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Molecular Mechanism Underlying the High Salt Stress-Regulated Gene Expression of Drug-Metabolizing Enzymes

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Summary

In this study, we evaluated the influence of high salt stress and hyperosmotic stress on the expression of drug-metabolizing enzymes in the cultured human hepatocyte. After the primary cultured human hepatocytes were exposed to the high salt or hypertonic media, cytochrome P450 (CYP) 1A1, CYP2E1 and UDP-glucuronosyltransferase (UGT) 2B4 were induced at RNA level. Furthermore, we identified the tonicity-response motif in the 5'-flanking region of CYP2E1, and revealed that this motif is related to the up-regulation of CYP2E1 genes through the interaction with tonicity response element binding protein (TonEBP). These novel findings indicate the possibility that hypertonic stress would influence the capacity of the drug metabolism in human liver, which may affect the therapeutic effect of drugs.