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Advanced hybrid theranostic nanoplatforms for an active drug delivery in the cancer treatment

PLATINUM CONJUGATED TO NOVEL GRAPHENE OXIDE NANOPLATFORMS AS ANTICANCER THERAPY FOR GLIOBLASTOMA AND BREAST CANCER

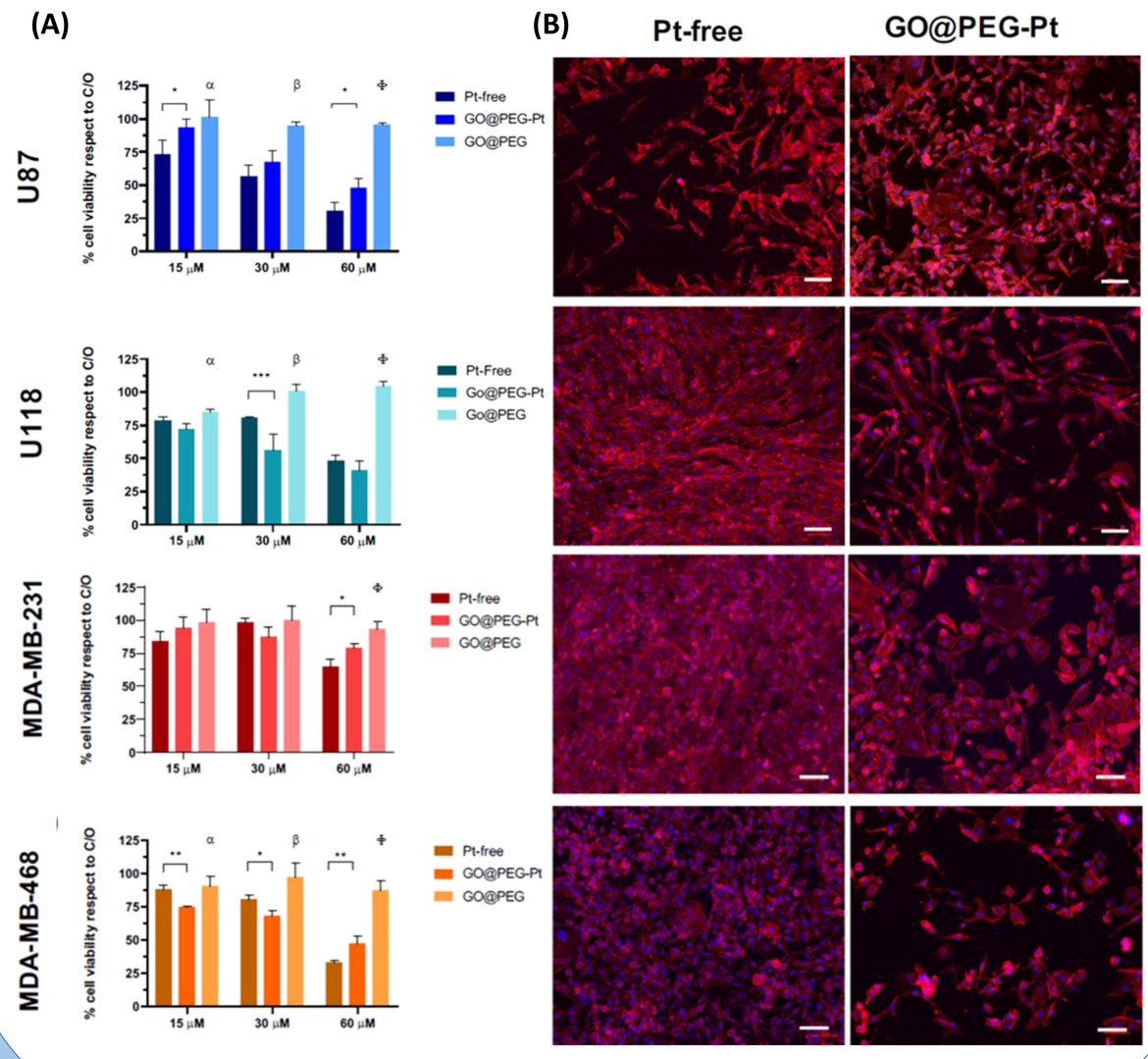
E. Giusto[1], A. Rossi[1,2,*], L. Zarska[3], D. F. Beirne[4], G. Bassi[1,5], A. Ruffini[1], M. Montesi[1], D. Montagner[4], V. Ranc[3], and S. Panseri[1]

[1] ISTEC-CNR, National Research Council, 48018, Faenza, Italy.
[2] University of Messina; Department of Chemical, Biological, Pharmaceutical and Environmental Sciences. 98166, Messina, Italy.
[3] Regional Centre of Advanced Technologies and Materials, Czech Advanced Technology and Research Institute, Palacký University, Olomouc, Czech Republic.
[4] Maynooth University, Maynooth, Ireland.
[5] University of G. D'Annunzio; Department of Neurosciences, Imaging and Clinical Sciences. 66100, Chieti, Italy.
*arianna.rossi@istec.cnr.it

INTRODUCTION: Chemotherapy is largely used to treat cancer and it is based on the use of molecules targeting the high cancer cell proliferation metabolism[1]. Platinum (Pt) and three of its isoforms (cisplatin, carboplatin, and oxaliplatin) are some of the most successful metal-based drugs to cure breast cancer and glioblastoma[2]. Despite Pt-based chemotherapeutics being effective, their side effects (high degradation before entering the cells, the off-target organs toxicity, and cell resistance) remain great drawbacks[3,4]. In this work, it was developed a Graphene Oxide (GO) nanoplatform functionalized with Pt as a promising smart delivery system that could increase the Pt cellular uptake reducing the Pt amount needed for cancer treatment and consequently the side effects.

CELL VIABILITY AND MORPHOLOGY EVALUATION

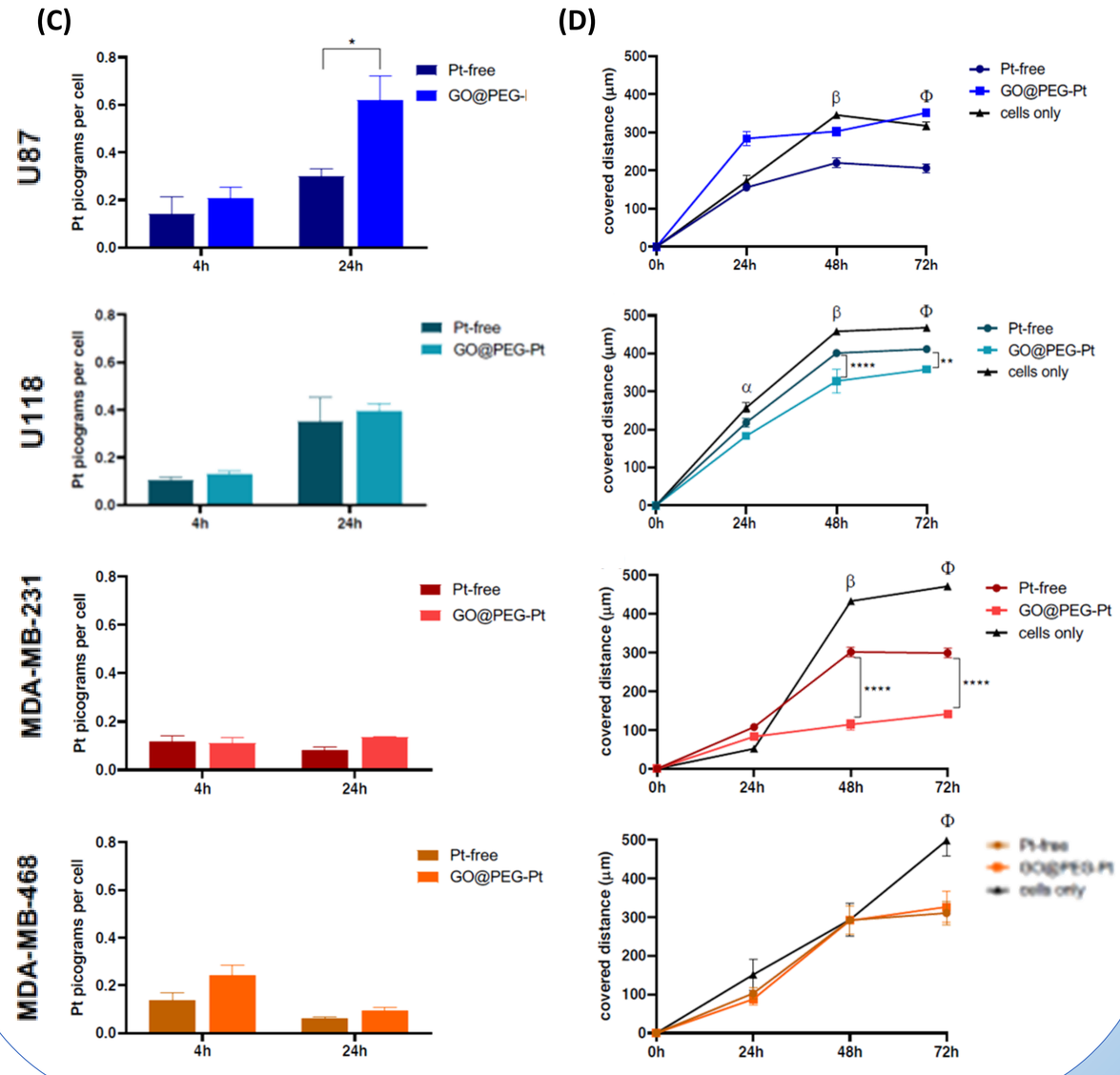
The cell viability was significantly lower in MDA-MB 468 and U118 cells at 30µM for GO-PEG-Pt group compared to Pt-free (<75%) (Fig. A), and even the cell morphology seemed to be compromised, in fact the cell density is lower in GO@PEG-Pt group compared to Pt-free with a round and smaller cell morphology shape and with actin filaments aggregated at the cell's edges (Fig.B).



EXPERIMENTAL: GO nanoplatforms were treated with 8-arm polyethylene glycol-amine (PEG) that permits to load Pt on the platform (GO-PEG-Pt) and an extensive in vitro screening was performed on two breast cancer cell lines with aggressive nature that lead to metastatic behavior (MDA-MB 231 and MDA-MB 468) and two glioblastoma cell lines (U87 and U118). The bioactivity of GO-PEG-Pt compared to Pt-free (15µM, 30µM, and 60µM) was analyzed by looking at the effect on cellular uptake (ICP-OES), viability (MTT Assay), morphology (DAPI and actin staining), and migration up to 72 hours (Scratch Assay).

PLATINUM UPTAKE AND CELL MIGRATION ANALYSIS

Cell viability results were highly related to the cellular uptake of GO-PEG-Pt which is significantly higher compared to Pt-free after 24h (Fig.C). In addition, GO-PEG-Pt mostly affected the cell migration compared to Pt-free, in particular, MDA-MB 231 showed a migration reduction of 60% (Fig.D), and this could be a great advantage in reducing the metastasis process.



CONCLUSIONS: This study demonstrated that the combination of Pt onto PEG-functionalized nano-sized GO provided numerous advantages for tumor therapy such as minimizing toxicity, enhancing the cellular uptake, and consequently we could reduce the side effects because a lower amount of Pt is necessary.

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