Transcriptome Analysis of Human Liver in Chimeric PXB-Mouse® for Risk Marker Identification Associated with Drug-Induced Liver Injury

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Purpose. We previously reported about the biomarker candidate genes whose amount of expression fluctuated under hepatotoxic drug administration to chimeric mice with highly humanized liver. In this study, we performed transcriptome analysis on the gene variation database derived from the study mentioned above, and identified more risk marker candidate genes associated with drug-induced liver injury (DILI).

Methods. We administrated 8 pharmaceutical products (Towa Pharmaceutical Co., Ltd.) in each of “hTOX” drugs (relatively higher rate of hepatotoxic incidents) and ”non-hTOX” drugs (negligible hepatotoxic incidents) to humanized chimeric mice “PXB-mice®” (PhoenixBio Co., Ltd.), and applied whole genome microarray profiling by “GeneChip®” (Human Genome U133 Plus 2.0 Array, Affymetrix Inc.) to the humanized liver. The gene expression data were analyzed using bioinformatics software “GeneSpring 13.1” (Agilent Technologies Inc.).

Results & Conclusion. Within the mRNAs that were not affected in the amount of expression by all of 8 non-hTOX drugs, we found 7 candidates whose amount were increased in all of 8 hTOX treatments. Among these 7 mRNAs, PIK3R1, RBAK and FKBP5 have been known for involvement in hepatic cytotoxicity-inhibition, cancer cell growth inhibition and cell proliferation, respectively, and seem to be promising as possible risk markers for DILI. This method might be useful to research of risk marker gene for DILI without clinical trials.