

Recent Basic Researches on Drug Interactions and Their Application for the Clinical Pharmacotherapy

○Tamihide Matsunaga and Shigeru Ohmori (Divi. of Pharm., Shinshu Univ. Hosp.)

Recently, a number of clinically important drug interactions were documented, and many of them occur because of changes in the activities of drug-metabolizing enzymes and drug transporters. Basic researches on the enzyme inhibition using subcellular fractions, purified enzymes and culture cells may be useful for estimation of clinically important interactions, although *in vivo* absorption and concentration of the drugs are necessary for projection of the magnitudes of drug interactions. On the other hand, induction of drug metabolizing enzymes and drug transporters requires a complex mechanism that is difficult to be duplicated *in vitro*. In consequence, most induction studies in the past have been conducted *in vivo* using experimental animals. While such studies are useful in pointing to the potential of induction to bring about metabolic interactions, definitive findings from human systems are necessary to extrapolate the results to humans with increased confidence. Human hepatocytes represent one possible approach to this dilemma. However, we have clarified that CYP3A4 and CYP3A7 mRNA expression levels were markedly up-regulated by dexamethasone, but not by rifampicin in human fetal hepatocytes. These data suggested that the induction mechanisms of CYP3As in human fetal hepatocytes may be different from those in the adult liver. In conclusion, selection of suitable basic research models is important for prediction of drug interactions in clinical pharmacotherapy.