10b Improved Oxygen Delivery to Hepatocytes Maintained within a Hollow Fiber Bioreactor Via Bovine Red Blood Cell Supplementation of Circulating Culturing Media

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Oxygen delivery to hollow fiber (HF) cultures, especially hepatic HF cultures, is believed to be a limiting nutrient because of large diffusion distances, small cell space diffusion coefficients, and low aqueous media oxygen solubility. Inadequate oxygen delivery to hepatocytes can reduce viability levels and hamper expression of differentiated function. This problem can potentially be alleviated via the addition of an oxygen carrier to a circulating bioreactor media feed stream. Consequently, we have initiated finite element modeling and experimental studies to examine the use of circulating bovine red blood cells (bRBCs) within hepatic HF cultures. The ultimate goal of this multifaceted project is to develop an efficient hepatic HF bioreactor operating under appropriate oxygenation conditions. The finite element model employed in these studies shows a marked improvement in oxygen delivery, and the provision of a greater range of oxygen tensions to hepatocytes over the length of the bioreactor with bRBC supplementation. It is expected that this model can be used to a priori optimize bioreactor process parameters and estimate oxygen delivery with varied bRBC supplementation, helping to focus corresponding experimental studies on the most likely culture conditions for providing optimum oxygenation conditions. The results for our experimental work showed decreased hepatocyte lactate production to glucose consumption ratios when bRBCs were added to the culture circulating media, indicating the presence of a more aerobic environment. Additionally, albumin synthesis was improved within the experimental culture. Our experimental results thus support the use of bRBCs to improve oxygen delivery to hepatocytes maintained within a HF bioreactor.