ALBUMIN IN CELL CULTURE MEDIA – AN EXAMINATION OF QUALITY AND FUNCTION

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The inclusion of human serum albumin into serum free cell culture media (SFM) has been shown to be extremely beneficial in expanding multiple therapeutically relevant cell types *ex vivo*. However, proteins isolated from human serum can have variable performance, the presence of questionable stabilizing reagents, and potential adventitious agent contamination risks. Thus, the investigation into the inclusion of a recombinant alternatives in serum free cell culture media is warranted.

Native albumins from two different vendors and recombinant human albumins from two different expression systems were compared for monomer purity, protein modification, and conjugated fatty acid profile. These initial studies indicated that recombinant versions, regardless of expression platform, offered superior monomer purity and percent unmodified protein over the native albumins in addition to significantly altered fatty acid compositions. Thus, given the profound effects of different lipid species in cell culture, as well as the unknown performance contribution of serum-derived undefined contaminates and protein modifications found in native albumins, it is currently unknown if these ultra-pure, highly unmodified and well-defined recombinant albumins are capable of equivalent or superior performance when compared to the native versions.

These same native and recombinant albumins were subsequently tested in quantifiable functional performance assays in multiple industry-relevant cell systems in order to better understand how these biochemical characteristics translate to overall albumin function in cell culture. This functional screen determined a cell type-specific albumin source preference that did not have a significant correlation to albumin monomer purity or total lipid load of each albumin tested. However, further analysis has shown that specific modifications and targeted optimization of the recombinant albumin significantly enhanced the performance in select cell systems.

Taken together, these studies indicate that different sources and protein characteristics of albumin can translate to differential abilities to expand cells *ex vivo*. More critically, however, the insights gained from this data indicates that recombinant albumin can be further optimized for use in efficiently expanding multiple cell types while retaining adequate cell phenotype and function. Thus, the feasibility of the incorporation of recombinant albumin into SFM formulations to generate fully animal component free media has been established and further exploration is warranted.