495c Preventing Hepatocyte Steatosis by Co-Culture with Adipocytes during Plasma Exposure

Deepak Nagrath, Vanessa Lopez, Francois Berthiaume, and Martin Yarmush

During bioartificial liver operation when extracorporeal bioartificial liver (BAL) systems (which consists of functioning, viable hepatocytes) are exposed to patient plasma/blood there is an increased accumulation of lipids which in turn leads to deterioration of liver-specific functions. Studies on whole-body metabolism have shown that adipose tissue is the preferential site for lipid storage, and adipocytokines secreted by adipocytes, such as leptin, adiponectin, TNF-a, and resistin, play an important roles in metabolic homeostasis by changing hepatic insulin sensitivity and peroxisomal b-oxidation. We hypothesized that coculturing adipocytes with hepatocytes would improve lipid metabolism and reduce intracellular lipid accumulation in hepatocytes. In coculture configuration, hepatocytes were seeded in a double gel sandwich culture on 6 well dishes and 3T3-L1 preadipocytes were seeded on the inserts and later differentiated into mature adipocytes. The coculture system was modulated for differential activation of fat storage in adipcocytes and catabolism of fatty acids and b-oxidation in hepatocytes through peroxisomal proliferator activated receptor (PPAR) ligands. The results clearly demonstrate that the lipids in plasma were differentially routed to adipocytes, thus preventing the accumulation of excess fat in hepatocytes. Additionally, we modulated the adipokines to increase the hepatic functions. The adiponectin and leptin expression was increased and resistin expression was decreased through PPAR ligands to increase the liver specific functions.