Graphene oxide surface functionalization of polymeric scaffolds for the recruitment and thermal ablation of tumor cells

Nicolò Mauro, Cinzia Scialabba, Anna Li Volsi, Giovanna Pitarresi, Gaetano Giammona

Laboratory of Biocompatible Polymers, Department of "Scienze e Tecnologie Biologiche, Chimiche e Farmaceutiche" (STEBICEF), University of Palermo, via Archirafi 32, 90123, Palermo, Italy;
nicolo.mauro@unipa.it

The control of metastatic spread of a primary tumor is related to good probability of eluding extravasation of cancer cells to target organs, thereby containing the progression of disease burden [1]. Circulating tumor cells (CTCs) in the bloodstream have been recently correlated to metastasis outbreak [2], therefore much attention has been focused on the capture of CTCs on functional biomaterials to limit tumor growth. We developed a electrospun microfiber scaffold composed of poly(caprolactone) layered with graphene oxide (GO) sheets at the microfiber surface, named PCL_{MF}-GO, able to simultaneously recruit CTCs and kill them by non-invasive near infrared-assisted photothermal ablation. Here, nitrogen plasma activation was used for scaffold engineering to provide functionalization of the scaffold surface with reactive amines, even if keeping bulk properties of the virgin polymeric material, and to enhance cell adhesion properties of hydrophobic polymers [3]. We investigated the covalent nature of the interactions taking place between GO and amines inserted through plasma exposure by DSC, FT-IR, SEM, AFM and XPS analyses. SEM was employed for the direct morphological study of the PCL_{MF}-GO scaffold. It is evident that microfibers did not display significant damage after the treatment with N_2 plasma (Fig. 2 A-B) and that GO sheets are closely adhered to the microfibers surface, even linking adjacent microfibers (Fig. 2A). AFM analysis shows (Fig. 2C) that PCL_{MF}-GO exhibited a surface characterized by rough and porous areas, typical of polymeric materials, near to highly smooth surface 1 nm thickness that can be credited to the GO monolayers, thus indicating that GO sheets are firmly attached to the mat by the covalent bonds established with amine intermediates provided by N_2 plasma activation. The in vitro preferential recruitment of breast cancer cells (MCF-7) instead of normal fibroblasts (HDFa) was studied as function of non-specific GO-mediated recognition, suggesting a potential pivotal role of GO in recruiting cancer cells in vivo (Fig 2D). We also display that GO deposition, thanks to the high near-infrared (NIR) absorbance, enable the discrete photothermal eradication of the captured cancer cells in situ (≈ 98%). Moreover, this technology can be used to capture circulating cancer cells in patients and, after proper ex vivo propagation, to develop biomarkers and tailor-made anticancer therapies.

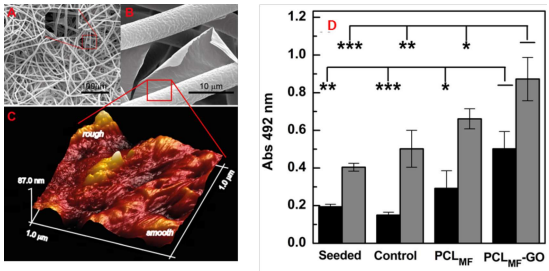

Figure 1. SEM (A and B) and AFM (C) of PCL_{MF}-GO. Cell adhesion properties of PCL_{MF}-GO using MCF-7 cells (D): the cell viability is reported after an incubation time of 6 and 24 h.

References

1. O.L. Griffith, J.W. Gray, *Breast Cancer Res.*, **2011**, *13*, 230.
2. S. Nagrath, L.V. Sequist, S. Maheswaran, D.W. Bell, D. Irimia, L. Ulkus, M.R. Smith, E.L. Kwak, S. Digumarthy, A. Muzikansky, P. Ryan, U.J. Balis, R.G. Tompkins, D.A. Haber, M. Toner, *Nature,* **2007**, 450, 1235.
3. L.C. Lopez, M.R. Belviso, R. Gristina, M. Nardulli, R. d'Agostino, P. Favia, *Plasma Process. Polym.*, **2007,** *4*, S402.