Further characterization of autologous NeoHepatocytes for in vitro toxicity testing.

Gold standard for in vitro toxicity tests and drug screenings is primary human hepatocytes (hHeps). Because of their limited availability efforts have been made to provide alternatives, e.g., monocyte-derived NeoHepatocytes. In the past years it has been critically discussed if gaining hepatocyte features is associated with trans-differentiation of monocytes or their activation towards a macrophage phenotype. Generating NeoHepatocytes in the presence of six different human AB sera, fetal calf serum (FCS) or autologous serum showed that yield and quality of NeoHepatocytes is inversely correlated to macrophage activation. Using autologous serum constantly the highest amount of cells with the best metabolic capacity was obtained.

Focus of this study was to further analyze bio-transformation capacity of the optimized NeoHepatocytes for use as in vitro toxicity test-system. Treatment of the optimized NeoHepatocytes with two different pro-teratogenic substances with corresponding metabolites and eight known hepatotoxins showed comparable toxicity to hHeps. Bio-transformation rates, assessed by testosterone metabolism, were comparable in both cell types. Our data reveal that use of autologous serum reduced macrophage activation which improved yield and function of NeoHepatocytes resulting in bio-transformation and toxicity profiles.
comparable to hHeps. Thus, their easy accessibility makes them an ideal candidate for in vitro toxicity studies.