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'Mad cow' proteins successfully detected in blood

Biochemical technique expected to yield new, more effective test for disease-causing prions in cattle and humans

GALVESTON, Texas -- Researchers at the University of Texas Medical Branch at Galveston (UTMB) have found a way to detect in blood the malformed proteins that cause "mad cow disease," the first time such "prions" have been detected biochemically in blood.

The discovery, reported in an article scheduled to appear online in Nature Medicine Aug. 28, is expected to lead to a much more effective detection method for the infectious proteins responsible for brain-destroying disorders, such as bovine spongiform encephalopathy (BSE) in cattle and variant Creutzfeldt-Jakob disease (vCJD) in humans. The blood test would make it much easier to keep BSE-infected beef out of the human food supply, ensure that blood transfusions and organ transplants do not transmit vCJD, and give researchers their first chance to figure out how many people may be incubating the disease.

"The concentration of infectious prion protein in blood is far too small to be detected by the methods used to detect it in the brain, but we know it's still enough to spread the disease," said UTMB neurology professor Claudio Soto, senior author of the Nature Medicine paper. "The key to our success was developing a technique that would amplify the quantity of this protein more than 10 million-fold, raising it to a detectable level."

Soto and the paper's other authors, UTMB assistant professor of neurology Joaquin Castilla and research assistant Paula Sa• applied a method they call protein misfolding cyclic amplification (PMCA) to blood samples taken from 18 prion-infected hamsters that had developed clinical symptoms of prion disease. PMCA uses sound waves to

vastly accelerate the process that prions use to convert normal proteins to misshapen infectious forms.

Successive rounds of PMCA led to the discovery of prions in the blood of 16 of the 18 infected hamsters. No prions were found in blood samples that were taken from 12 healthy control hamsters and subjected to the same treatment.

"Since the original publication of a paper on our PMCA technology, we've spent four years optimizing and automating this process to get to this point," Soto said. "The next step, which we're currently working on, will be detecting prions in the blood of animals before they develop clinical symptoms and applying the technology to human blood samples."

Tests for infectious prions in cattle and human blood are badly needed. Because current tests require post-slaughter brain tissue for analysis, in the United States only cattle already showing clinical symptoms of BSE (so-called "downer cows") are tested for the disorder. This is true even though vCJD potentially can be transmitted by animals not yet showing symptoms of the disease. (Only two cases of BSE have been found in American cows so far.) And although British BSE cases have been in decline since 1992, scientists believe the British BSE epidemic of the 1980s could have exposed millions of people in the UK and Europe to infectious prions. The extent of the vCJD epidemic is yet unknown. So far the disease has killed around 180 people worldwide, but numbers could reach thousands or even hundreds of thousands in the coming decades. Prions have also been shown to be transmissible through blood transfusions and organ transplants.

"Who knows what the real situation is in cattle in the United States? And with people, we could be sitting on a time bomb, because the incubation period of this disease in humans can be up to 40 years," Soto said. "That's why a blood test is so important. We need to know the extent of the problem, we need to make sure that beef and the human blood supply are safe, and we need early diagnosis so that when scientists develop a therapy we can intervene before clinical symptoms appear--by then, it's too late."

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