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Dual chemotherapy and photodynamic therapy: A synergistic strategy to improve cancer treatment

Ana Lazaro Carrillo[1], **Bruno M Simões**[2], **Robert B Clarke**[2] and **Angeles Villanueva**[1,3]
[1]Autonomous University of Madrid, Spain
[2]Manchester Cancer Research Centre - University of Manchester, UK
[3]IMDEA Nanoscience Institute, Spain

Nowadays different strategies are being introduced in order to enhance photodynamic therapy (PDT) effectiveness, such as combination of PDT with chemotherapy or improvement of photosensitizer (PS) features. A new combined PDT-chemotherapy treatment comprising two drugs widespread in clinical research - the hydrophobic zinc(II)-phthalocyanine (ZnPc) as PS and the common chemotherapeutic agent doxorubicin (DOX) - were tested. Cytotoxicity assay showed that this combination remarkably increases the effectiveness of the treatment by inducing a synergistic cell death effect (lower than 10%) when compared to DOX or ZnPc monotherapy (cell surviving around 80%). In addition, annexin-V detection by flow cytometry, analysis of active caspase-3 and cytochrome c by immunofluorescence and time-lapse videomicroscopy corroborated a fine-tunable effect depending on light dose, leading to apoptotic or necrotic mechanism of cell death. Using DCFH-DA (dichlorodihydrofluorescein diacetate) probe, we demonstrate that a significant higher reactive oxygen species generation into cells was the main cause of the synergistic effect of this combined treatment. Further, mammosphere formation efficiency assay showed a reduced breast cancer stem cell activity in established cell line and primary cells obtained from patients, even using DOX at much lower concentration than clinical level. Finally, studies in human breast cancer xenografts indicated a high efficiency also *in vivo*. All these results provide novel and valuable information that contribute to consider chemophototherapy as a promising tool in current antitumoral treatments, potentially overcoming resistance to cancer chemotherapy and targeting cancer stem cells.

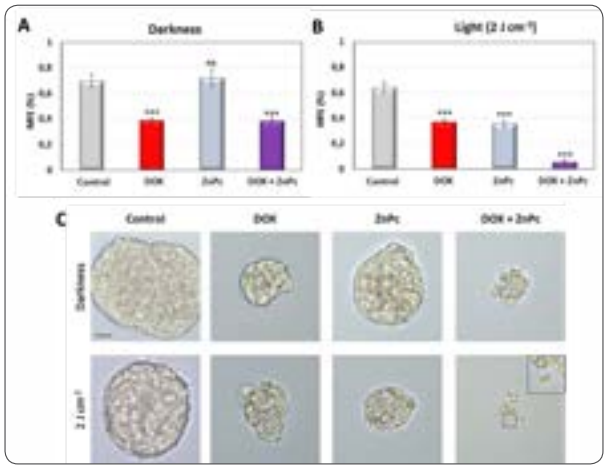

Figure 1: Effect in cancer stem cells (CSCs) in MCF-7 cell line. Evaluation of mammosphere formation efficiency in control cells or after the different treatments under **(A)** dark condition or **(B)** irradiated with a light dose of 2 J cm-2. **(C)** Morphology of the mammospheres formed after the different treatments in dark and light condition

Biography

Ana Lazaro Carrillo has completed her PhD from Autonomous University of Madrid (Spain) with mention of best thesis in 2017 granted by SEBC (Spanish Society of Cell Biology). She is a Teaching Assistant in the Department of Biology, a premier research organization. She has participated in more than 30 international congresses and more than 70 meetings, workshops and courses. She has published 7 papers in journals of high recognition and has been serving as Reviewer of repute journals. In addition, she has participated in research and dissemination activities related to Multifun project, funded by the European Union and has been a Research Member of two projects funded by Spanish Ministry for Economy and Competitiveness. Her research interest include: cell biology; photodynamic therapy and chemotherapy for cancer treatment; internalization, biocompatibility and efficient delivery of nanostructures *in vitro* (cell cultures); cell death mechanisms and cellular inactivation; activity of cancer stem cells (established cell lines and patient samples).

ana.lazaro@uam.es