Development of a multi-marker live animal diagnostic specific to TSE disease in blood plasma

Area of research interest: Foodborne pathogens
Study duration: 2007-04-01
Project code: M03062
Conducted by: Institute for Animal Health

Background

The development of TSE diagnostic tests to date has been focused on the detection of PrPSc (the scrapie form of prion protein) as the only established marker of infection. While this single marker approach has been adequate for surveillance testing purposes in post mortem brain tissue, PrPSc may not deliver the specificity and sensitivity required for a blood based pre-clinical assay.

Research Approach

Rather than look for single markers, the research used an established proteomic technology, based on protein expression difference mapping (which has been successful in the diagnosis of other diseases), to establish a panel of protein markers in blood plasma for use as a pre-clinical TSE diagnostic test. To establish a panel of protein markers for TSEs in sheep, a series of blood samples was taken from donor sheep at several time points throughout the course of disease. Biomarkers were established initially in the terminal animals infected with a TSE and then in a time course series. A panel of markers was constructed taking into consideration markers present at the terminal stage and markers which appear at earlier time points thus providing a robust panel which were used to build a mathematical classification model algorithm. Markers were tested and validated in a blind study to assess their sensitivity and specificity.

Results

Many proteins were found which differentiated between TSE disease and normal control animals. A panel of protein markers (11 proteins) at the clinical stage of disease in the scrapie infected samples distinguished between scrapie and normal animals.

In the BSE animals, proteins were found to have some predictive power in distinguishing BSE at 2 months (a panel of 8 proteins), 4 months (panel of 8), 6 months (panel of 7), 8 months (panel of 10), 10-12 months (panel of 11),18-28 months (panel of 9) and the clinical stage of disease (panel of 8).The most predictive sets of markers were found at six months and at the terminal stage of disease. Seven of the proteins from the scrapie panel were also found to differentiate between the diseased and control animals at least one or more of the time points in the BSE-infected sheep.

The panels of proteins at each time point were then tested against additional plasma samples which had not been included in the search for predictive proteins to establish that the proteins found were specifically predictive for BSE and not general signs of disease. Protein markers

found at the clinical stage of disease predicted that toxoplasma samples were non-BSE and that all but two BSE animals which were still alive (12 BSE animals still alive and 3 non-positive animals) as non-BSE. This confirmed that the panel of protein markers found at the clinical point of disease were specific for the detection of BSE.

The researchers attempted to purify some of the proteins which were differentially expressed and formally identify them. Proteins formally identified were plasminogen and fibrinogen as a complex, immunoglobulin lambda light chain, haemoglobin subunit beta and ApoN protein.

Research report

England, Northern Ireland and Wales

PDF
View Development of a multi-marker live animal diagnostic specific to TSE disease in blood plasma research report as PDF(Open in a new window) (2.69 MB)