Pharmacogenomics J. 2017 Dec 27. doi: 10.1038/s41397-017-0011-3. [Epub ahead of print]

The impact of genetic polymorphisms on CYP1A2 activity in humans: a systematic review and meta-analysis.

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Abstract

A large interindividual variation in the activity of cytochrome P450 1A2 (CYP1A2) raises concern about therapeutic failure or toxicity when medical professionals prescribe drugs extensively metabolized by CYP1A2. To date, a number of studies have assessed the association between genetic polymorphisms and CYP1A2 activity; however, there are controversies as to the functional importance of CYP1A2 polymorphisms on the metabolism of CYP1A2 substrates. This systematic review and meta-analysis assessed the effects of genetic polymorphisms on CYP1A2 activity, as measured by caffeine metabolism, in a total of 3570 individual subjects. Higher enzyme activity was observed among those who were homozygous or heterozygous for the -163C>A polymorphism (rs762551), when compared to the wild-type individuals (SMD = 0.40, 95%CI = 0.12-0.68, p = 0.005; SMD = 0.32, 95%CI = 0.11-0.54, p = 0.003, respectively) and this was more pronounced among smokers (SMD = 0.92, 95%CI = 0.27-1.57, p = 0.005; SMD = 0.56, 95%CI = 0.22-0.90, p = 0.001, respectively). For other CYP1A2 polymorphisms, altered caffeine metabolic ratios were not seen. Our results indicate the functional importance of -163C>A polymorphism on CYP1A2 inducibility in humans.

PMID: 29282363 DOI: 10.1038/s41397-017-0011-3