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Using Mass Spectrometry to Diagnose Prion diseases: Can we do that?

Christopher J. Silva[1], Bruce C. Onisko[2], Irina Dynin[1], Melissa L. Erickson[1] and J. Mark Carter[1]

[1]United States Department of Agriculture, USA
[2]OniPro Biosciences, USA

Prions (PrP^{Sc}) are infectious proteins. They are able to convert a normal cellular protein (PrP^{C}) into a prion and, thereby, propagate an infection. We have used mass spectrometry to quantitate the prions present in infected hamsters, mice, and sheep. Calibration curves relating the area ratios of the selected analyte peptides for each species and their oxidized analogs to stable isotope labeled internal standards were prepared. The limits of detection (LOD) for human, sheep, deer, cow, and mouse PrP were determined to be below 100 attomoles (10^{-18} moles; ~1,000,000 molecules). We included characteristic non-analyte peptides in the multiple reaction monitoring method. These peptides had LODs that were much lower than those of the analyte peptides. By combining these approaches we can both quantitate and confirm the presence of prions in the attomole range. This method was used to quantitate the prions present in brains of hamsters or mice five weeks after inoculation (*ic*) with either four hamster-adapted prion strains or four mouse-adapted prion strains. The prions from different brain regions of a sheep naturally infected with scrapie were also quantitated. All of the rodent-adapted prion strains were detectable in the asymptomatic animals. In sheep, prions were detectable in the obex, anterior portion of the cerebrum, and the non-obex/non-anterior portion of the cerebrum. This mass spectrometry-based approach can be used to quantitate and confirm the presence of prions before pathological changes are detectable.

Biography

Christopher J. Silva received his Ph.D. in organic chemistry from Stanford University. He is currently a Research Chemist for the Agricultural Research Service of the USDA in Albany, California, USA. His is the author or co-author of 27 peer-reviewed scientific publication, book chapters, and/or published patent applications. His research interests include protein analysis using mass spectrometry and prion biology.