Prions in the brain eliminated by homing molecules

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Toxic prions in the brain can be detected with self-illuminating polymers. The originators, at Linköping University in Sweden, has now shown that the same molecules can also render the prions harmless, and potentially cure fatal nerve-destroying illnesses.

Linköping researchers and their colleagues at the University Hospital in Zürich tested the luminescent conjugated polymers, or LCPs, on tissue sections from the brains of mice that had been infected with prions. The results show that the number of prions, as well as their toxicity and infectibility, decreased drastically. This is the first time anyone has been able to demonstrate the possibility of treating illnesses such as mad cow disease and Creutzfeldt-Jacobs with LCP molecules.

"When we see this effect on prion infections, we believe the same approach could work on Alzheimer's disease as well," says Peter Nilsson, researcher in Bioorganic Chemistry funded by ERC, the European Research Council.

Along with professors Per Hammarström and Adriano Aguzzi and others, he is now publishing the results in The *Journal of Biological Chemistry*.

Prions are diseased forms of normally occurring proteins in the brain. When they clump together in large aggregates, nerve cells in the surrounding area are affected, which leads to serious brain damage and a quick death. Prion illnesses can be inherited, occur spontaneously or

through infection, for example through infected meat – as was the case with mad cow disease.

The course of the illness is relentless when the prions fall to pieces and replicate at an exponential rate. When researchers inserted the LCP molecules into their model system, the replication was arrested, possible through stabilizing the prion aggregates.

The variable components in an LCP are various chemical subgroups attached onto the polymer. In the published study, eight different substances were tested, and all of them had significant effect on the toxicity of the prions.

"Based on these results, we can now customise entirely new molecules with potentially even better effect. These are now being tested on animal models," Nilsson says.

Researchers want to go even further and test whether the molecules will function on fruit flies with an Alzheimer's-like nerve disorder. Alzheimer's is caused by what is known as amyloid plaque, which has a similar but slower course than prion diseases.

More information: Polythiophenes inhibit prion propagation by stabilizing PrP aggregates by I. Margalith, C. Suter, B. Ballmer, P. Schwarz, C. Tiberi, T. Sonati, J. Falsig, S. Nyström, P. Hammarström, A. Åslund, K. P. R. Nilsson, A. Yam, E. Whitters, S. Hornemann and A. Aguzzi. *The Journal of Biological Chemistry*, online early edition 6 April 2012.

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