a varied prevalence across the globe. Excessive oxidative stress is the underlying cause of the Renin Angiotensin Aldosterone System (RAAS) imbalance leading to elevated blood pressure (BP). Evidence-based medicine (EBM), along with suitable lifestyle modifications, assists in managing the disease and lowering the risk of disease-associated cardiovascular morbidity and mortality. Losartan, an angiotensin receptor blocker (ARB), is one of the first-line drugs available. One of the complications of HTN is hyperuricemia, a metamorphosis in urate homeostasis. Studies have highlighted the uricosuric action of losartan along with its antihypertensive effects. However, varied therapeutic outcomes are observed in patients due to genetic polymorphisms based on different ethnical backgrounds. Haroon and colleagues reviewed single nucleotide polymorphisms (SNPs) affecting Losartan's antihypertensive and uricosuric action. Among other genes, they identified nephrin (NPHS1) and URAT1 genes and discussed how they affect losartan's antihypertensive and serum uric acid (SUA) lowering effects, respectively.

Editorial Staff