MS09-7 **Comparison of the function of transporters involved in the hepatic and renal uptake of drugs between monkeys and humans**

◯Kazuya MAEDA[1], Yuichi SUGIYAMA[1]

[1]Grad. Sch. of Pharm. Sci., The Univ. of Tokyo

The importance of drug transporters in the detoxification of drugs has been recently well recognized through various in vitro experiments and clinical studies. It is very difficult to directly extrapolate animal data to human pharmacokinetics of substrates by several reasons such as the difference in the function and expression of transporters. Moreover, isoforms of OATP family transporters in rodents don't genetically correspond to those in humans. Thus, monkey is thought to be a more suitable model animal for the prediction of pharmacokinetics in humans. In our lab, monkey OATP1B1, an important transporter for hepatic uptake of anions, and OAT1 and OAT3, responsible transporters for their renal uptake, have been cloned and characterized. In the kidney, the uptake clearance of several compounds in monkey OAT1 and OAT3 well correlated with that in human isoforms, whereas transport properties of some substrates in rat OAT3 were different from those in human OAT3. Drug interaction between famotidine and probenecid has been observed in humans, but it cannot be reproduced in rats. This is caused by the relative contribution of OAT3 and OCT1 to the renal uptake of famotidine in rats and humans. On the other hand, this OAT3-mediated interaction was also observed in monkeys. In the liver, at the moment, inhibition constants and transport activities of many compounds in monkey OATP1B1 well correlated with those in human OATP1B1. Though further quantitative characterization will be needed, it is suggested that transport properties of substrates of uptake transporters in humans are very similar to those in monkeys.