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How droplet-based microfluidics can play a key role in cancer treatment research?

Droplet-based microfluidics can be used to create multicellular tumor spheroids (MCTSs), that are a very powerful tool to mimic in vivo solid tumors. MCTSs can simply be described as aggregates of cancer cells, thus forming a three-dimensional (3D) tumor model.[1] Among all the different generation methods, droplet-based microfluidics enables a rapid and efficient generation of spheroids, a good control of spheroid size and the automatization of the procedure. An aqueous phase containing the cells and an oil phase are mixed together to generate droplets enclosing single tumor cells in suspension (Figure 1). The generated droplets are collected from the microfluidic device and incubated in a cell incubation system.[2] Upon cell culture, these cells in suspension aggregate, undergo tight interactions and form a compact spherical structure: a spheroid.[3] A single MCTS has been formed inside almost each droplet. In order to generate stable droplets with a good cell encapsulation, the use of a surfactant like FluoSurf™ is highly recommended.

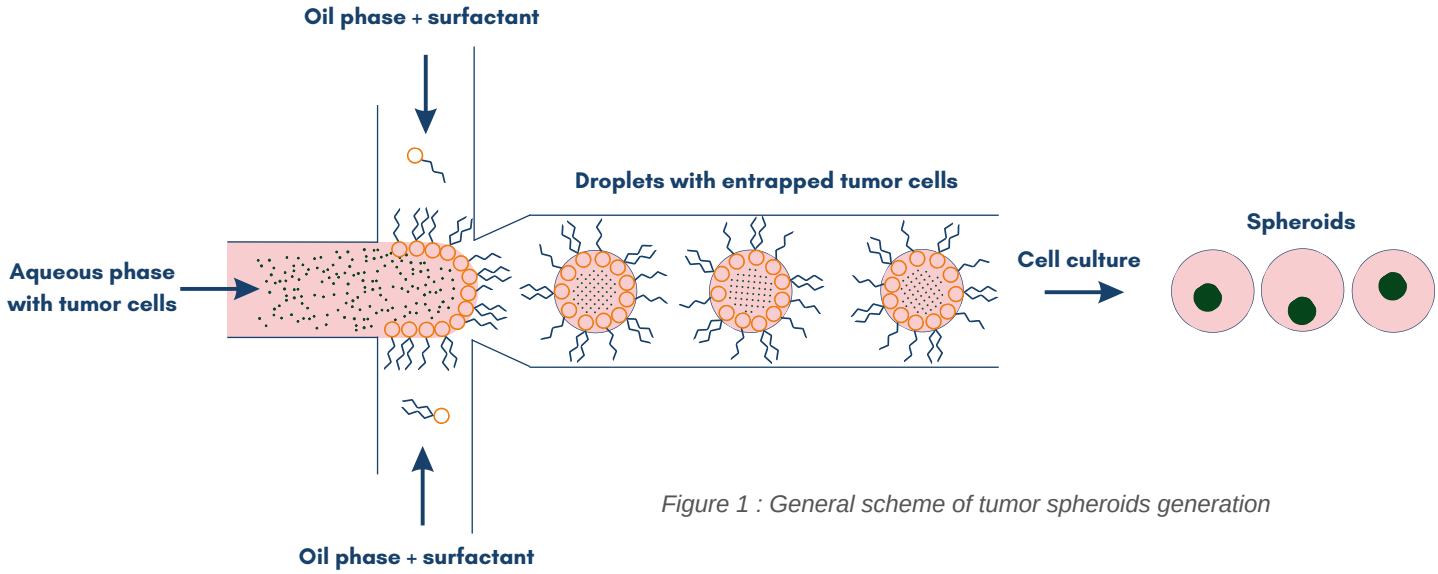

Figure 1 : General scheme of tumor spheroids generation

Because tumor cells are tightly packed within the spheroids, they present strong cell-cell interactions. However, two-dimensional (2D) models like monolayer cell cultures are not able to recreate these interactions with precision. Therefore, they lead to the overestimation of drug efficiencies and do not allow the prediction of drug behavior in vivo.[4] 3D models that are MCTSs are gradually replacing 2D models, as they allow to better mimic cell-cell interactions and thus to closely mimic in vivo solid tumors' main features. MCTSs are an intermediate step which comes between 2D monolayer models and in vivo solid tumors. Therefore, MCTSs are an essential tool for cancer treatment research.

Spheroids are mainly applied to the study and characterization of anticancer treatments. Their use opens new ways to tumors drug screening for chemotherapy, a drug treatment using chemicals to destroy cancer cells. Droplets are used as micro-reactors in which different reagents are added at determinate times. Dose-response curves to chemotherapy give insights on the effect of the reagent, or chemotherapeutic compound, on the spheroids.[3] It allows the screening of different drug concentrations, of a wide range of drug combinations and of the reagents' cytotoxicity. These in vitro studies are performed before in vivo ones.

The next step in drug development implies in vivo studies on laboratory animals. By a better selection of drug candidates, spheroids help in reducing the number of animals used for preclinical studies.[4] In the future, these in vitro experiments could even replace in vivo ones and avoid the use of laboratory animals.

Spheroids generated by droplet-based microfluidics can also be utilized in photothermal therapy. Photothermal therapy is a technique that kills the tumor cells by converting light into heat energy. Tumor spheroids are treated with a photothermal agent and then irradiated with a near-infrared laser. After irradiation, the cells viability within tumor spheroids is assessed. To determine whether cells are living or dead after irradiation, all the cells are stained with dyes and the results are examined using fluorescence analysis. The decrease of the viability of cancer cells demonstrates that the effect of photothermal therapy is to induce the cells death within tumor spheroids.[5]

In order to accurately mimic cancer tumors, 3D models like MCTSs play a critical role. Creating these tumor spheroids is crucial for anticancer treatment research, as they enable the characterization of various anticancer treatments. Droplet-based microfluidics allows a high-throughput generation of uniform spheroids that can be automated, and thus address the limitations of conventional methods for the generation of tumor spheroids.

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