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Merging cold plasmas and biomaterials for osteosarcoma therapy

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Biomaterials are employed for tissue and organs regeneration or functional repair, including delivery of therapeutics. In bone regeneration and repair, incorporation of drugs to biomaterials has been investigated as a means of providing additional functionalities to the material, and plasma processes contributed to bone biomaterials ie. through polymerisation processes to modulate the drug release[1]. With the evolution of plasma devices, great advances have been made in therapies based in cold atmospheric plasmas (CAP) [2,3]. Production of reactive oxygen and nitrogen species (RONS) in liquids (water, saline solutions, cell culture media) resulting from treatment by cold atmospheric plasma has been focus of interest in the last years [4]. Plasma chemistry leads to the generation of an abundance of reactive species such as H_2O_2, NO_2^-, NO_3^-, O_3^-, $ONOO^-$, etc [2,4,5] which are suspected to play a key role in selective cancer cell death without damaging surrounding healthy tissues. Such effects of plasmas in liquids open the door for minimally invasive therapies that we aim at investigating for osteosarcoma, and expand from liquids to biomaterials which allow a sustained release of the plasma-generated RONS to the diseased site. In fact, the development of efficient vehicles which allow local confinement and delivery of RONS to the diseased site is a fundamental requirement. In this sense, biocompatible polymers with ability to form 3D networks can be an alternative to deliver the plasma-generated RONS locally. We discuss the use of different hydrogels [6,7] for plasma treatment and their outcomes, as compared to Plasma Conditioned Liquids (PCM) [8,9]; in general, their physic-chemical properties remain unchanged by the plasma treatment. Their capacity to generate RONS during plasma jet treatment is highly dependent on the chemistry of the polymer solution, but often several-fold higher concentrations can be obtained than in a typical isotonic saline solution. The hydrogels show capacity for sustained release of the RONS. The biological effects of the treated hydrogels in osteosarcoma are discussed with regard to the different reactive species generated in the PAM (ie. [H_2O_2], [NO_2^-], short-lived RONS). Lastly, we discuss the implications of using 3D models to evaluate the effects of PCM, by comparing both mouse OS tumour sections in organotypic culture [10], as well as in a tumor model generated from a composite scaffold.

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Short Bio: Cristina Canal is Associate professor at the Department of Materials Science and Engineering, at the Technical University of Catalonia (UPC), within the Biomaterials, Biomechanics and Tissue Engineering Group. She serves as Resarch Deputy Director of the Center for Research in Biomedical Engineering (CREB). She has participated and led a number of research projects, as well as technology transfer projects in the areas of Textile materials, Biomaterials and Cold Plasmas. She published more than 60 publications, and has given several invited talks in conferences. Her research has been recognized with different awards, including the L'Oreal-Unesco fellowship "For Young Women in Science" (2012) and the "2018 Early Career Award in Plasma Medicine". Her interests are focused in cold plasmas for biomedical applications, particularly: i. surface modification of biomaterials to control parameters such as adhesion or biological behaviour; ii. Control of drug release from biomaterials; and iii. Therapeutical appications of cold plasmas, for instance, in bone cancers. She is currently leader of a European Research Council Starting Grant project in the field of Plasma Medicine, her main axis of research being currently focused in the atmospheric pressure plasma therapy of bone cancer treatment in combination with biomaterials.

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