**Human hepatoma HepaRG cells: a unique model system for xenobiotic metabolism and toxicity studies**

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**INTRODUCTION**

Recently, a new human hepatoma cell line named HepaRG has been established. These cells, derived from a human liver carcinoma, are characterized by a high pattern of differentiation after 2 weeks at confluence in presence of 2% DMSO (Gripion et al., PNAS, 2002).

The aim of this work was to analyze the expression of the main xenobiotic metabolizing enzymes and drug transporters in HepaRG cells and to determine whether these cells could mimic human hepatocytes in drug metabolism and toxicity studies.

**Fig. 1** Differentiation and transdifferentiation of hepatocyte-like cells through bipotent progenitors

**Fig. 2** Drug metabolism activities. HepaRG cells were cultured for 30 or 33 days. At day 15, 2% DMSO was added to the culture medium until day 30. Then the cells were cultured for 24h (day 31) or 72h (day 33) without 2% DMSO or were seeded at high density and cultured for 24h or 72h with or without 2% DMSO.

**Fig. 3** mRNA expression of several transporters. Transcripts were measured in confluent HepG2 and undifferentiated proliferating (P) or differentiated (D) HepaRG cells. The values are expressed as percentages compared to 1-day human hepatocyte cultures.

**CONCLUSIONS**

We report for the first time that a human hepatoma cell line is able to express the major CYP-related activities as well as other liver-specific functions. These unique functional properties make HepaRG cells a suitable model for metabolism and acute and chronic hepatotoxicity studies of chemicals.