

Synthetic prion series created for the first time

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At times, to understand something well, it is useful to rebuild it from scratch. It happens with prions as well: in collaboration with the BESTA Institute in Milan, the Laboratory of Prion Biology at SISSA in Trieste assembled artificial prions, devising a method for synthesizing them in a series. Lab tests showed that synthetic prions act like their biological counterparts. Results will be published on Dec. 31, 2015, in one of the most respected journals in the industry, *PLoS Pathogens*.

"They will help us understand the precise mechanisms by which prions cause illnesses like Mad Cow or Creutzfeldt-Jakob disease." SISSA, in collaboration with the Carlo Besta Neurological Institute in Milan, established ideal lab conditions to create synthetic prions which act like biological ones, in a repetitive manner. "It is the first time that something like this has been done, and the consequences for research are significant."

Synthetic prions produced in a series allow precise control over their pathogenic behavior in experiments," explains Giuseppe Legname, coordinator of the study whose lab techniques and results will be published in *Plos Pathogens*. Working with 'natural' prions is not always so simple. "They are complex and heterogeneous," says Legname, noting they are often complicated to use. "The synthetic ones we created ourselves, however, are easier to control, homogeneous and structurally defined. And yet they still show the same consequences as biological ones. Our ultimate goal, of course, is to identify mechanisms which can block the pathogenic effect, in order to develop treatments for disease."



In the study, Legname and colleagues synthesized mouse prions, verifying their role in causing illness, which proved comparable to natural prions. "When we 'characterized' them, we also observed that they were very similar to the ones responsible for Mad Cow and Creutzfeldt-Jakob disease, the human form of the illness."

Not just 'Mad Cow'

"Naturally, our line of research is already evolving. We will be working with human prions, and we have other projects as well," says Legname. He is referring to the hypothesis which is becoming more and more scientifically sound, that at the base of most neurodegenerative disease there are molecules with mechanisms similar to those of prions. "We are thinking about the molecules responsible for Alzheimers, like amyloid beta, or Parkinsons, or even amyotrophic lateral sclerosis. In these cases as well, having synthetic molecules available could be an important step forward."

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