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Study of genetic variants that result in loss of activity of major drug metabolizing enzymes such as CYP3A5, CYP2D6 and SULT1A1

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We have carried out a comprehensive study on the occurrence of major SNPs in the genes encoding CYP3A5, CYP2D6 and SULT1A1. CYP3A5 and CYP2D6 are cytochrome P450 enzymes involved in phase I drug metabolism whereas SULT1A1 sulphonates drugs and thus helps in the clearance from the system. CYP3A5 and CYP2D6 are known to metabolize 50% and 25% respectively of the currently prescribed drugs. Functional SNPs in these genes are known to impair the metabolism of commonly prescribed drugs apart from anti-cancer drugs. Hence, the objective of the study was to screen individuals for the presence of the SNPs; CYP3A5*3 (rs776746), CYP2D6*4 (rs3892097) and SULT1A1*2 (rs9282861). Our results indicate that a significant proportion of Indian population do carry SNPs of the enzymes and are likely to be poor responders to various commonly prescribed drugs, including tamoxifen, most widely used to breast cancer. The prevalence of the SNPs observed in the present study differed significantly from those reported by western countries. On a significant note one of the SNPs exhibited association with cancer. Our results therefore indicate a strong need for developing Indian/population specific databases for treating various ailments more effectively with fewer side effects.

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