New test detects toxic prions in blood

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The first cases of Mad Cow disease in humans (properly called variant Creutzfeld Jakob Disease, or vCJD) occurred in the late 1990s and are thought to be the consequence of eating contaminated beef products. Since then, several cases of secondary infections caused by transfusions with blood from donors who subsequently developed vCJD have been reported, raising concerns about the safety of blood and blood products. A paper published in *PLOS Pathogens* on June 12th now describes an assay that can detect prions in blood samples from humans with vCJD and in animals at early stages of the (asymptomatic) incubation phase.

To develop the assay, Olivier Andréoletti, from the Ecole Nationale Vétérinaire de Toulouse, France, and colleagues first optimized a method called PMCA (for Protein Misfolding Cyclic Amplification). The method mimics in a test tube the process by which misfolded (toxic) prions propagate, and the researchers determined experimental conditions that enable efficient PMCA amplification of the vCJD agent in the blood.

Having defined such conditions, they show that the assay can detect vCJD in asymptomatic but infected animals in the early phase of the incubation period. They examined blood samples collected from infected sheep and macaques (vCJD-infected macaques are considered the best model of the human disease). In both models, the assay can accurately identify infected animals and detect the presence of vCJD prions in blood from macaques shortly after the initial infection (and several years before clinical disease onset).

Samples from human vCJD patients are rare, and none exist from individuals at preclinical stage of the disease. To test the assay in human blood, the researchers obtained samples from vCJD patients and non-infected controls and analyzed them blindly (i.e. the people who did the assays did not know which samples were which) in two different laboratories. The assay correctly and consistently identified three of the four vCJD affected patients, and yielded no false-positive result in any of the 141 healthy controls. The negative result in one of the vCJD samples raises the question of the potential absence of vCJD agent in the blood of certain patients.

The authors say their "results represent substantial progress towards an applicable vCJD blood detection assay. Such assay could be used to identify vCJD infected but asymptomatic individuals and/or for screening donated blood for the presence of the vCJD agent".

More information: Lacroux C, Comoy E, Moudjou M, Perret-Liaudet A, Lugan S, et al. (2014) Preclinical Detection of Variant CJD and BSE Prions in Blood. *PLoS Pathog* 10(6):e1004202. DOI: 10.1371/journal.ppat.1004202