CJD foundation grant progress report

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Title: Detection of residual prions from decontaminated medical and laboratory surfaces.

Project objective. To investigate the interplay of prion strain, surface type, and surface treatment on residual prion detection. We will contaminate laboratory and clinically relevant surfaces with prion strains from rodents, livestock, or primates, and determine the detection sensitivity of our system. Then we will evaluate the detection of surface residual prions under optimized conditions with three levels of decontamination: effective, partially effective, and ineffective. Finally, we will perform a safety survey in prion-exposed laboratories and clinics. The results of these studies will validate our innovative detection methodology for compatible surface residual prions that are optimized for laboratory or clinical settings.

Summary of accomplishments. Prion diseases are untreatable fatal transmissible neurodegenerative diseases that affect a wide range of mammals including humans that are caused by PrP^{Sc}, the infectious self-templating conformation of the host encoded protein, PrP^{C}. Prion diseases can be transmitted via surfaces in laboratory and clinical settings. Here we use a combination of surface swabbing and real time quaking induced conversion (RT-QuIC) to test for residual surface associated prions following prion disinfection. We found that treatment of several prion-contaminated laboratory and clinically relevant surfaces with either water or 70% EtOH resulted in robust detection of surface associated prions. In contrast, treatment of surfaces with sodium hypochlorite resulted in a failure to detect surface associated prions. RT-QuIC analysis of prion contaminated stainless-steel wires paralleled the findings of the surface swab studies. Importantly, animal bioassay and RT-QuIC analysis of the same swab extracts are in agreement. We report on conditions that may interfere with the assay that need to be taken into consideration before using this technique. Overall, this method can be used to survey laboratory and clinical surfaces for prion infectivity following prion decontamination protocols.

Key findings. We found that swabbing of prion contaminated surfaces can rapidly determine the efficacy of surface prion decontamination. Importantly, we determined examination of surface extracts with RT-QuIC and animal bioassay produced similar findings suggesting that this method can accurately assess reduction in prion titer. We found that a reduction of RT-QuIC seeding activity of the surface swabs corresponded with a reduction in RT-QuIC seeding activity of the surface. We identified surface contaminants that interfere with the assay that may be found in clinical and laboratory settings. Overall, this method can enhance clinical and laboratory prion safety measures.

Next steps related to prion research. In combination with the recent outstanding publication from Dr. Caughey's group (Orru et al., 2024 PMID: 38640117) on RT-QuIC detection of alpha synuclein, tau and PrP prions from solutions bathing surfaces, two independent groups have developed practical methods to assess prion contamination in medical and laboratory settings. It is known that prions when bound to a surface (e.g. stainless steel wire, soil particle) remain infectious. What is unknown is if prion conversion occurs on PrP^{Sc} bound to the surface or if desorption of PrP^{Sc} from the surface is required to establish prion infection. Sara Simmons, who did the work described here as part of her Master's thesis, has transitioned to a doctorate program and will be investigating the mechanism of establishment of prion infection when bound to a surface.