425b Engineering Select Physical Properties of Cross-Linked Red Blood Cells and a Simple *a Priori* Estimation of Their Efficacy as an Oxygen Delivery Vehicle within the Context of a Hepatic Hollow Fiber Bioreactor

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Bovine red blood cells (bRBCs) can potentially provide a simplistic and economic means of improving oxygen delivery to hollow fiber (HF) bioreactor cell cultures. Bovine RBCs are also interesting since many of their physical properties can be altered as a result of glutaraldehyde cross-linking. Cross-linking bRBCs produces an oxygen carrier that is expected to be beneficial under specific circumstances (i.e. delivery of oxygen to cells that are sensitive to free hemoglobin (Hb), and cells that require low inlet oxygen tensions). We have examined the osmotic stability and electrophoretic mobility of cross-linked bRBCs, and observed that cross-linking improves osmotic stability while minimally impacting electrophoretic mobility. The oxygen binding properties (P_{50} and n) of cross-linked bRBCs were also measured and under the reported reaction conditions, cross-linking increased the oxygen affinity and reduced the cooperativity of bRBCs. A Krogh tissue cylinder model was then utilized to provide an *a priori* estimate of oxygen delivery to hepatocytes housed within a HF bioreactor with both normal and cross-linked bRBC media supplementation. This model showed that bRBCs generally improved oxygen delivery to HF cell cultures, and that cross-linked bRBCs are more beneficial than normal bRBCs in specifically targeting oxygen delivery to cells maintained at low inlet oxygen tensions. Additionally, the model showed that bRBC supplementation can significantly improve oxygen delivery without requiring extreme bRBC concentrations, and that a significant media flow rate increase is required to offer the same improvement in oxygen delivery that is achieved through bRBC supplementation at a minimal hematocrit