Accepted Manuscript

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Andrei Soutyrine, Hongsheng Huang, Olga Andrievskaia, Ines Walther, Gordon Mitchell

PII: S0034-5288(17)30507-6
DOI: doi: 10.1016/j.rvsc.2017.09.007
Reference: YRVSC 3418

To appear in: *Research in Veterinary Science*

Received date: 5 May 2017
Revised date: 24 August 2017
Accepted date: 3 September 2017

Please cite this article as: Andrei Soutyrine, Hongsheng Huang, Olga Andrievskaia, Ines Walther, Gordon Mitchell , A novel approach for scrapie-associated prion (PrPSc) detection in blood using the competitive affinity of an aggregate-specific antibody and streptavidin to PrPSc. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Yrvsc(2017), doi: 10.1016/j.rvsc.2017.09.007

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ACCEPTED MANUSCRIPT

A Novel Approach for Scrapie-Associated Prion (PrP^{Sc}) Detection in Blood Using the Competitive Affinity of an Aggregate-Specific Antibody and Streptavidin to PrP^{Sc}

Andrei Soutyrine, Hongsheng Huang, Olga Andrievskaia, Ines Walther, Gordon Mitchell

Ottawa Laboratory (Fallowfield), Canadian Food Inspection Agency, Ottawa, Ontario, CANADA

*Corresponding author at: Ottawa Laboratory (Fallowfield), Canadian Food Inspection Agency, 3851 Fallowfield Road, Ottawa, Ontario, K2H 8P9, Canada. Tel.:+1 343 212 0264. E-mail address: andrei.soutyrine@inspection.gc.ca .

Abstract

Scrapie is a fatal neurodegenerative disorder affecting sheep and goats, originating from exposure to disease-associated prions (PrP^{Sc}). An ante-mortem screening test that can detect native PrP^{Sc} in body fluids remains unavailable due to insufficient sensitivity of current detection methods that involve proteinase or denaturation treatments. We adopted an approach to detect PrP^{Sc} in whole blood using a simple proteinase- and denaturation-independent immunoassay, based on the competitive affinity of an aggregate-specific monoclonal antibody and streptavidin to PrP^{Sc}. First, we demonstrated the ability of native PrP^{Sc} to bind to streptavidin and the inhibition of this interaction by 15B3 antibody ($P<0.05$). This led to a new two-step assay that involved capturing native prions from infected blood on a solid-state matrix and detection of PrP^{Sc} aggregates by evaluating the conformation-dependent conjugate catalytic activity ratio in samples against a pre-determined threshold. This test showed capacity for detecting scrapie prions in 500 µL of sheep whole blood spiked with scrapie brain homogenate containing approximately 5 ng of total brain protein, and estimated to have 500 fg of PrP^{Sc}. The test also discriminated between blood samples from scrapie-negative (6 sheep, 4 goats) and scrapie-infected animals (3 experimentally infected sheep, 7 naturally infected goats). Collectively, with the proposed high-throughput sample-processing platform, these initial studies provide insights into the development of a large-scale screening test for the routine diagnosis of scrapie.

Key words: scrapie, prion disease blood test, streptavidin, aggregate-specific antibody, immunoassay.

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