Coculture systems of CD34+ cells with hepatocytes as models for induction of hepatic differentiation

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Published online on 16 May 2007

Adult human haematopoietic stem cells possess high plasticity that was demonstrated with respect to their differentiation into organ specific cell types. Using differential experimental design, studies have indicated that adult stem cells can differentiate into hepatocytes-like cells which differ in hepatic marker expression profiles and functional properties. However, methods are still being developed for induction of stem cell differentiation and the contribution of direct cell-cell-contact or soluble factors is under investigation. For hepatic differentiation of CD34+ cord blood cells we investigated models with respect to contributions of direct stem cell - hepatocyte interactions and secreted factors from hepatocyte culture.

CD34+ stem cells were cocultured with different cell types as murine hepatocytes line AML-12, human hepatocarcinoma HepG2 and murine hepatocytes. Flow cytometric analysis using dye transfer technique showed that stem cells get in contact with hepatocytes. Video imaging revealed a high CD34+ motility. FACS and Western Blot techniques demonstrated that CD34+ cells express Connexin43 and the hepatocytes Connexin32. Through these gap junctions cells may communicate and perhaps support differentiation into hepatic-like cells. Furthermore, conditioned cell culture media from HepG2 cells induced early endodermal differentiation (SOX17, FOXA2, AFP) of CD34+ stem cells, suggesting the involvement of secreted soluble factors. Conditioned hepatocyte media and coculture of CD34+ cells with hepatic cells represents a valuable model for studying hepatic differentiation processes.