

Genes-4U

UGT1A1 (TA)6/7

(UDP-glucuronosyl transferase 1A1, Gilbert's syndrome)

UGT1A1 metabolizes primarily **bilirubin** but also **drugs, xenobiotics** and other **endogenous compounds** like **hydroxyestrogens and thyroid hormones**. **Gilbert's syndrome**, i.e. mild hyperbilirubinemia in adults enhanced by fasting, is mostly caused by common insertion / deletion mutations in the promoter of the UGT1A1 gene with 5, 6, 7 or 8 thymidine-adenine (TA) repeats. In caucasians, the wild type form is (TA)6 / (TA)6, and the most common mutation, **(TA)7**, occurs in 5-15 % of individuals (1). Molecular testing allows direct detection of these abnormalities, so that the long series of serological and biochemical tests previously used to arrive at the exclusion diagnosis "Gilbert's syndrome" is no more necessary (2). In newborns with hemolytic syndromes (e.g. Rhesus or ABO bloodgroup incompatibility), pronounced icterus with the danger of **kernicterus** is associated with these UGT1A1 mutations (3). Notably, there are more than 50 other rare mutations in UGT1A1 that lead to either Gilbert's syndrome, or the more severe Crigler-Najjar syndrome of impaired bilirubin metabolism. Patients with variant UGT1A1 promoter genotypes are prone to toxicity of the cancer drug **Irinotecan** due to impaired glucuronidation of the active metabolite SN-38 (4). The antiretroviral drug **Indinavir** may precipitate jaundice in these patients due to competitive inhibition (5). 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 (6).

References

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