

## NOTA DE PRENSA

# CIC bioGUNE researchers take part in a project to control the prion epidemic affecting deer in the USA

The discovery, made in collaboration with the University of Kentucky (USA), has been published in the prestigious "Science" journal.

(*Bilbao, 13 May 2010*).- Researchers at the Centre for Cooperative Research in Bioscience, CIC bioGUNE, in collaboration with the University of Kentucky (USA), have discovered a new way to control the stability of certain types of prions (the pathogen agents responsible for transmissible spongiform encephalopathies or TSEs) by means of selecting certain proteins. This gives the opportunity to control prion disease in deer, which has become an epidemic in the USA and Canada. The discovery was published last week in the prestigious scientific journal *Science*.

While the most prevalent prion disease in Europe is *scrapie* in sheep and goats and the bovine spongiform encephalopathy, or mad cow disease, which appeared in the 90s, in the USA it is the deer prions that are of most concern to the scientific community. Although there is no statistical evidence that deer prions can infect humans, the disease in wild animals is continuously expanding in numerous states and has already reached some Canadian states.

The chronic wasting disease (CWD) is a transmissible spongiform encephalopathy that affects pet and wild ungulates. Deer prions infect several types of different deer species, the most common being the mule deer and the Canadian deer. The first signs diagnosed date back to 1967 and were found in a mule deer (Odocoileus hemionus hemionus) held in captivity in Colorado (USA).

Epidemiological data suggest that CWD is a self-sustaining disease and it seems that it can be transmitted horizontally in captive populations. Recent studies indicate that the transmission of prions in wild populations may occur through contaminated urine, faeces and saliva.



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Because of the significance of the epidemic, the disease is being researched at the Prion Laboratory at the Proteomics Unit of the CIC bioGUNE, which started its work earlier this year at the Bizkaia Technology Park under the direction of Joaquín Castilla, a researcher hired by the IkerBasque Agency, Agencia Ikerbasque, with the main objective of "furthering knowledge of transmissible spongiform encephalopathies (TSEs)".

#### The role of prion strains

The CIC bioGUNE researchers who were part of an international team coordinated by Professor Glenn Telling from the University of Kentucky studied the role of the various properties of the prion strains in the transmission and spreading of the prion disease in depth.

For this study, transgenic mice susceptible to prion disease in cervids were designed and generated. For the first time, these animals helped identify two biologically distinguishable strains of CWD prions; this has led to the conclusion that the two prion strains are interrelated. Whilst the transgenic mice, designed to replicate Canadian deer prions, showed a stable propagation of each of the prion strains, the transgenic mice designed to replicate prions from mule deer propagated an unstable mixture of CWD strains, preventing their separation on the basis of their biochemical properties.

The significance of this study is due to the fact that it is the first time that a single difference in the primary sequence of amino-acids of the protein responsible for prion diseases (Canadian deer versus mule deer) is shown, allowing the selection of prion strains. This discovery makes it possible to control the stability of some prion strains by modifying the primary structure of the protein responsible. For the first time, the study also shows the existence of at least two types of CWD strains with clearly distinct pathogenic behaviours.

In the last decade much has been achieved in the understanding of prions. In this regard, the epidemic of the bovine spongiform disease in Europe ("mad cow" disease) has sparked an increase in the number of research groups devoted to investigation of this type of infectious agents. Nonetheless, nowadays prions are still mostly unknown entity. According to Castilla, prions are probably "one of the most intriguing pathogenic agents in nature since their alleged composition relates them to only one protein and the emergence of clearly distinct strains gives them incomparable scientific value".



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Their replication mechanism is similar to what happens during the development of diseases such as Alzheimer's or Parkinson's disease, making them a unique pathogen. "But if we add that we still do not know what a prion is, this turns it into an irresistible subject of study for people like those in my group and for myself", concludes Castilla.

One of the great unknowns in the area of prion diseases to which Prof. Castilla's group devote themselves is how a single protein is capable of infecting some species and not other. Although great strides in this direction are being made thanks to new techniques that have recently emerged, there is still a long way to go.