CIC biomaGUNE research enables the attachment of proteins to nanoparticles in the blood to be studied

The research, published in Nature Communications, sheds light on the behaviour of nanoparticles on coming into contact with the human body

When nanoparticles are introduced into the body, proteins present in the blood spontaneously form a surface coating on the nanoparticles referred to as the "protein corona"

Nanomaterial surface design may be key in biomedical applications for the treatment of various diseases such as cancer

The findings of the team led by CIC biomaGUNE researchers Wolfgang J. Parak and Mónica Carril (an Ikerbasque researcher) pave the way for analysis of the protein corona in vivo using magnetic resonance technology

(Donostia-San Sebastián, 12 December 2017). A CIC biomaGUNE research team has determined a new application of magnetic resonance for the study of the protein corona through nanoparticle size change. Study of the protein corona, a spontaneous surface coating of nanoparticles, which inevitably forms when nanoparticles come into contact with the proteins naturally found in abundance in blood, is key in the field of nanomaterial design for biomedical applications.

This research has made it possible to study the protein corona in real blood samples and opens up the potential for measuring it directly in a living organism using a magnetic resonance imaging (MRI) scanner.

Mónica Carril, Ikerbasque researcher in CIC biomaGUNE, explains: "Our team has studied the protein corona in blood and in the presence of cells. To do so, we have used fluorine-labelled nanoparticles. The signal from the nucleus of fluorine enables the

diffusion coefficient of the nanoparticles to be measured free from interference using magnetic resonance".

The research, published in the journal Nature Communications, not only allows protein corona to be studied in real blood samples but also opens up the potential for measuring it directly in a living organism using MRI. This is already under investigation in CIC biomaGUNE.

Use of nanoparticles in the diagnosis and treatment of various pathologies

The field of nanomedicine is growing significantly. In recent years, a multitude of potential applications of different nanomaterials in the diagnosis and treatment of various pathologies has arisen.

However, an in-depth knowledge of what really goes on when nanoparticles come into contact with the human body is highly important before nanomedicine can be considered a viable alternative in the clinical field. An important part of the explanation of the behaviour of nanoparticles for biomedical applications lies in their surface design, as this is often modified with biomolecules with a therapeutic function or to direct the nanomaterial towards a specific type of tissue such as tumours. Mónica Carril explains further: "It is important to study the protein corona as it could be masking the surface properties of the nanomaterials designed by us, potentially changing their stability or excretory pathway".

Measurement of the increase in radius caused by the protein corona

The attachment of proteins to the surface of nanoparticles produces a logical increase in the size of those nanoparticles, which is what has been measured. "Using magnetic resonance, we have observed how nanoparticles diffuse in fluids. The size of nanoparticles has a direct impact on how they diffuse: the larger they are, the slower they move and the less area they cover. Many of the techniques currently in use for studying the protein corona are based on the same principle. However, one of the prerequisites of those techniques is that the fluid in which the nanoparticles diffuse must be clean to avoid interferences. The particularity of our research lies in the fact that we have based our measurements on the signal obtained from the fluorine nucleus used to decorate our nanoparticles, thereby eliminating all concerns regarding interference due to the absence of fluorinated molecules in the physiological media", Mónica Carril adds.

Laboratory models used up to now are mere approximations of what really goes on inside the body. In this sense, to obtain a technique enabling the formation of the protein corona to be studied in real time inside the human body would represent significant progress. The fluorine-based MRI technique could make this possible, and Mónica Carril's group in CIC biomaGUNE is working on the practical demonstration of this solution.

Apart from Mónica Carril, other participants in the study include Daniel Padro, Pablo del Pino, Carolina Carrillo-Carrión, Marta Gallego and Wolfgang J. Parak. The study has mainly been conducted in CIC biomaGUNE.

The research project has been ongoing for over two and a half years and has had to overcome several difficulties. “As a chemist, the most important challenge has been to find suitable fluorinated nanoparticles. We needed nanoparticles with a high fluorine content to obtain a good signal. You have to bear in mind that one of the characteristics of fluorine is its hydrophobicity, or tendency to repel water. We also needed the nanoparticles to be soluble in water to be able to study the protein corona in physiological media. The most difficult thing was to find that balance between a suitable fluorine signal and solubility in water”, Mónica Carril concludes.

About CIC biomaGUNE

The Centre for Cooperative Research in Biomaterials (CIC biomaGUNE), located in the Donostia-San Sebastián Technology Park, conducts cutting-edge research at the interface between Chemistry, Biology and Physics, and particularly on the properties of molecular level biological nanostructures and their biomedical applications.