USE OF HEPATOCYTE AND KUPFFER CELL CO-CULTURE MODELS IN
ASSESSMENT OF CYTOCHROME P450 METABOLISM

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Abstract

Primary human hepatocyte cultures have long been the gold standard for assessment of liver metabolism of xenobiotic compounds. In the liver, the response to infection and inflammation by tissue associated immune cells can alter gene expression, including cytochrome P450 (CYP) expression. Hepatocytes are macrophages which are part of the liver sinusoidal and mediate many of these responses. Hepatocyte/kupffer cells co-culture offer a more comprehensive model to understand the effects of the liver inflammatory response and microenvironmental modulation of critical drug metabolizing enzymes for better in vivo predictions. Freshly isolated human primary hepatocytes and hepatocytes were chemotactically attracted to separate monolayers and in co-culture at distances ranging from physiological (1:9) to highly inflamed (1:1). Tropin type II culture was used to assess viability of isolated cells. The phagocytic properties of hepatocytes were restored in culture. The specific uptake of latex beads by Kupffer cells was reduced in co-culture. The data showed that Kupffer cells were chemotactically attracted to hepatocytes, which was confirmed by immunohistochemistry. The data showed that Kupffer cells were chemotactically attracted to hepatocytes, which was confirmed by immunohistochemistry. The data showed that Kupffer cells were chemotactically attracted to hepatocytes, which was confirmed by immunohistochemistry.

Introduction

Kupffer cells are the resident macrophage population in the liver, where they reside within the lumen of the liver sinusoid and mediate a number of immune functions. They were first identified by Karl Wilhelm von Kupffer, for whom they are named. Kupffer cells have a number of functions, including the phagocytosis of non-self materials, the regulation of immune responses, and the modulation of liver metabolism. They are known to be involved in the regulation of liver metabolism through the stimulation of liver enzyme expression. Kupffer cells are also known to be involved in the modulation of the inflammatory response in the liver, which can have a significant impact on liver function and health. Therefore, understanding the role of Kupffer cells in liver metabolism is crucial for the development of effective therapies for liver disease.

Methods

Hepatocyte and Kupffer Cell Co-Cultures: Functional Co-cultures can be established with Kupffer cells and hepatocytes. This model is useful for understanding the impact of immune mediators on liver metabolism.

Figure 1. Flow cytometric analysis of the uptake of 1um latex beads by Kupffer cells in freshly isolated rat Kupffer cells.

Figure 2. Uptake of 1um latex beads by Kupffer cells in co-culture with hepatocytes.

Results:

Kupffer cells show increased phagocytosis when added to hepatocytes, which is dependent on the Kupffer cell content of the co-culture. This data indicate that the functional role of Kupffer cells and hepatocytes can be evaluated and used to better define the impact of immune mediation on liver metabolism.

Figure 3. ED2 (2004) immunofluorescence in cultured Kupffer cells.

Conclusions

Kupffer cells can be isolated from SD Rat livers at high purity. Kupffer cells can be visualized using the macrophage specific marker ED2 or fluorescent 1um beads in culture. Functional Co-Cultures can be established with Kupffer cells and hepatocytes.

Figure 4. IL-6 secretion by cultured Kupffer cells in co-culture with hepatocytes.

Acknowledgments

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References