432i Effect of Aggregate Morphology of a Non-Disease Associated Protein on the Cellular Metabolic Response and Viability of Human Epithelial Cells in Vitro

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Protein aggregation has been associated with the pathologies of more than twenty human diseases in a range of tissues. Recent studies have shown that non-disease related proteins can form aggregates with morphologies similar to those associated with disease. Further, such aggregates have been shown in certain instances to be cytotoxic to *in vitro* cell culture. These results suggest that there are common mechanisms for aggregate formation, as well as their toxic effects on cells. The elucidation of such mechanisms is crucial to the development of strategies to prevent disease. Here we present results pertaining to the toxicity of aggregates of the 63 amino acid protein L. Protein L forms a stable tertiary structure in aqueous solution, and thus a variety of alcohol denaturants were explored to induce self-association. The resulting aggregates bind both Congo Red and Thioflavin T dyes in a manner consistent with the presence of amyloid fibrils. We observed with TEM a number of distinct solvent dependent fibril morphologies. The impact of different fibril morphologies on the *in vitro* cellular metabolic response and cytotoxicity in both cancerous and non-cancerous epithelial human cell lines will be discussed. In addition, we will present similar data on the effect of fibrillar maturity to determine if mature fibrils of protein L exhibit a lowered toxicity, as has been observed for many disease related aggregates. In conclusion, we will use these results to suggest possible methods of preventing the formation of toxic protein aggregates *in vivo*.