CIC biomaGUNE explores the insides of tumours grown in smart three-dimensional scaffolds

The 4DbioSERS project, funded by the ERC to the sum of €2.4 million, aims to respond to numerous as yet unanswered questions about cancer

The goal is to find a way to monitor cells in real time and record the release of tumour metabolites and other indicators under different conditions

San Sebastián, 4 February 2021. The Biomaterials Research Centre, CIC biomaGUNE, is currently working on a number of different projects that seek to understand, diagnose and treat different types of cancer. In the context of World Cancer Day, CIC biomaGUNE seeks to explain to the public how it works on a daily basis to fight against this disease, which continues to pose so many as yet unanswered questions.

The CIC biomaGUNE BioNanoPlasmonics research team, led by Ikerbasque Professor Luis Liz Marzán (one of the most influential scientists in the world, according to Clarivate Analytics' Highly Cited Researchers list), has spent the last two years immersed in the 4DbioSERS project, which aims to study cancer, particularly melanoma and breast cancer, in order to gain greater insight into tumour growth and dynamics. The project has been awarded funding by the European Research Council (ERC) to the sum of €2.4 million, within the prestigious ERC Advanced Grant programme.

'We have managed to grow three-dimensional tumours in scaffolds containing plasmonic nanoparticles, which we can use to monitor the metabolites secreted by a cell, as well as other indicators such as temperature and pH at different time points. This in turn enables us to see how cells move around inside the tumour, in order to help us understand what happens in that environment over time,' explain Malou Henriksen and Dorleta Jimenez de Aberasturi, two members of the research team. Henriksen has a PhD in biology and is responsible for growing the cells with which the tumour models are constructed: 'it is important to start growing tumours in three-dimensions, because in reality, cells do not behave as they do in 2D cultures'. The study has already obtained several different cellular compositions: 'a mix of tumour cells, other kinds of cell and other components, such as the extracellular matrix, among others,' adds Henriksen.

For her part, Jimenez de Aberasturi is an Ikerbasque Fellow and a specialist in the production of plasmonic nanoparticles: 'we coat these nanoparticles to make them biocompatible, and then we functionalise them so we can use them as sensors and contrast agents. We use Surface Enhanced Raman Scattering or SERS to understand what is going on inside the tumours without touching them. Our aim is to understand what happens inside a tumour and how it evolves; the cells are alive and move around (in metastases also)'.

Satisfaction and future prospects

The two researchers express their satisfaction with the results obtained so far by this multidisciplinary team: 'we have achieved many of our initial goals and are well on the way to successfully finishing the project'. To date, using a 3D bioprinter capable of inserting plasmonic nanoparticles, they have managed to build the scaffolds that serve both as a support and a means of detection. As well as growing tumours in these scaffolds, through the co-culture of different cell types they have also managed to 'use different plasmonic particles to measure different metabolites (such as, for example, those secreted by cells when they die), as well as the temperature and pH in different parts of the tumour,' explains Henriksen.

The two researchers are also hopeful about the future: 'we hope to measure more, because tumours are highly complex systems that evolve over time. We have managed to measure different elements at a specific moment, but we now need to include the time variable,' clarifies Jimenez de Aberasturi. 'For example, we want to use imaging techniques to monitor the evolution of a cell and measure its metabolites over time.' There are many unanswered questions in the field of cancer research. 'If we manage to gain a greater understanding of these cellular models, we will be able to find some of these answers. For example, we still do not understand why, in metastases, some cells abandon the tumour while others do not, or what exactly it is that these cells secrete when the metastasis breaks away,' adds Henriksen.

The 4DbioSERS project opens up a multitude of opportunities for future cancer research, since the team plans to conduct pharmacological trials and even apply photothermal therapies to tumours in order to advance current knowledge in this field. The BioNanoPlasmonics group is carrying out cutting-edge research in this area and its facilities are equipped with state-of-the-art technology. Thanks to the combination of human experience in biomaterials, imaging and nanoplasmonics, and the technology available at CIC biomaGUNE, the team is a world leader in the study of cancer.

In addition to the 4DbioSERS project, CIC biomaGUNE is also involved in several other initiatives in collaboration with other research centres. The research team led by Aitziber L. Cortajarena has developed a new formulation of immunostimulant-decorated nanoparticles which fosters the basal activity of immune system cells (T lymphocytes and NK cells) to fight against cancer cells. The project has received funding from the AECC (Spanish Agency for the Fight against Cancer) and the Basque Government Health Department, in collaboration with IIS Biocruces. There is one study aimed at developing a simple, cheap and fast method of detecting lung cancer, and another oriented towards developing cancer therapies using boron neutron capture (BNTC). The centre also heads up a European project aimed at developing oxygen nanocarriers and photosensitising agents for the treatment of cancer through photodynamic therapy. Finally, *Asparia Glycomics*, a spin-off launched by CIC biomaGUNE, is focused on developing its own technology for the diagnosis and prognosis of cancer and other autoimmune diseases.

About CIC biomaGUNE

The Biomaterials Research Centre, CIC biomaGUNE, is a member of the Basque Research and Technology Alliance (BRTA) and carries out cutting-edge research on the interface between Chemistry, Biology and Physics, with special focus on the study of the properties of biological nanostructures at a molecular scale, and their biomedical applications. In 2018 it was officially designated a 'María de Maeztu' Unit of Excellence for complying with certain requisites denoting

outstanding quality in the field of research at a worldwide level, coupled with a high level of impact and a high degree of competitiveness.

Photo 1: 3D co-culture of breast cancer epithelial cells and fibroblasts (Beatriz Molina Martinez / CIC biomaGUNE).

Photo 2: Scaffold with attached epithelial cancer cells (Beatriz Molina Martinez / CIC biomaGUNE).

Photo 3: One of the researchers from the BioNanoPlasmonics team at CIC biomaGUNE, working the lab.