Graphene oxide complexed with integrin antagonists for targeting plasma membrane receptors in glioblastoma cells

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Graphene oxide (GO) is one of the most promising two-dimensional materials, holding potential for various applications, especially in medicine. GO has already been used as a carrier for biomolecules such as proteins, peptides and nucleic acids. We have established that GO predominantly interacts with the plasma membrane of cancer cells, rather than being taken up. Therefore, we hypothesize that GO functionalized with therapeutic molecules could target specific signalling pathways, integrin receptor-dependent, emerging from the plasma membrane.

We used two glioblastoma cell lines: expressing high (U87) or low (U251) amounts of integrin receptors, as well as a negative control, non-cancer cell line (Beas-2B). GO was complexed a linear integrin antagonists (lRGD), using the non-covalent approach (GO:lRGD). We found that 89.1% ± 3.2% of the lRGD was bound to GO, with 40% of the lRGD released after 24 h. We confirmed by Atomic Force Microscopy that GO:lRGD exhibited the same size and thickness as GO. The successful functionalization was proven by X-ray crystallography and X-ray photoelectron spectroscopy. The GO:lRGD spectra was shifted to lower angle than the GO, indicating the intercalation of lRGD into GO. In addition, GO:lRGD exhibited higher atomic percentage of Nitrogen (2.88%) in comparison with GO (0.77%).

We looked at cellular viability, motility and directionality; all correlated with the inactivation of RGD-dependent integrin receptors. The time-lapse microscopy analysis revealed that the velocity, directionality and mean square displacement of U87 and U251 cells were significantly reduced when compared to the controls (untreated, RGD or GO-treated cells) after 24h. On the other hand, BEAS-2B cells were not significantly affected, as expected.

Our results indicate that GO:lRGD can have specificity for targeting relevant glioblastoma cells and affecting their motility as well as that the toxicity of lRGD can be reduced in non-cancer cells when in complex with GO.

#Nanomedicine #Glioblastoma #Graphene oxide #Integrin receptors