

Prion propagates in foreign host

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Prions -- infectious, oddly-folded proteins that are the main suspects in fatal neurodegenerative diseases such as Cruetzfeldt-Jakob and bovine spongiform encephalopathy, or "mad cow" -- remain mostly a mystery to scientists. Very few prions have been fully described. How they infect and propagate is not fully understood.

New insights into prion propagation reported in the July 6 issue of *Molecular Cell* by Susan Liebman, distinguished university professor of biological sciences at the University of Illinois at Chicago, may help tug back the veil on the behavior and variety of these potentially lethal molecules.

The work was done with former UIC post-doctoral fellow Vibha Taneja and University of Bordeaux researchers Sven Saupe, Marie-Lise Maddelein and Nicholas Talarek.

Previously, Liebman focused her studies on prion-forming proteins found in baker's yeast, while Saupe's research looked at prion protein in another fungus.

A key difference between the two is that the yeast prion proteins are rich in the amino acids glutamine and asparagine in the regions of the protein used to transform them into a prion. In contrast, the fungal prion lacks a rich supply of these amino acids -- a characteristic it shares with the prion-forming protein in mammals, which is otherwise dissimilar.

The researchers showed, by fusing the prion-forming domain of the

fungal protein to a reporter protein, that the fungal prion could propagate in yeast.

"We showed that the fusion formed a prion in yeast and it was infectious," Liebman said. "It's the first time a prion from one organism has been propagated in another organism that normally lacks that prion. It demonstrates that totally heterologous prion propagation is possible.

"Surprisingly, the presence of a glutamine and asparagine-rich yeast prion that helps other yeast prions to form also helped this one to form," Liebman said, showing that prions of one type can interact with a dissimilar type.

Liebman said the finding suggests the possibility that yeast itself may contain non-glutamine and asparagine-rich prions. "We just haven't looked for them," she said.

The finding also underscores the value of the yeast model for studying factors necessary to propagate prions, now that it's been shown that propagation is not necessarily host-specific.

Liebman said the research emphasizes the need to look for new prions.

"How many more are there" Are there lots that we haven't looked at" How do we look for them" These are open questions."

Source: University of Illinois at Chicago

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