New hight troughput technologies reveal the impact of nanomaterials with human primary immune cells

Marco Orecchioni [1], Davide Bedognetti[2], Francesco M Marincola[2], Gianni Cesareni[3], Kostas Kostarelos[4], Alberto Bianco[5] and **Lucia Gemma Delogu[1*]**

lgdelogu@uniss.it

[1] University of Sassari, 07100 Sassari, Italy, [2] Research Branch, Sidra Medical & Research Centre, Doha, Qatar, [3] Department of Biology, University of Rome Tor Vergata, Rome, Italy [4] Nanomedicine Laboratory, Faculty of Medical & Human Sciences, University of Manchester, Manchester M13 9PT, UK, [5] CNRS, Institut de Biologie Molèculaire et Cellulaire, Laboratoire d'Immunologie et Chimie Thérapeutiques, 15 rue René Descartes, 67000 Strasbourg, France.

Abstract

Nanotechnology nowadays is expanding its legacy in medicine by implementing approaches aimed to delivering therapeutics and developing new diagnostic and imaging tools [1]. However, before any translational application of nanotechnology in medicine, a critical step is represented by the assessment of their impact on the complexity of the immune system [2]. In this context, is mandatory to study the immunological impact of some of the main promising nanomaterials for biomedical applications such as carbon nanotubes (CNTs), graphene, lipid nanocapsules (NCs) and super paramagnetic iron oxide nanoparticles (SPIONs) on the different immune cell populations. Recently we focused our attention on these new nanomaterials in order to clarify their potential to be applied in therapy and diagnostic applications, taking also advantage from their intrinsic immunomodulayory properties. One example of this approach is here reported for graphene, particularly on its oxidized form (GO). We investigated the effects of several types of thoroughly characterized GO sheets, different in their lateral dimension and functionalization, on human primary lymphomonocytes from healthy donors. Wide range of assays looking at cell viability, cell activation, and molecular interaction were done. Moreover, to better dissect the immunological effects of these nanomaterials on individual cells, we applied single-cell mass cytometry to evaluate the effect of functionalized GOs on 15 cellular populations corresponding to 200 nodes of distinct but logically interconnected cell sub-populations. We than used whole-transcriptomic analysis (Illumina BeadArray) for functional and molecular characterization of GOs on human T-cells and monocytes. Notably, only the functionalized GO ($GONH_2$) 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 (TNFα, IL6, and CCL4) [**Fig.1**]; inducing also the overexpression of pathways critical for the development of an effective anti-tumor immune response (i.e. interferon signaling) [**Fig.2**]. A positive impact of nanomaterials on the immune system, able to trigger both immune suppression or immune activation, is a new concept helpful in the development of new nanoscale platforms in medicine. These new platforms, indeed can be investigated as immunotherapy tools, vaccine carriers, adjuvants, and drug delivery systems to target pathology or inflammatory and inflammation-associated disorders.

References

[1] Vincent Dusastre. The invisible revolution. Nature 451, 770-77 (2008).

[2] Orecchioni M, et al and Delogu LG, Impact of carbon nanotubes and graphene on immune cells. Journal of translational medicine (2014).

Figures

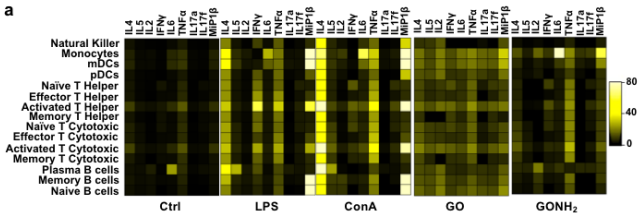

Figure 1. **Analysis of the immune cell behavior using CyTOF2**

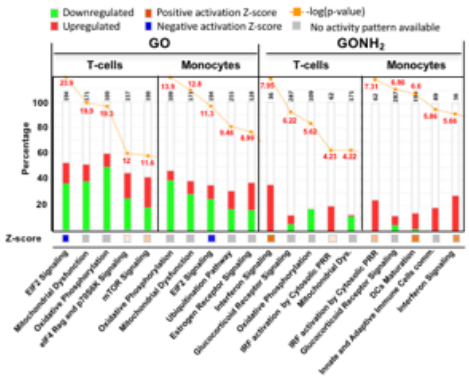

Figure 2. **Gene expression impact of GO and $GONH_2$ on T- and monocyte cell lines**