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Implication of human UGT2B7, 2B15 and 2B17 in 19-norandrosterone metabolism

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Abstract

The identity of the enzymes involved in nandrolone glucuronidation *in vivo* together with their relative contribution and regulation remain unknown. Inhibition assays using human liver microsomes incubated with 19-norandrosterone and selective inhibitors revealed that UGT2B7 and UGT2B15 are involved in 19-norandrosterone glucuronidation. Human liver microsomes were genotyped for UGT2B15 D85Y, UGT2B7 H268Y and the UGT2B17 deletion polymorphism.
The glucuronidation activity on 19-norandrosterone was significantly higher in UGT2B15 DD than in the other genotypes ($p<0.05$). However, stratification by UGT2B7 or UGT2B17 polymorphisms did not reveal any significant difference in glucuronidation activity. Since the metabolism mainly takes place in the liver, human liver cancer HepG2 cells were cultured and exposed to androgens to determine if the transcriptional activity of the genes of interest was affected. Surprisingly, only UGT2B7 mRNA expression was significantly increased in HepG2 after incubation with nandrolone decanoate (1.8-folds).
These results show that the UGT2B7 and UGT2B15 are involved in 19-norandrosterone glucuronidation and that UGT2B15 polymorphism (D85Y) is the only UGT genetic variation that influences the glucuronidation activity. This could partly explain the inter-individual variation in 19-norandrosterone excretion.

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