Graphene and immune cells: a box of opportunities

Lucia G. Delogu[1,5]
Marco Orecchioni[1], Davide Bedognetti[2], Valentina Bordoni[1], Alberto Bianco[3], Kostas Kostarelos [4]

[1] University of Sassari, 07100 Sassari, Italy. [2] Research Branch, Sidra Medical & Research Centre, Doha, Qatar. [3] CNRS, Institut de Biologie Molèculaire et Cellulaire, Laboratoire d'Immunologie et Chimie Thérapeutiques, 67000 Strasbourg, France [4] Nanomedicine Laboratory, Faculty of Medical & Human Sciences, University of Manchester, Manchester M13 9PT, UK. [5]Department of Chemical and Pharmaceutical Sciences University of Trieste, Trieste, Italy.
lgdelogu@units.it

Abstract
Despite significant progress of nanotechnology also in medicine, the development of new nanomaterials able to treat and prevents diseases such as cancer is still one of the biggest challenges [1]. In this challenge, a critical step is represented by the assessment of their impact on the complexity of the immune system [2]. Graphene oxide (GO), has attracted tremendous interest being explored for many potential applications in medicine [3]. To clarify its action on the immune cells, here, we propose an integrative analytical pipeline encompassing genomic and cellular characterization of the impact of graphene on primary immune cells. We used whole-transcriptomic analysis (Illumina BeadArray) for functional and molecular characterization of GO and GO functionalizated through the addition of amino groups ($GONH_2$) on human T-cells and monocytes. We then employed single cell mass cytometry. We identify 15 cellular main populations corresponding to 200 nodes of distinct but logically interconnected cell sub-populations. Notably, thanks to several analytical tools (i.e.SPADE and viSNE) we found that only the functionalized $GONH_2$ was able to induce a specific dendritic cell and monocyte activation skewed toward a Th1/M1 response, as demonstrated by the increased production of classic M1 cytokines (TNFa, IL6, and CCL4) [Figure 1]. This effect was proved also by the overexpression of pathways critical for the development of an effective anti-tumor immune response (i.e. interferon signalling, CCR5 and CXCR3 ligands) [Figure 2]. Our findings report a new pipeline able to carefully analyse the immunological impact of new nanoscale platforms for a successful application in medicine.

References

[1] Vincent Dusastre. Nature (2008). The invisible revolution.
[2] Orecchioni M, Bedognetti D, Sgarrella F, Marincola FM, Bianco A, Delogu LG. Journal of translational medicine (2014). Impact of carbon nanotubes and graphene on immune cells.
[3] Kostas Kostarelos. Nature Reviews (2016). Translating graphene and 2D materials into medicine.

Figures

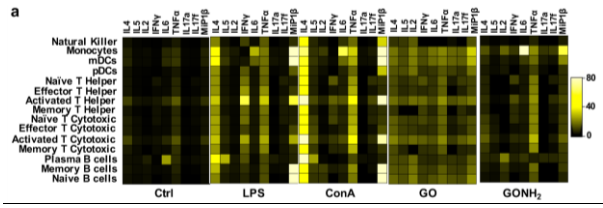

Figure 1: Heat map analysis of the immune cell behavior using CyTOF.

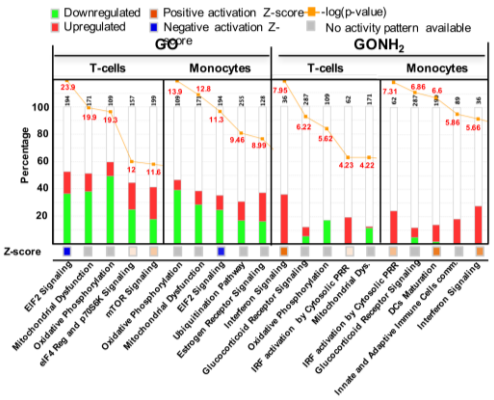

Figure 2: Gene expression impact of GO and $GONH_2$ on T- and monocyte cell lines.