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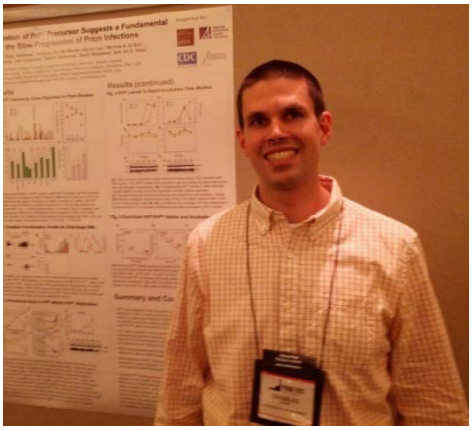

Originally from Tennessee, United States, I completed my B.Sc. with a major in Microbiology and minor in Animal Sciences at the University of Tennessee. I relocated to pursue a M.Sc. at the University of Kentucky in the Department of Animal Sciences with a thesis research project focused on the reproduction of beef cattle. My close association with cattle during the time of my Master's work coincided with the first discoveries of bovine spongiform encephalopathy (BSE) in North America, which occurred in Alberta, Canada. This event heightened my curiosity into these neurodegenerative diseases that initiated what has now been an eight year devotion to prion research. Soon thereafter, I was fortunate to be able to transition to the Department of Microbiology at the University of Kentucky for Ph.D. studies, where I was assigned a project aimed at understanding prion propagation by developing a cell culture model for prion disease, optimizing an *in vitro* prion conversion assay, identifying factors regulating prion replication, and investigating methods for intervention. After I finished my graduate studies, I was recruited and gladly welcomed the opportunity for a postdoctoral position under the guidance of Dr. David Westaway, where I could continue research in the prion field at the newly established Centre for Prions and Protein Folding Diseases at the University of Alberta.

With the support of an Alberta Innovates Health Solution Fellowship, I have been able to address a critical question regarding the possibility of a host response during prion pathogenesis. The cellular prion protein (PrP^{C}) is recognized as the obligate substrate for the replication of PrP^{Sc}, which is the infectious component of a prion that is associated with mammalian prion diseases. The hypothesis for my research project was that PrP^{C} levels are decreased by prion infection. This hypothesis is based on a discovery by the Westaway laboratory just prior to my joining, where the PrP-like Shadoo (Sho) protein levels were shown to be reduced in parallel with PrP^{Sc} accumulation in a prion disease specific manner. Until now, the disease status of PrP^{C} has been under-explored because of its unaltered steady-state levels of mRNA and the confounding excess of PrP^{Sc}. By utilizing a new technology to monitor the different forms of PrP during a variety of prion diseases, we were able to detect that brain cells respond by downregulating PrP^{C} preclinically. Reduction of PrP^{C} early in prion infection helps to explain the latency of prion infections. Realization of this previously unappreciated element of pathogenesis offers promise that drug enhancement of this natural protective response is now a therapeutic option.

This publication is definitely the result of a collaborative effort. For this reason, I would like to thank all of contributors and co-authors. In particular, the collaboration with Dr. Jiri Safar at Case Western Reserve played a central role in making this investigation possible. I also must acknowledge Dr. David Westaway, whom I am grateful for his continuous support and advice, as well as being engaged in mentoring me to achieve my goals as a scientist.