P72 Radium-223 in metastatic prostate cancer: comparison of 2D and 3D cultures

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Introduction & Objectives: Nowadays, castration resistant prostate cancer is a stage of the disease that still presents a high mortality rate, although there are some therapy options to manage it, raising survival and providing more life quality to the patients. One of these options is the Radium-223, an alpha particle emitter radiopharmaceutical that has a positive effect on the increasing of overall survival of patients, while also lowering the risk of symptomatic skeletal events.
The main objectives of this experimental work were to optimize and characterize a three-dimensional cell culture model in a prostate cancer cell line, and then assess the effects of the Radium-223 on the model.

Materials & Methods: In the first phase of the work, it was used the magnetic levitation method in order to form three-dimensional spheroids of PC3, using histochemical staining to study spheroid structure and viability, immunocytochemistry for protein expression and flow cytometry to learn about the culture's viability and cell death pathways. The effects of the Radium-223 irradiation were then studied by the SRB assay, to evaluate total protein content, and by Alamar Blue, to study cell proliferation.

Results: The PC3 3D structures displayed a spherical conformation and presented extensive necrotic and apoptotic zones, since the size of the spheroid was in the order of mm^2. Besides, the spheroids also exhibited different expression in some key proteins when compared with control cells cultured in monolayer, an important fact when testing cancer therapeutics.
After the irradiation of the spheroids with Radium-223, all doses tested presented a decrease compared to the control whether it was in total protein content or cell proliferation. The results also showed that the Radium-223 treatment exhibited a lower efficacy in the spheroids when compared with monolayer cells, which can be due to the fact that the three-dimensional structures are closer to mimicking the in vivo scenario, and so the cytotoxicity of the Radium-223 is decreased. Also, as alpha particles have low penetration ranges and the spheroid has a large size, the radiopharmaceutical might not be properly entering the three-dimensional structure.

Conclusions: Thereby, with this work it was possible to conclude that, as expected, the Radium-223 acts differently when tested in monolayer and in three dimensional cultures, as shown by the primary results obtained. Thus, it is very important to evaluate this and, in the future, other drugs or radiopharmaceuticals, using in vitro three-dimensional spheroids before passing to in vivo studies, as they can function as a bridge between the two and give more information than standard two-dimensional cell culture.
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