MedicalXpress

Study shows infectious prions can arise spontaneously in normal brain tissue

July 26 2010

In a startling new study that involved research on both sides of the Atlantic, scientists from The Scripps Research Institute in Florida and the University College London (UCL) Institute of Neurology in England have shown for the first time that abnormal prions, bits of infectious protein devoid of DNA or RNA that can cause fatal neurodegenerative disease, can suddenly erupt from healthy brain tissue.

The catalyst in the study was the metallic surface of simple steel wires. Previous research showed that prions bind readily to these types of surfaces and can initiate infection with remarkable efficiency. Surprisingly, according to the new research, wires coated with uninfected brain homogenate could also initiate prion disease in cell culture, which was transmissible to mice.

The findings are being published the week of July 26, 2010, in an advance, online edition of the journal Proceedings of the National Academy of Sciences (*PNAS*).

"Prion diseases such as sporadic Creutzfeldt-Jakob disease in humans or atypical bovine spongiform encephalopathy, a form of mad cow disease, occur rarely and at random," said Charles Weissmann, M.D., Ph.D., chair of Scripps Florida's Department of Infectology, who led the study with John Collinge, head of the Department of Neurodegenerative Disease at UCL Institute of Neurology. "It has been proposed that these events reflect rare, spontaneous formation of prions in brain. Our study offers experimental proof that prions can in fact originate spontaneously,

and shows that this event is promoted by contact with steel surfaces."

Infectious prions, which are composed solely of protein, are classified by distinct strains, originally characterized by their incubation time and the disease they cause. These toxic prions have the ability to reproduce, despite the fact that they contain no nucleic acid genome.

Mammalian cells normally produce harmless cellular prion protein (PrPC). Following prion infection, the abnormal or misfolded prion protein (PrPSc) converts PrPC into a likeness of itself, by causing it to change its conformation or shape. The end-stage consists of large aggregates of these misfolded proteins, which cause massive tissue and cell damage.

A Highly Sensitive Test

In the new study, the scientists used the Scrapie Cell Assay, a test originally created by Weissmann that is highly sensitive to minute quantities of prions.

Using the Scrapie Cell Assay to measure infectivity of prion-coated wires, the team observed several unexpected instances of infectious prions in control groups where metal wires had been exposed only to uninfected normal mouse brain tissue. In the current study, this phenomenon was investigated in rigorous and exhaustive control experiments specifically designed to exclude prion contamination. Weissmann and his colleagues in London found that when normal prion protein is coated onto steel wires and brought into contact with cultured cells, a small but significant proportion of the coated wires cause prion infection of the cells - and when transferred to mice, they continue to spawn the disease.

Weissmann noted that an alternative interpretation of the results is that

infectious prions are naturally present in the brain at levels not detectable by conventional methods, and are normally destroyed at the same rate they are created. If that is the case, he noted, metal surfaces could be acting to concentrate the infectious prions to the extent that they became quantifiable by the team's testing methods.

More information: The first author of the study, "Spontaneous Generation of Mammalian Prions," is Julie Edgeworth of the UCL Institute of Neurology.

Provided by The Scripps Research Institute