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Clinical pharmacogenetics of CYP3A4 in MAT for OUD: A case for diversity

Bradford D Wilson[1], Earl B Ettienne[1], Edwin Chapman[2], Mary Maneno[1], Adaku Ofoegbu[1], Beverlyn Settles-Reaves[2], Melissa Clarke[2] and Georgia Dunston[1]

[1]Howard University, USA

[2]Medical Home Development Group, USA

Opioid use disorder (OUD) and the associated increase in overdose deaths has become a U.S. national health priority. Medication-assisted therapy (MAT) is a treatment approach commonly used in OUD management. Buprenorphine, a partial mu-opioid receptor agonist and kappa-opioid receptor antagonist, has been shown to be an effective MAT option for OUD management. Buprenorphine is primarily metabolized by the cytochrome P450 3A4 (CYP3A4) enzyme. The CYP3A4*1B allele confers an ultra-rapid metabolizer phenotype and is found at a significantly higher frequency in African populations compared to non-African populations. This genetic difference in CYP3A4 metabolism leaves some patients being managed on buprenorphine undertreated and at an increased risk for relapse. Clinical pharmacogenomics (CPGx) testing of CYP3A4 has been shown to improve MAT outcomes in African American patients. PGx-guided buprenorphine dosing reduced the number of relapses on OUD patients exhibiting the CYP3A4*1B genotype. Reduced relapse translates into additional downstream benefits including reduction in risk of hepatitis C and/or HIV infection. The functional significance and clinical utility of this variant demonstrate the need for diversity in CPGx studies and pharmacogenomics testing algorithms.

Biography

Bradford D Wilson is a Geneticist with over a decade of experience in DNA sequencing, bioinformatics and genomics research. He has conducted research in breast and prostate cancer, hypertension and pharmacogenomics at the National Human Genome Center and the W. Montague Cobb Laboratory at Howard University. His approach to identifying the genetics underlying the biology of health disparities leverages genetic diversity and utilizes sequence variation to elucidate the pathophysiology.

Bradford.wilson@howard.edu

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