

A New Assay For The Detection Of Misfolded Prion Protein (PrP^{SC}) In Blood. Cindy Orser PhD, Tao Pan PhD, Jasmeet Sethi PhD, Craig Nelson, Pete Andreotti PhD, and Alan S. Rudolph PhD MBA. Adlyfe Inc. 9430 Key West Ave, Rockville, MD 20850

We have developed a new in vitro diagnostic assay for the rapid detection of misfolded prion protein (PrP^{SC}) in blood. Small peptides structurally designed with fluorescent probes have been synthesized. Upon interaction with PrP^{SC} in a blood sample, the peptides undergo a conformational change from alpha helix to beta sheet that mimics the folding reaction known to occur as PrP^C converts to the infectious and deleterious PrP^{SC} (J. Biomolecular Structure and Dynamics 21:353-365 2003). The conformational change in the synthetic peptide is accompanied by formation of an excimer state of the fluorescent probes on the peptide which is easily monitored over the timecourse (30-180 minutes) of the reaction. Superior sensitivity of the assay is achieved due to signal amplification as additional peptides are recruited in solution to undergo a similar conformation change. This has enabled the detection of PrP^{SC} in blood plasma and serum of animals infected with disease. In a controlled model of infection in hamsters, we have shown that this method can detect disease presymptomatically and considerably earlier than current ELISA or Western Blot tests which are currently unable to detect disease in blood. We have also demonstrated the detection of PrP^{SC} in the blood of animals with endemic disease including Sheep Scrapie and BSE. The test is currently being optimized for large scale automated high throughput testing for PrP^{SC} for live animal surveillance of disease as well as human blood screening for vCJD.