Quantification of PrPd and correlation with infectivity in scrapie-infected tissues destined for human consumption

Area of research interest: Foodborne pathogens
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Background

A quantitative approach to measure the infectivity levels in edible foods was established in order to underpin a proportionate response for estimating the risk of disease transmission. Establishing infectivity levels in edible tissues and their potential risk is not easily solved as the assumption that misfolded PrP is the sole cause of prion disease is contentious. In addition, the levels of PrPres measured by current diagnostic tests for TSEs do not always correlate with disease.

Research Approach

PrPd levels and properties were investigated in muscle, lymph nodes and peripheral nerve associated with tissues normally destined for human consumption. The hypothesis that muscle spindles are a likely source of infectivity in muscle will be investigated. PrPd will be quantified using methods that were inclusive of forms of PrPd that normally fall outside the standard measurement parameters in diagnostic tests. PK sensitive forms of PrPd were determined in PK titration assays and by binding to PrPd specific ligands (polyanions) and antibodies (anti-YYR) and quantified relative to recombinant ovine PrP. Infectivity was measured in a mouse line transgenic for the ovine PrP gene containing the VRQ allele. The specific outcome was a measurement of PrPd in tissue that correlates with infectivity in a specific bioassay model. These data were used to calculate measurement of infectious load in edible tissues so as to inform on the likely risk when compared with infectivity in relevant species models.

Results

The bioassay response is very dependent on the mouse model chosen for assay (for example, the tg338 model was not suitable for assaying MRI Suffolk sheep prions) and similarly different sources of prions (for example, atypical scrapie prions Vs Suffolk prions) differ in their response to various commercial BSE/scrapie diagnostics tests.

Considering the biological variability of the bioassay and the poorer biochemical sensitivity of rapid tests compared to bioassay, there was a good correlation between the level of prions in brain and the high end-point dilution of this tissue in the biochemical assays. A similar ranking of bioassay titre and tissue end-point dilution value is seen for pre-scapular lymph node, sciatic nerve and ocular muscle although the rate of decline of the biochemical signal at high dilutions

seemed to be faster than for prion titre itself. In practice this could lead to an under-estimation of infectious load solely based on biochemical assay if this effect is not taken into account.

Published Papers

- Everest, S.J., Ramsay, A.M., Chaplin, M.J., Everitt, S., Stack, M.J., Neale, M.H., Jeffrey, M., Moore, S.J., Bellworthy, S.J. & Terry, L.A. (2011) Detection and localisation of PrPSc in the liver of sheep infected with scrapie and bovine spongiform encephalopathy. PLOS One 6(5), e19737
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Research report

England, Northern Ireland and Wales

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