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A Novel Long-Term Culture Method for Activating Cytochrome P450 and Liver-Specific Function of Hepatocytes Utilizing a Collagen Vitrigel Membrane Chamber

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[Introduction] In drug discovery, it is important to predict *in vivo* human pharmacokinetic and toxicological properties from *in vitro* tools, and hepatocyte is one of the useful *in vitro* tools. However, current hepatocyte models do not always reproduce *in vivo* physiological functions as hepatocytes. Since CYP has been reported to be involved in hepatotoxicity by reactive metabolites, maintenance of CYP activities comparable to *in vivo* human liver would be important to predict hepatotoxicity of drug candidate more preciously. In addition, long-term culture of hepatocytes is difficult in the conventional mono-layer culture. Therefore, new culture method of hepatocytes for activating their functional properties including CYP activities is highly demanded. In this study, we have established a novel culture method of hepatocytes by utilizing a collagen vitrigel membrane chamber to maintain CYP activity and liver functions at high levels for a long period. **[Methods]** Human chimeric hepatocytes freshly isolated from liver-humanized mice were used. To quantitatively assess the profile of liver-specific function, time course changes of albumin secretion and urea synthesis were measured. In addition, 5 major CYP activities were compared. **[Results and Discussion]** Throughout 3-week culture period, liver-specific function was significantly higher in vitrigel culture than in mono-layer culture. In addition, vitrigel culture showed equal to or higher CYP activities for all CYP isoforms tested for longer period. These results indicated that vitrigel culture was superior to the conventional mono-layer culture in terms of the liver-specific function including CYP activity and suggested that the vitrigel culture would be potentially applied to multiple *in vitro* cell assays to assess liver-specific function and hepatotoxicity.