Scientists discover a novel methodology for the detection of amyloid fibers, structures associated to neurodegenerative diseases

The research, publishedin the Proceedings of the National Academy of Sciences of the USA, opens the door toward new diagnostic methods for Alzheimer's, Parkinson's or prionic diseases

The technique is based on the link of gold nanoparticles to the fibers and observation of an optical signal characteristic of their organization into a helicoidal structure

It allows a simple detection of very small amounts of fibers at early stages of their formation

(Donostia-San Sebastián, march 12, 2018). A team of researchers, with participation of CIC biomaGUNE, CIC bioGUNE, University of Antwerp, University of Extremadura and University of Vigo, has developed a new method for the detection of amyloid fibers from proteins that are usually implicated in Parkinson's disease and other neurodegenerative diseases such as Alzheimer's or those from prions.

Amyloid fibers are structures based on misfolded proteins which get organized into a helicoidal fiber. The misfolded proteins comprising these fibers are characterized by a strong union to each other, creating structures that are extraordinarily resistant to elimination. This type of structuras are observed in the encephalon of people affected by various neurodegenerative diseases such as Alzheimer's, Parkinson's or prionic diseases (mad cow, etc.), in which neuronal death occurs because of the presence of such fibers. One of the features that these diseases share is the propagation of a specific protein that does not fold properly and accumulates in the form of the amyloid fibers.

The results of this work, which has been published by the Proceedings of the National Academy of Sciences of the USA, open the door to new diagnostic methods for these neurodegenerative diseases. "Although the damage is made in the brain, it is believed that the fibers also form in other parts of the body and therefore we can think of an analysis system that helps complementing existing tests. Furthermore, from a more fundamental perspective, this technique allows us to carry out kinetic studies, i.e. investigating the rate of formation of the fibers under different conditions and, perhaps, understanding which

are the parameters that can accelerate the process or even those that can stop it", explains Luis Liz-Marzán, scientific director of CIC biomaGUNE, where he also works as a researcher of the Ikerbasque program, and coordinator of the work entitled *"Detection of Amyloid Fibrils in Parkinson´s Disease Using Plasmonic Chirality"*.

A multidisciplinary project

This project that now sees the light was initiated in January 2017, thanks to the funding of a Marie Slodowska Curie grant by the European Union, which allowed the incorporation of Dr. Jatish Kumar to Liz-Marzán's group in CIC biomaGUNE. This incorporation was key to kick off a multidisciplinary project where several groups from the Basque Country and elsewhere have participated. The team that carried out the research was composed by Jatish Kumar as the main researcher and Luis Liz-Marzán as coordinator and director of the work. Next to them also participated Elena López and Aitziber Cortajarena (CIC biomaGUNE) in the preparation of proteins and amyloid fibers; Hasier Eraña and Joaquín Castilla (CIC bioGUNE) in the preparation of prion and brain samples; Nathalie Claes and Sara Bals (University of Antwerp) in electron microscopy and tomography; and Víctor Martín (University of Extremadura) and Diego Solís (University of Vigo) in computational modeling.

"Given the multidisciplinar character of the research, it has been necessary to find a common language between the different teams of chemists, biochemists, biologists and physicists, so that the collaboration could work. It was also essential to design the appropriate nanoparticles to ensure an efficient link to fibers with specific dimensions, while providing a sufficiently intense signal. On the other hand, access to clinical samples provided the work with a dimension that was much closer to the real application", explains Liz-Marzán, when mentioning the difficulties that had to be overcome to ensure the success of the research.

The complexity of the project required the use of specific instrumentation at the various groups involved. Thus, they used techniques for production and purification of proteins, high resolution electron microscopy, optical spectroscopy and circular dichroism, apart from advanced computational tools.