

## **UDP-glucuronosyltransferase UGT1A6 : T181A and R184S amino acid substitutions**

Several polymorphisms that alter UDP-glucuronosyltransferase (UGT) activities have been identified. In the UGT1A6 gene, two linked missense mutations on one allele of UGT1A6 (UGT1A6\*2) result in T181A and R184S amino acid substitutions and reduced activity against phenolics, such as 4-nitrophenol, 4-hydroxycoumarin (Oral Anticoagulants !) and butylated hydroxy anisole. In a recent study, genotype frequencies for UGT1A6\*2 were 0.478, 0.392, 0.029, 0.090, 0.012 for wild-type (wt)/wt, wt/T181A + R184S, wt/R184S, T181A + R184S/T181A + R184S and T181A + R184S/R184S, respectively. These highly prevalent polymorphisms, which result in modified activity of UGT 1A6, may influence susceptibility to cancers associated with altered metabolism of endogenous and xenobiotic compounds. Interestingly, UGT1A6 is not only expressed in the liver, but also in human brain where it has been found to metabolise 5-hydroxytryptamine. UGT1A6 could play an important role in the glucuronidation of 5-hydroxytryptamine in vivo, therefore terminating the actions of the neurotransmitter.

### References

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