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3D Engineered Models in Plasma Oncology: Investigating the Efficiency of Plasma-Activated Ringer's Saline in Osteosarcoma

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The use of Cold Atmospheric Plasma in oncology is an emerging field due to its huge potential as novel anti-cancer therapy [1]. However, the beneficial effects of plasma and of plasma-treated liquids for treating cancer have mostly been demonstrated in 2-dimensional cultures of cells [1, 2], which do not mimic the complexity of the 3-dimensional (3D) tumor microenvironment.

In this work we will focus in a kind of cancer of pediatric prevalence, Osteosarcoma (OS). OS is the most common bone malignant neoplasm. Although chemotherapy has improved long-term survival over the past few decades, the outcome for patients with metastatic or recurrent OS remains dismally poor.

The aim of this study is to obtain mechanistic insights on the action of plasma-activated Ringer's saline (PAR) in relevant 3D models of OS. Thus, in order to evaluate its effects in a relevant context, we have investigated two strategies: 1st. Ex-vivo studies employing organotypic cultures of murine OS, and 2nd. Development of a 3D tissue-engineered model of osteosarcoma using a composite bone-like scaffold produced from an organic matrix and inorganic nanoparticles.

Both models confirmed the time-dependant cytotoxicity observed in 2D. Histological analysis in the murine model showed a decrease in proliferating cells (lower Ki-67 expression), being the differential intracellular reactive oxygen species increase and DNA damage between OS cells and hBM-MSCs key mediators for cell apoptosis [3]. The 3D tissue-engineered model of human OS exhibits excellent osteomimicry. Significantly different functional behaviors have been observed between monolayer and the engineered tumor when treated with PAR. Our data reveal that the 3D environment protects cells from PAR-induced lethality by scavenging and diminishing the amount of reactive oxygen and nitrogen species generated by CAP. We have been able to investigate the stemness phenotype of OS cells under PAR treatment and it will be discussed in the talk.

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