PRESS RELEASE

A new link between Alzheimer's and prion diseases.

- Researchers from CIC bioGUNE and the University of Texas Medical School reveal a new link based on the misfolding of a protein involved in both diseases.

- The study suggests that the protein's misfolding process may be an important risk factor for the development of a second pathology.

(Bilbao, March 2010). Researchers from the Co-operative Research Center, CIC bioGUNE, and from the University of Texas Medical School, Houston (USA), discovered a new link between Alzheimer's and prion pathologies, which is based on the misfolding of a protein involved in both diseases.

The study has been published in the *Journal of Neuroscience.*

The study, carried out by Joaquín Castilla (CIC bioGUNE) and Claudio Soto from the University of Texas Medical School of Houston, is based on the hypothesis that despite the diversity of clinical symptoms associated with diseases involving misfolding of proteins, there are several similarities that suggest that lots of those diseases can be connected at a molecular mechanism level.

The main goal of this study was to analyse the interaction of the protein misfolding processes involved in Alzheimer's and prion diseases.
For this purpose, prions have been inoculated in a transgenic mouse used as an Alzheimer's model that develops amyloid plaques.

"*Our findings show a dramatic acceleration and exacerbation of both pathologies. The onset of prion disease symptoms in transgenic mice appeared significantly faster with a concomitant increase on the level of misfolded prion protein in the brain. We also observed a striking increase in amyloid plaque deposition that is characteristic of Alzheimer's disease*", said Joaquín Castilla, responsible for the Prion Laboratory of the Proteomics Unit of CIC bioGUNE.

Histological and biochemical studies showed the physical association of the two misfolded proteins in the brain, and in vitro experiments showed that protein misfolding

can be enhanced by a cross-seeding mechanism (i.e., the prion protein accelerates the misfolding of the protein developing Alzheimer's plaques).

As a conclusion, the results suggest that there is a profound interaction between Alzheimer's and prion pathologies, meaning that the protein misfolding process may be an important risk factor for the development of a second pathology.

"*This study may have important implications to understand the origin and progression of diseases related to protein misfolding disorders*", concludes Castilla.

The techniques used are applied to both pathologies, prion diseases and Alzheimer's disease, as the inoculation of animal models and the histopathological and immunohistochemical studies, which are biochemical techniques and in vitro protein misfolding studies.

- **Prion diseases**

Prions are pathogens that cause the TSDs, which are also called prion diseases. TSD diseases belong to a group of fatal neurodegenerative diseases that affect human beings and animals, for which there is no therapy available so far. These diseases can have various origins: hereditary, sporadic (supposedly spontaneous) and infectious.

Scrapie, the disease that affects sheep and goats, is probably the oldest prion disease. Nonetheless, it is the BSD (Bovine Spongiform Disease) the disease that caught most public attention, due to its implication in the generation of a new disease in humans and its proved transmission to most of other species. There is another disease, Creutzfeldt Jacob's one, that causes 1-2 cases per year in a million inhabitants and is still unknown to a great extent, specially in its sporadic version, where the origin remains a mystery. In the Basque Country, there is an uncommon situation. A high percentage of all the fatal familial insomnia cases in the world, which is a genetic prion disease that affects humans, is located in the Basque Country.

According to Castilla, prions are probably "*one of the most intriguing pathogens of nature, since their supposed composition is linked to only one protein and the appearance of clearly differential strains makes them of incomparable scientific value*". Their replication mechanism, which is similar to the development of such diseases as Alzheimer's or Parkinson, makes them a unique pathogen. "*Additionally, we still do not know what a prion is, so they are an irresistible subject of study for such people as the researchers of our group and for myself too*", concludes Castilla.