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## Nanomedicine

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### Isolation of glioblastoma cancer stem cells by sedimentation field flow fractionation for the development of 3D models in supramolecular hydrogels

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3D culture has revolutionized cell biology research and opened the door to new discoveries in terms of cell behavior and realistic response to chemotherapeutics. When cancer cells are grown in a hydrogel mimicking the physiological extracellular matrix, they develop into multicellular tumor spheroids (MCTS) representative of solid tumors like Glioblastoma. The 3D cancer culture combined with a complex microenvironment provides a platform to study tumor development but also to evaluate the toxicity of physicochemical entities such as nanoparticles. One of the main challenges of 3D culture and nanotoxicity studies is the reproducibility of the spheroids, therefore the repeatability of the response after treatment. In order to overcome this limitation, it is necessary to control both the nature of the gels and that of the implanted cell populations.

In this work we will present the use of bola-amphiphilic molecules, low molecular weight gelators of the glycosyl-nucleo-bola-amphiphilic-bis-amide type. They have a sol-gel transition temperature

suitable for cell culture, and at concentrations of 0.25% in the culture medium, form fibrillar networks with a viscoelasticity compatible (0.4 -1.0 kPa) with the cell culture of cells from GBM.

As far as the cell population is concerned, we have routinely produced homogeneous populations enriched in cancer stem cells (CSC) from the U87-MG line (human glioblastoma). CSCs are a key point and a rare cell type of the tumor niche. They contribute to aggressiveness, therapeutic resistance, metastasis and tumor recurrence. The study of CSCs is of major importance in the design of cancer eradication strategies. The development of a technique to isolate and characterize them is crucial to contribute to the development of diagnostic, prognostic and theranostic tools. It will also provide a solid basis for the development of targeted therapies against CSCs. Then, CSCs are of major interest for three-dimensional cell culture. It is in this sense that we use CSC subpopulations sorted by the Sedimentation Field Flow Fractionation (SdFFF) technique, to routinely generate reproducible spheroids, future study support for the action of nanoparticles for therapeutic purposes.