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Translational and clinical applications of pharmacogenomics in cardiovascular medicine

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Pharmacogenomics (PGx), a cornerstone of personalized medicine and optimal health care, has become common place in the practice of cardiovascular medicine. PGx testing can inform drug- and dose-selection strategies to improve efficacy and minimize the risk of adverse effects. The US FDA-approved drug labeling of warfarin recommends VKORC1 and CYP2C9 testing to determine initial doses of warfarin, and testing has resulted in significantly decreased rates of warfarin-associated adverse events. Clopidogrel drug labeling describes the use of CYP2C19 testing to identify patients less likely to respond to clopidogrel so that alternate therapies can be considered. PGx testing also has indication for improving the safety of statins, one of the most commonly prescribed classes of medication worldwide. The Clinical Pharmacogenetics Implementation Consortium (CPIC), a shared project between the US National Institutes of Health (NIH) Pharmacogenomics Knowledgebase (Pharm GKB) and the NIH Pharmacogenomics Research Network (PGRN), recommends SLCO1B1 testing to identify patients at higher risk of simvastatin-associated myopathy. Findings from our ongoing research suggest polymorphisms in CYP3A4 and CYP3A5, the primary metabolizing enzymes for several statins, may to play an important role in characterizing simvastatin myopathy risk. Clinical outcomes associated with beta-blockers, another prominent class of cardiovascular medications, may also be improved with PGx testing. Findings from our ongoing research suggest CYP2D6 testing may prove useful in establishing goals for maintenance dose of beta-blockers in patients with heart failure. This presentation offers a contemporary overview of PGx testing, briefly discussing implications and limitations of emerging validated tests relevant to various classes of cardiovascular pharmacotherapies (e.g., anticoagulants, beta-blockers, and statins). A review of the clinical and translational research used to establish current official guidelines for PGx applications in cardiovascular medicine, will be followed by an in-depth description of our ongoing research involving promising novel PGx applications for statin and beta-blocker pharmacotherapies.

Biography

Joseph Kitzmiller is an NIH Translational Scholar in Pharmacogenomics and Faculty Member at The Ohio State University (Colleges of Engineering and Medicine). His research focuses on investigating the interplay among genetics, nutrition and cardiovascular pharmacotherapies. With active funding from the American Heart Association and the National Institutes of Health, he leads basic, translational, and clinical research of the largest classes of cardiovascular medications, statins and beta-blockers. He is a Board-Certified Pharmacologist, a Clinical Consultant for Gnome Diagnostics, and a Clinical Investigator at Ohio Clinical Trials. At Gnome Diagnostics, he provides Medical Leadership for the clinical implementation of pharmacogenomics testing, and his work at Ohio Clinical Trials involves implementation of early phase drug development studies. At the Ohio State University, he is an Associate Director of the Center for Pharmacogenomics and Director of the Clinical Pharmacology and Pharmacogenomics Fellowship Training Program.

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