S11-5 The utilization of chimeric mice with humanized liver in drug discovery and development.

◯Tae INOUE[1,2], Masakazu KAKUNI[1], Hiroki OHSHITA[1], Kazumi SUGIHARA[2], Shigeyuki KITAMURA[2,3], Shigeru OHTA[2], Toru HORIE[1], Chise TATENO[1]

[1]PhoenixBio Co., Ltd., [2]Graduate School of Biomedical Sciences, Hiroshima University, [3]Nihon Pharmaceutical University

Chimeric mice with humanized liver are used world wide as a model animal in drug discovery and development for the prediction of human *in vivo.* At present the main focus is in preclinical pharmacokinetics and drug metabolism studies and the screening of anti hepatitis B or C viral agents as a hepatitis virus model animal. The hepatic mRNA expression of human drug-metabolizing enzymes, such as CYPs, Phase Ⅰ, Phase Ⅱ enzymes and transporters has been confirmed to occur at similar levels to those reported in human. We compared the drug metabolizing capacity of the chimeric mice to humans by examining the *in vivo* human pharmacokinetics and metabolic disposition characteristics of model drugs such as ketoprofen, *S*-warfarin, diazepam and zaleplon, which exhibit marked species differences in their metabolic pathways and were able to demonstrate that the data obtained from chimeric mice with humanized liver reflected reported human data. We have also established an HCV/HBV infectable chimeric mouse model with humanized liver for the screening of anti viral agents. This HCV/HBV animal model has reportedly proven useful in assessing the efficacy of anti viral drug (interferon or Ribavirin et al.). Recently, chimeric mice with humanized liver have also shown promise as an *in vivo* screening model for the evaluation of next generation liver regeneration agents with new mechanisms. We think that the research data from chimeric mice with humanized liver can help provide more accurate human *in vivo* predictions and thus aid in optimizing and speeding up the drug discovery and development process.