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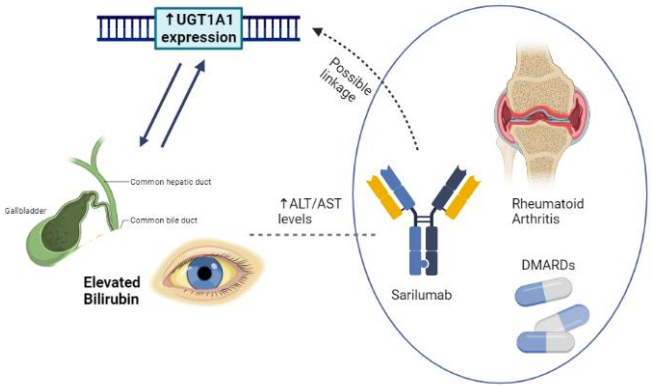
Editor's Choice

Editor's Selection of the Important Research Investigations in the Field of Precision Medicine from Around the World

Editorial Staff

Association of UGT1A1 Genetic Variants with Increases in Bilirubin Levels (doi.org/10.55627/pmc.002.001.0094)

For patients that are intolerant or resistant to the disease-modifying-antirheumatic-drugs (DMARDS) or suffer from mild to moderate rheumatoid arthritis (RA), a human monoclonal antibody targeting interleukin (IL)-6Rα called Sarilumab is approved for use. Patients who are given Sarilumab are reported to have mild abnormalities in the AST/ALT levels.



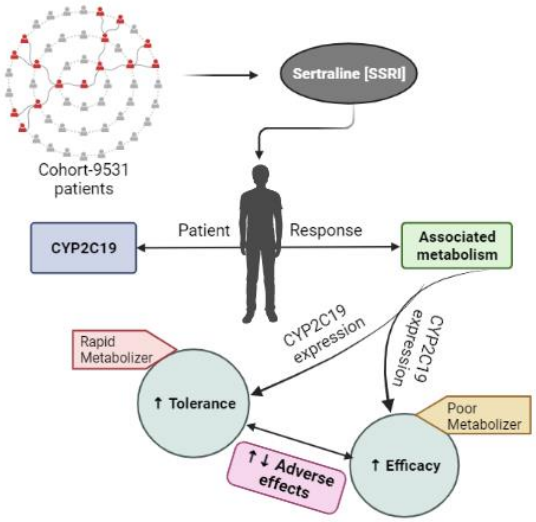
Lin and colleagues performed a genome-wide investigation into the elevated levels of bilirubin in patients suffering from RA and are being administered Sarilumab. DNA samples of 1075 patients were subjected to exome sequencing and genotyping. Their findings reveal that maximum elevations in bilirubin levels are associated with variants of the UGT1A1 gene (rs4148325; $p = 2.88 \times 10^{-41}$) but ALT/AST elevations harbored no such association. Other independent loci failed to have any associations in Sarilumab-prescribed patients having bilirubin elevations. The authors argue that variants of the UGT11 gene are associated with a bilirubin increase in RA patients taking Sarilumab. ***Pharmacogenomics J***. 2022 May;22(3):160-165.

Selective Serotonin Reuptake Inhibitors Response and the Impact of CYP2C19 Metabolizer Status (doi.org/10.55627/pmc.002.001.0097)

A particular class of antidepressants called selective-serotonin-reuptake-inhibitors (SSRIs) are subjected to altered metabolism as a result of variations in the *CYP2C19* gene. Clinicians do take into account the *CYP2C19* variations whilst making a pharmacogenomic recommendation. However, the clear links between the efficacy and safety of the drugs to the genetic variations in metabolism are yet to be established.

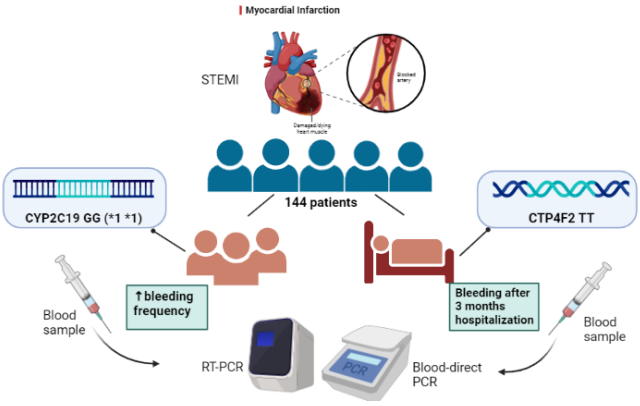
Campos et al, intended to address this question by investigating CYP2C19 polymorphisms and the associated metabolism as well as patient-reported response in a cohort of 9531 patients subjected to SSRIs as part of their regimen. CYP2C19 alleles were the determining factor for metabolizer status. Rapid metabolizers demonstrated higher

tolerability but poor metabolizers reported higher efficacy, across all medications. Greater differences were seen in reporting adverse effects for sertraline in various metabolizer groups. The results for tolerability, efficacy and adverse effects, and metabolizer state were in line with previous predictions. Their study did not see slow metabolizers to be at a greater risk for side effects without clinical titration adjustments. Still, both interventional and longitudinal studies such as randomized clinical trials including the whole spectrum of metabolizers are essential to determine the association between CYP2C19 metabolizers and the effects on SSRI treatment efficacy and adverse effects. ***Pharmacogenomics J.*** 2022 Mar;22(2):130-135.



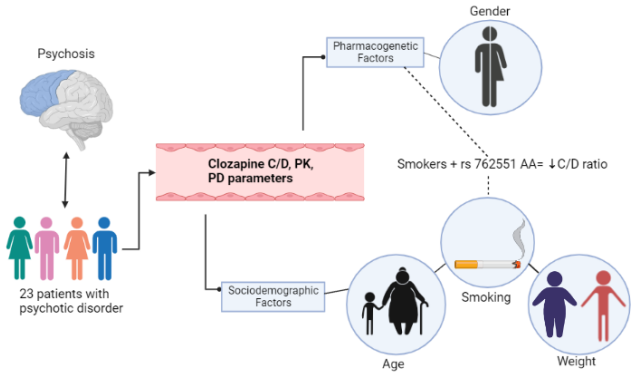
Blood Direct PCR for Detection of CYP2C19 and CYP4F2 Variants (doi.org/10.55627/pmc.002.001.0095)

Tatarunas et al, intended to develop and introduce into clinical practice a technique that can rapidly determine CYP2C19 rs4244285 and CTP4F2 rs3093135 genotypes from blood samples of patients. They recruited 144 consecutive patients with ST-elevated myocardial infarction for their study. Real-time PCR and Blood-direct PCR were performed to identify the variants. Their results show that CYP2C19 GG (*1*1) was more common in patients with an increased frequency of bleeding events. Patients who still had bleeding problems after 3 months of hospitalization had a higher frequency of the CYP4F2 TT variant. ***Per Med***. 2022 May;19(3):207-217.



Plasma Level Determination and Pharmacogenetics of Clozapine (doi.org/10.55627/pmc.002.001.0098)

Sanguesa et al., undertook an investigation to discern the differences in the levels of Clozapine (CLZ) in plasma and determine the pharmacogenetic and sociodemographic factors that influence it as well as introduce these tools in a clinical setting.

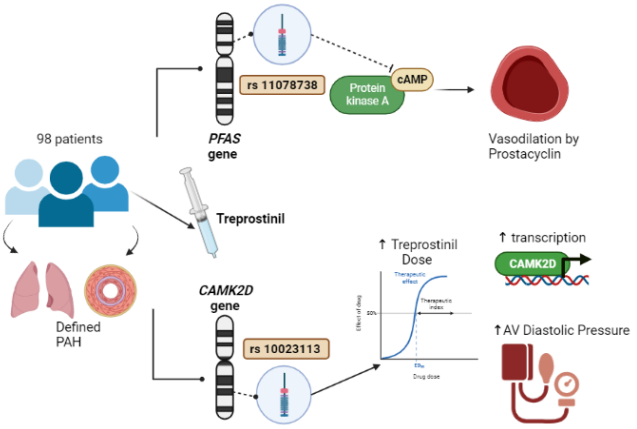


In a group of 23 patients diagnosed with psychotic disorders CLZ concentration in plasma were measured alongside CLZ pharmacokinetic and pharmacodynamic parameters. Their findings revealed that smoking status, age, and weight were significantly associated with mean concentration/dose ratio (C/D). Gender and mean CLZ concentrations also demonstrated a

significant difference. Smokers having the genotype rs762551 AA had a significantly lower well as classical factors produced greater individualization of treatment. ***Per Med***. 2022 May;19(3):181-192.

Treprostinil Dose in Pulmonary Arterial Hypertension and the Role of Two Polymorphic Genetic Loci (doi.org/10.55627/pmc.002.001.0096)

Although with different dosing requirements and varied clinical responses, prostacyclin as an infusion, still is an effective treatment for pulmonary arterial hypertension (PAH). Thomas and colleagues described novel biological markers that can aid in predicting the heterogenicity in response to prostacyclin treatment.



C/D ratio. The authors concluded that measuring CLZ levels in plasma with pharmacogenetics as

They recruited 98 patients from two academic medical centers with hemodynamically defined PAH. Their findings suggest the involvement of two main loci, rs11078738 in phosphoribosylformylglycinamidine synthase (PFAS) gene and rs10023113 SNPs in calcium/calmodulin-dependent protein kinase type II subunit delta (CAMK2D) gene. Cyclic AMP production, which serves as the primary mediator of vasodilation stimulated by prostacyclin was inhibited by the missense variant rs11078738 (p.L621P) in cell lines. A higher treprostinil dose along with an enhanced ventricular transcription of CAMK2D demonstrated an association with of rs10023113 variant. Increased right mean atrial and ventricular diastolic pressures showed an association with the same allele as mentioned above during the initial diagnostic catheterization in a separate cohort of patients. The authors argue in their manuscript that these two gene loci exhibit an association with pharmacodynamic response and right ventricular function in PAH to the treprostinil dose. ***Pharmacogenet Genomics***. 2022 Jun 1;32(4):144-151

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