

Genes-4U

UGT1A6 T181A

(UDP-glucuronosyl transferase 1A6 T181A)

UGT1A6 is one of the 15 members of the UGT family (1). Also known as 'phenol UGT', it **metabolizes** primarily planar phenols and arylamines (2), **aspirin, salicylate, 5-hydroxytryptamine or serotonin and coumarin derivatives**.

The missense mutation **T181A** (A541G at nt level) is usually linked with a second one, R184S (A552C at nt level, haplotype frequency 0.29) and causes decreased enzymatic activity of UGT1A6 (2,3).

Recently, the protective effect of aspirin on colon adenoma and polyp formation was found associated with the UGT1A6 T181A mutant (4).

Most patients with **Gilbert's syndrome** (see UGT1A1 (TA)_{6/7}) also show the UGT1A6 T181A mutation, and may thus have abnormalities in glucuronidation of aspirin or coumarin- and dopamine-derivatives (5).

References

(1) Miners JO, McKinnon RA, Mackenzie PI. Genetic polymorphisms of UDP-glucuronosyltransferases and their functional significance. *Toxicology* 2002 Dec 27;181-182:453-6 (PMID: 12505351)

(2) Lampe JW, Bigler J, Horner NK, Potter JD. UDP-glucuronosyltransferase (UGT1A1*28 and UGT1A6*2) polymorphisms in Caucasians and Asians: relationships to serum bilirubin concentrations. *Pharmacogenetics* 1999 Jun;9(3):341-9 (PMID: 10471066)

(3) Bigler J, Whitton J, Lampe JW, Fosdick L, Bostick RM, Potter JD. CYP2C9 and UGT1A6 genotypes modulate the protective effect of aspirin on colon adenoma risk. *Cancer Res* 2001 May 1;61(9):3566-9 (PMID: 11325819)

(4) King CD, Rios GR, Assouline JA, Tephly TR. Expression of UDP-glucuronosyltransferases (UGTs) 2B7 and 1A6 in the human brain and identification of 5-hydroxytryptamine as a substrate. *Arch Biochem Biophys* 1999 May 1;365(1):156-62 (PMID: 10222050)

(5) Peters WH, te Morsche RH, Roelofs HM. Combined polymorphisms in UDP-glucuronosyltransferases 1A1 and 1A6: implications for patients with Gilbert's syndrome. *J Hepatol* 2003 Jan;38(1):3-8 (PMID: 12480553)