＜PXB マウス関連発表＞

P241 In vitro evaluation of human hepatocytes isolated from chimeric mice with humanized livers (PXB-mice®) transplanted using cells from three different donors

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[Background]

Fresh human (h)-hepatocytes are regarded as the best *in vitro* model for xenobiotic metabolism and cytotoxicity studies. However, an "on demand" supply of fresh h-hepatocytes from the same donor is not possible. Chimeric mice with humanized livers (PXB-mice®) are considered a useful animal model for predicting h-type drug metabolism and toxicity, and a good tool for supplying fresh h-hepatocytes on demand. In a previous study, we showed that during culture the expression pattern of several h-CYP and UGT mRNAs, the level of h-albumin (h-alb) secretion, and the activity of CYP3A4 in h-hepatocytes isolated from the PXB mice (PXB-cells), were similar to those found in commercially available cryopreserved h-hepatocytes.

[Purpose]

Here, we evaluated the differences in individual hepatic functions such as h-alb secretion, hCYP and transporter mRNA expression, CYP3A4 activity levels, and CYP induction abilities, between PXB-cells isolated from Chimeric mice transplanted with three different donor hepatocytes.

[Methods and Results]

PXB mice were produced by transplanting commercially available cryopreserved h-hepatocytes (2-year-old Hispanic girl, 5-year-old African American boy and 2-year-old Caucasian girl) into cDNA-urokinase-type plasminogen activator-transgenic/SCID mice. The PXB-cells were isolated from three PXB mice per donor by using the collagenase perfusion method. Isolated PXB-cells were cultured on type I collagen-coated dish for three weeks, and their hepatic functions were analyzed. Irrespective of the plateability of the original donor cells, all the PXB-cells were plateable and cultured at least for 3 weeks. H-albumin levels in the culture medium were maintained throughout the culture period. Expression levels of several hCYPs and transporters in the cultured PXB-cells were comparable to those in freshly isolated PXB-cells. There were no significant differences in the CYP3A4 activities between the freshly isolated PXB-cells and those cultured for three weeks. CYP1A1, 1A2 and 3A4 induction abilities were also maintained for three weeks *in vitro*. The PXB-cells derived from different donors retained the individuality of hepatic functions between the donors and the inter-donor deviations between the PXB-cells were small.

[Conclusion]

The chimeric mouse with humanized liver may be a useful tool for supplying fresh h-hepatocytes from the same donor on demand. The isolated "PXB-cells" can maintain several hepatic functions on the culture plate, and should be a valuable tool for *in vitro* metabolic and pharmacotoxicological studies.