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Precision Medicine Communications

DOI: doi.org/10.55627/pmc.003.002.0481-0485

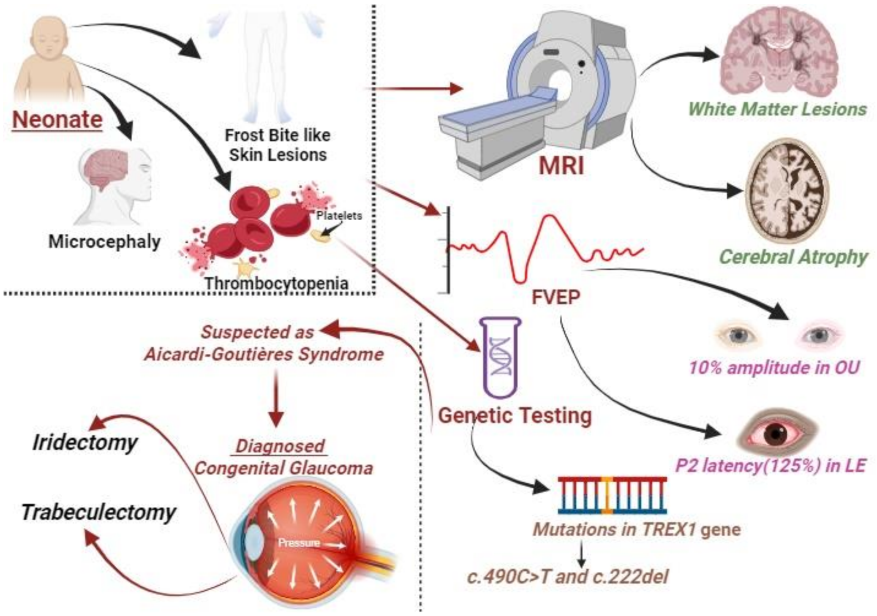
Editor’s Choice

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

Editorial Staff

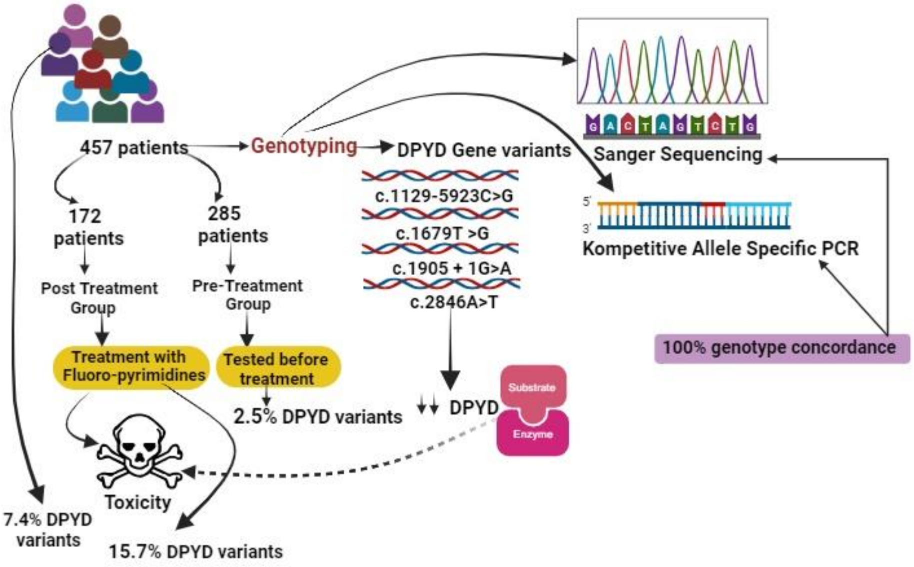
TREX1 Mutation in Aicardi–Goutières Syndrome with Congenital Glaucoma

Aicardi–Goutières syndrome (AGS) is a rare genetic disorder that primarily affects the brain, the skin, and the immune system. It is characterized by a group of symptoms that mimic the effects of a viral infection, leading to inflammation in various tissues. Świerczyńska and colleagues presented a case of a neonate with hypotrophy, microcephaly, frostbite-like skin lesions, thrombocytopenia, elevated liver enzymes, and hepatosplenomegaly and showed that she had ‘three prime repair exonuclease 1’ (*TREX1*) gene mutations. The genetic investigation found pathogenic mutations, c.490C>T and c.222del (novel mutation) in TREX1 gene showing AGS type 1 (AGS1). High serum IFN-α levels were also found. Later examination showed multiple ocular abnormalities including intraocular pressure (IOP) of 51 mmHg in the right eye and 49 in the left eye. The patient was diagnosed with congenital glaucoma, and it was managed with trabeculectomy with a basal iridectomy of both eyes, resulting in a reduction and stabilization in the IOP to 12 mmHg in the right eye and 10 mmHg in the left eye without any hypotensive eyedrops. This case report adds to the growing evidence of the involvement of the pathogenic c.490C>T and c.222del mutations in *TREX1* in ophthalmic abnormalities. J Pers Med. 2023 Nov 15;13(11):1609. doi: 10.3390/jpm13111609.



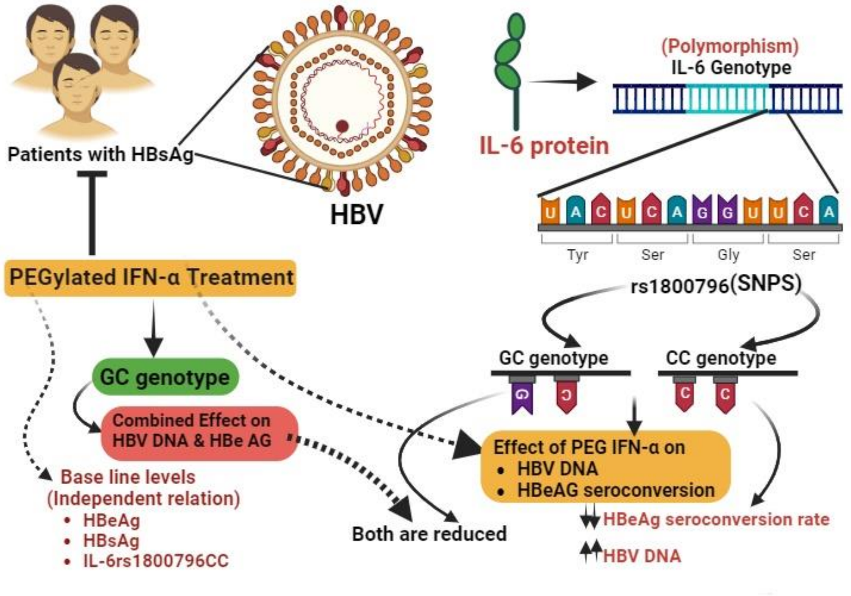
Rapid & Low-Cost DPYD Genotyping to Guide Fluoropyrimidine Treatment in Cancer Patients

DPYD (dihydropyrimidine dehydrogenase) genotyping is relevant in the context of cancer treatment, particularly with fluoropyrimidine-based chemotherapy drugs such as 5-fluorouracil (5-FU) and capecitabine. Dihydropyrimidine dehydrogenase is an enzyme involved in the metabolism of these drugs, and certain genetic variants in the DPYD gene can lead to reduced enzyme activity, potentially causing severe and life-threatening toxicities. The implementation of upfront DPYD genotyping involves testing patients for specific DPYD variants before starting fluoropyrimidine-based chemotherapy. Pinheiro and colleagues assessed the frequency of the four most common and well-established DPYD variants associated with fluoropyrimidine toxicity and implemented a relatively low-cost and high-throughput genotyping assay for their detection. Their study comprised 457 patients that were genotyped for the DPYD c.1129-5923C>G, c.1679T>G, c.1905 + 1G>A and c.2846A>T variants, either by Sanger sequencing or kompetitive allele-specific PCR (KASP) technology. Of these, 172 patients presented toxicity during treatment with fluoropyrimidines (post-treatment group), and 285 were tested before treatment (pretreatment group). A little more than 7% patients were DPYD homozygous. The most common variant they found was c.2846A>T. The KASP assays designed in this study presented 100% genotype concordance with the results obtained by Sanger sequencing. The authors concluded that the combined assessment of the four DPYD variants increases the identification of patients at high risk for developing fluoropyrimidine toxicity. They also found KASP genotyping a low-cost and rapid turnaround time assay. Pharmacogenet Genomics. 2023 Oct 1;33(8):165-171. doi: 10.1097/FPC.0000000000000505.



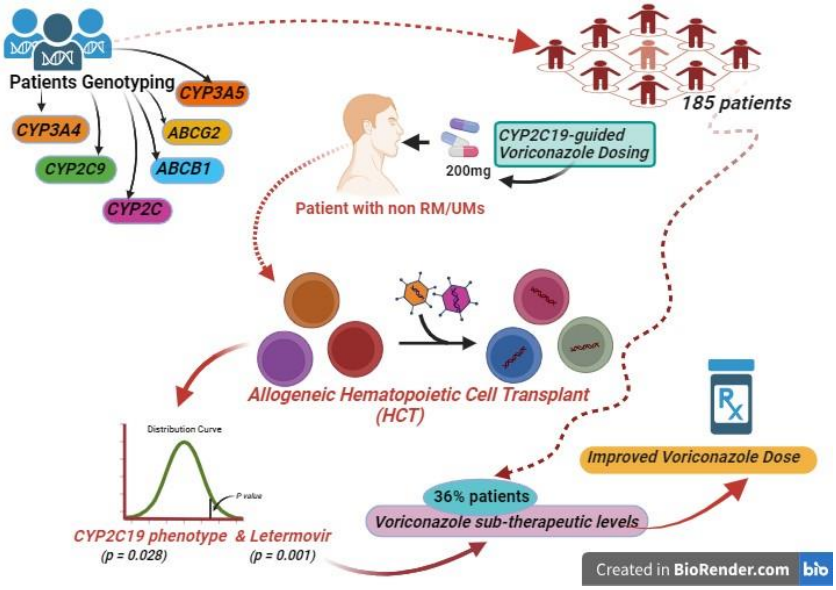
Prediction of PEGylated INF-α Treatment Response in Hepatitis B Patients

Genetic polymorphisms can influence the response to antiviral therapy in patients with chronic hepatitis B (CHB). The variability in treatment response is multifactorial, and genetic factors play a role in how individuals metabolize and respond to antiviral medications. Wang and colleagues investigated the genetic association of the *IL-6* rs1800796 polymorphism with PEGylated IFN-α (PegIFN-α) treatment response in hepatitis B surface antigen (HBsAg)-positive CHB patients. After sequencing the patients' samples, they found that more patients with the combined response (n = 95) carried *IL-6* rs1800796 GC genotypes, while CC genotype carriers possessed reduced HBeAg seroconversion rate and high values of hepatitis B virus DNA. They also found that PegIFN-α treatment response was also associated with the baseline HBsAg and HBeAg and *IL-6* rs1800796 CC genotype. The authors concluded that PegIFN-α response may be predicted by detecting *IL-6* rs1800796 genotype in CHB patients. Per Med. 2023 Nov;20(6):503-510. doi: 10.2217/pme-2023-0089.



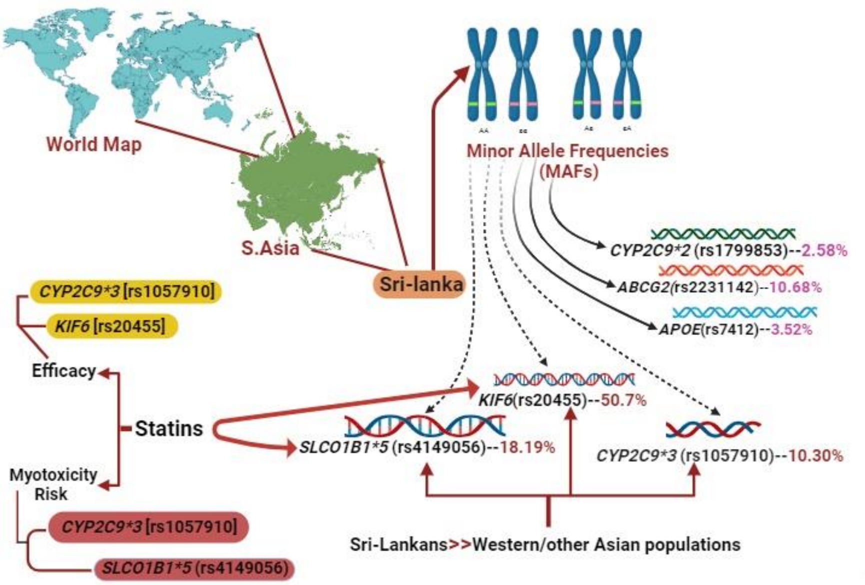
Predictors of Voriconazole Concentration in Hematopoietic Stem Cell Transplant

The variability in individual response to voriconazole can be influenced by both genetic factors (pharmacogenetics) and clinical factors. Understanding the pharmacogenetic and clinical predictors of voriconazole response is important for optimizing its use and minimizing adverse effects. Patel and colleagues investigated the association of genetic polymorphisms in ABCB1, ABCG2, CYP2C9, CYP3A4, CYP3A5, and the CYP2C genes with voriconazole trough concentrations in patients receiving CYP2C19-guided dosing. They performed a retrospective study in allogeneic hematopoietic cell transplant patients receiving CYP2C19-guided voriconazole dosing. They found that 36% of 185 patients were subtherapeutic. They also found that CYP2C19, age, and letermovir use were associated with voriconazole concentrations. Variations in the ABCG2 gene were associated with voriconazole concentrations in patients receiving 200 mg dose. Genetic polymorphisms in CYP2C19 and letermovir use were associated with subtherapeutic status. They concluded that CYP2C19 phenotype and letermovir use were significantly associated with subtherapeutic voriconazole concentrations and may be used to improve voriconazole precision dosing. Pharmacogenomics J. 2023 Nov;23(6):201-209. doi: 10.1038/s41397-023-00320-z.



Pharmacogenomic Variants Affecting Statins Response in Sri Lanka

Pharmacogenomic variants can influence the efficacy and toxicity of statins, which are commonly prescribed medications for managing cholesterol levels and reducing the risk of cardiovascular events. Statins work by inhibiting HMG-CoA reductase, an enzyme involved in cholesterol synthesis. Ranasinghe and colleagues investigated the diversity of pharmacogenetic variants of statins among Sri Lankans. They compared the minor allele frequencies (MAFs) of 426 Sri Lankans with other populations. They observed the following MAFs in common genes usually associated with statins response and toxicity.



The MAF of *SLCO1B1*5* (rs4149056 [T>C]) was 18.19% (95% CI: 14.53-21.85), MAFs of *CYP2C9*2* (rs1799853 [C>T]) and *CYP2C9*3* (rs1057910 [A>C]) were 2.58% (95% CI: 1.08-4.08) and 10.30% (95% CI: 7.75-13.61), respectively, MAFs of rs2231142 (G>T) (*ABCG2*), rs7412 (C>T) (*APOE*) and rs20455 (A>G) (*KIF6*) variants were 10.68% (95% CI: 7.76-13.60), 3.52% (95% CI: 1.77-5.27) and 50.7% (95% CI: 45.96-55.45), respectively. They found the frequency of two variants higher in the Sri Lankan populationcomparedd to the Western and other Asian populations (rs20455 (A>G), *CYP2C9*3* (A>C) and *SLCO1B1*5* (T>C)). They concluded that genetic polymorphisms affecting efficacy of statins (*KIF6* [rs20455], *CYP2C9*3*) and increase risk of statin-induced myotoxicity (*SLCO1B1*5* and *CYP2C9*3*) were prevalent in higher frequencies among Sri Lankans compared with Western populations. Pharmacogenomics. 2023 Oct;24(15):809-819. doi: 10.2217/pgs-2023-0149.

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