

PXB-Mouse[®] Study Services in DMPK and Safety Studies

Comparison of mRNA expression levels between PXB-Mouse[®] and human liver by microarray analysis

The gene expression of hepatocytes derived from PXB-mice and human hepatocytes derived from liver tissue was compared using Affymetrix[®] U133 Plus 2.0 human 47000 transcripts

Only PXB-Mouse hepatocytes highly expressed : 6.3%
Signal strength > 2
(PXB-Mouse hepatocytes > Human hepatocytes derived from liver tissue)

Only Human tissue derived hepatocytes highly expressed : 9.2%
Signal strength < 0.5
(PXB-Mouse hepatocytes < Human hepatocytes derived from liver tissue)

Both hepatocytes
PXB-Mouse and human tissue derived) :
highly expressed
0.5 < Signal Strength < 2

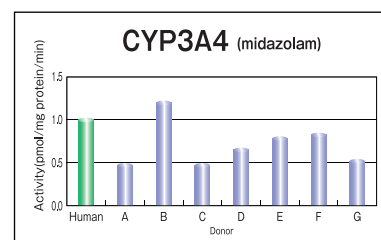
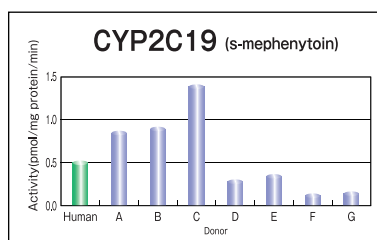
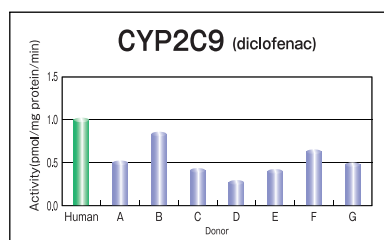
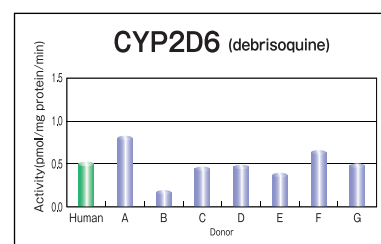
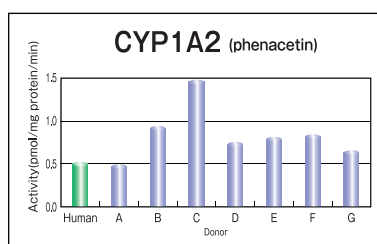
Tateno, et al., SOT Meeting, 2007

Enzymatic activities of major human cytochrome P450s in PXB-Mouse[®]

PXB-mice were produced from several donor hepatocyte lots and the enzymatic activities for major CYPs were confirmed



PXB-mice Donor			
Donor	Age	Gender	Race
A	3mo	Male	Caucasian
B	1ye	Male	Caucasian
C	5ye	Male	African American
D	14ye	Male	Caucasian
E	22ye	Male	African American
F	22ye	Male	Asian
G	35ye	Male	Caucasian

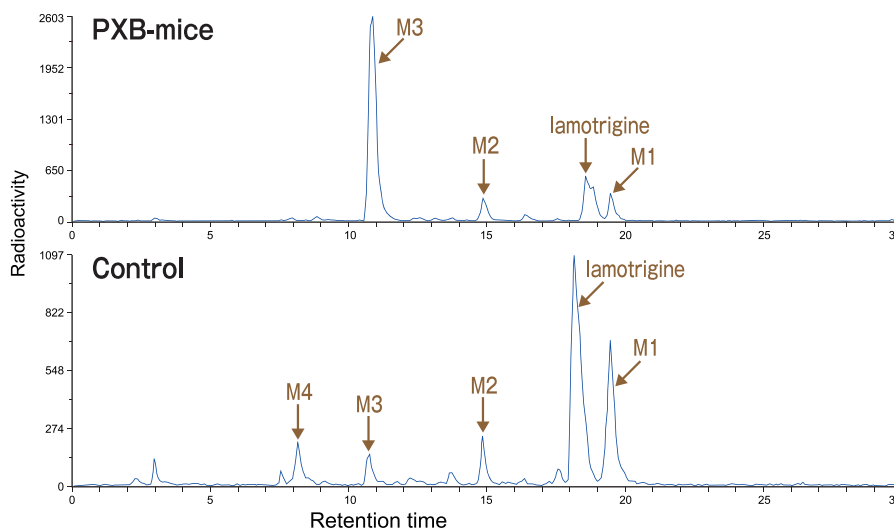
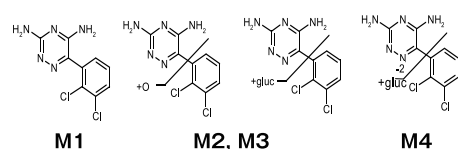
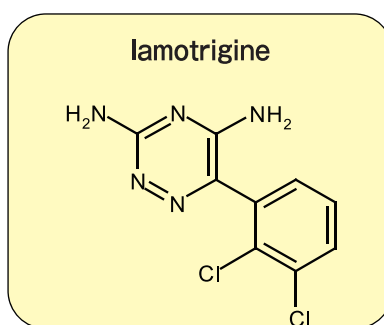


Oshita, et al., JSSX Meeting, 2010

Profiling of human specific metabolites

4 authentic compounds (lamotrigine, NK-1 antagonist, diclofenac and propafenone) were used to qualitatively profile human metabolites in PXB-mice

Collaboration Study with Merck & Co., Inc

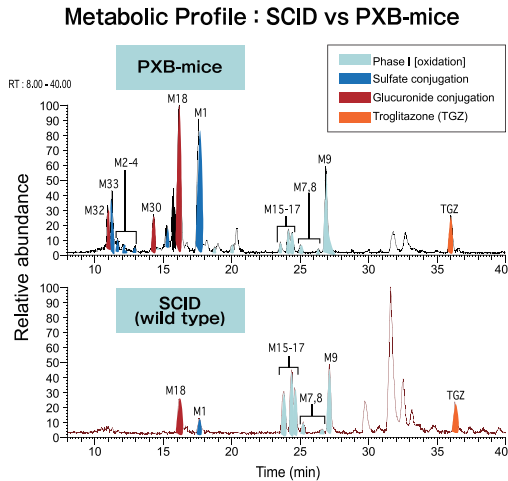


Kumar, et al., ISSX Meeting, 2009

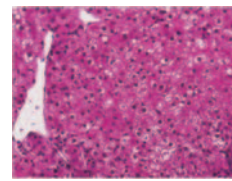
Detection of reactive metabolites and histopathological analysis of effects of troglitazone on PXB-Mouse®

Troglitazone caused reactive metabolite formation and consequent histopathological liver damage which had not been detectable in other animal models was confirmed in PXB-mice

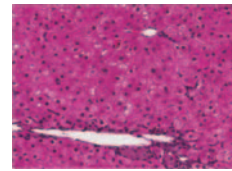
Study Service Performed for AstraZeneca UK Ltd.



H&E Staining : PXB-mice

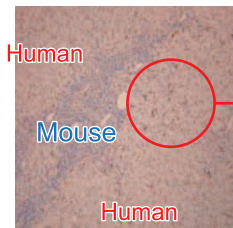


Vehicle treated
Macrovesicular vacuolation

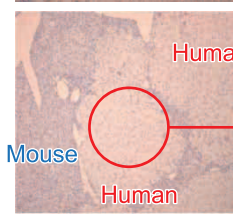


Troglitazone treated (600mg/kg)
Microvesicular vacuolation

MRP2 LHC : PXB-mice



Vehicle treated



Troglitazone treated (600mg/kg)

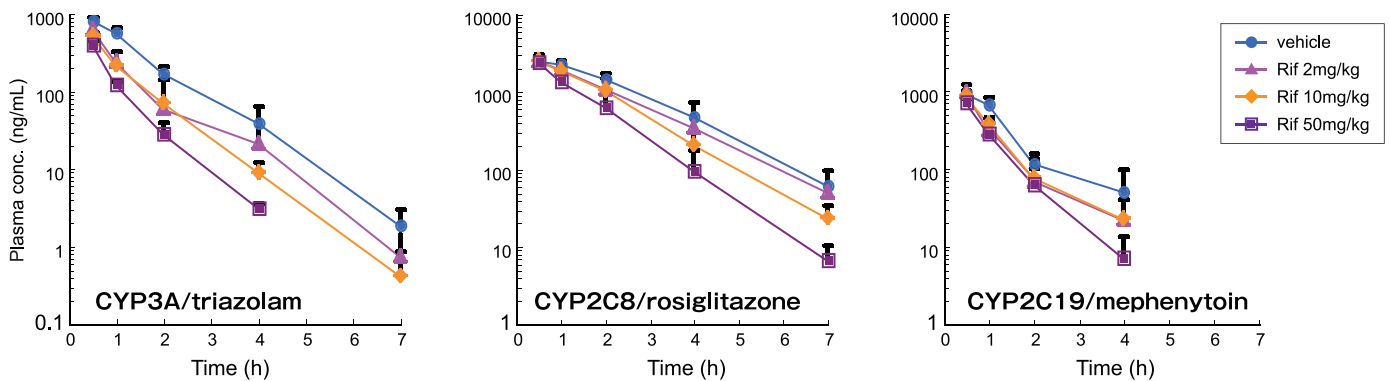
Foster, et al., ISSX Meeting, 2010

Enzyme induction study in PXB-Mouse®

Evaluation of the enzyme induction caused by 4 day repeat dosing of rifampicin

Rifampicin induced the enzymatic activities dose dependently and the induction effects were in line with reported clinical results

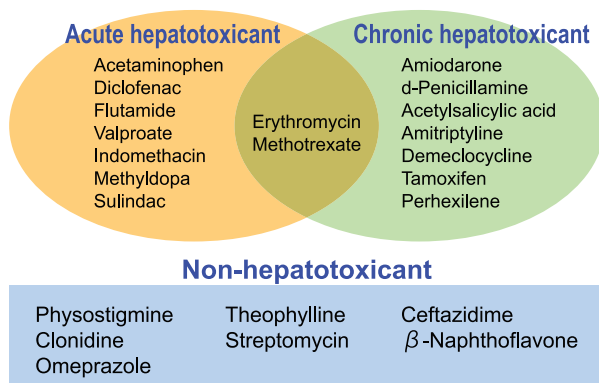
Collaboration Study with Kyowa Hakko Kirin Co., Ltd.



Toxicogenomics analysis in PXB-Mouse®

PXB-mice enable an accurate prediction of human toxicity

Collaboration Study with Sekisui Medical Co., Ltd.



Comparison of Simulated Toxicity Score and Actual Toxicity

Animal Species	Result		
	Match	Borderline	No match
Rat	17	2	4
PXB-Mouse	21	2	0

Contact Information



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