

In depth-spheroid phenotypic characterizations: effects of 5-Fluorouracil on cohesion

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MultiCellular Tumor Spheroids (MCTS), which mimic the 3-Dimensional (3D) organization of a tumor, are considered as better models than conventional cultures in 2-Dimensions (2D) to study cancer cell biology and to evaluate the response to chemotherapeutic drugs. A real time and quantitative follow-up of MCTS with simple and robust readouts to evaluate drug efficacy is still missing. Here, we evaluate the chemotherapeutic drug 5-Fluorouracil (5-FU) response on the growth and integrity of MCTS two days after treatment of MCTS and for three colorectal carcinoma cell lines with different cohesive properties (HT29, HCT116 and SW480). We found different sensitivity to 5-FU for the three CRC cell lines, ranging from high (SW480), intermediate (HCT116) and low (HT29) and the same hierarchy of CRC cell lines sensitivity is conserved in 2D. We also evidence that 5-FU has a strong impact on spheroid cohesion, with the apparition of a number of single detaching cells from the spheroid in a 5-FU dose- and cell line-dependent manner. We propose an innovative methodology for the chemosensitivity evaluation in 3D MCTS that recapitulates and regionalizes the 5-FU-induced changes within MCTS over time. These robust phenotypic read-outs could be easily scalable for high-throughput drug screening that may include different types of cancer cells to take into account tumor heterogeneity and resistance to treatment.