

# Immune cells and graphene: interactions and potentiality

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Before any successful translational application of nanomaterials in medicine, a critical step is represented by the assessment of their impact on the complexity of the immune system and immune cells [1]. We present our results on carbon nanomaterials, in particular on graphene, and their interactions with the blood immune cells [2-9]. We here discuss different scenarios of interest where the immune response can have a key role in the carbon nanomaterials applications: from cancer therapy, to space biology, to immunotherapy, to bone regeneration. We discuss how an immune design of graphene and other nanomaterials can facilitate their translation into the everyday clinical practice. Indeed, the understanding of the interactions between nanoparticles and immune cells is hindered by the scant implementation of high throughput technologies in nanotechnology. A novel tool for flow cytometry analysis has been developed, gaining leverage with the precision of mass spectrometry. The combination of the two techniques, Single-cell mass cytometry, provides the measurement of more than 40 simultaneous cellular parameters at a single-cell resolution with over 100 available detection channels. As suggested by Goldberg (Cell 2015), we propose, for the first time in the context of nanotechnology, a new analytical strategy taking advantage of this powerful method, able to deconvolve the immunological impact of nanomaterials, at the single-cell level [2]. The analytical pipeline we recently reported encompasses the immunological characterization of the most studied nanomaterial in the last years: graphene. Mass cytometry enables us to describe the immune cell interactions of thin graphene oxide (GO) flakes and GO functionalized by amino groups (GONH<sub>2</sub>) on 15 cellular populations corresponding to 200

nodes of distinct but logically interconnected cell sub-populations. Together we performed whole-transcriptomic analysis for functional and molecular characterization on human T-cells and monocytes as a representative for the adaptive and innate responses. Our results emphasize the importance of the functionalization on enhancing the biocompatibility of GO-based nanomaterials. Notably, only the functionalized GONH<sub>2</sub> was able to induce a specific monocytoïd dendritic cell and monocyte activation skewed toward a T helper 1/M1 response. The positive impact of GONH<sub>2</sub> on specific immune cells could serve as a starting point for the development of new nanoscale platforms in medicine as novel immunotherapy, vaccine carrier, or nanoadjuvant tools. Our recent study[2] paves the way for the future use of single-cell mass cytometry for a deep characterization of immune responses to any nanomaterials useful for biomedical applications.

Moreover, we will present our results on graphene-based tools in the context of osteoimmunology and their applications for bone loss-related diseases.

## References

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- 2 Single cell mass cytometry reveals the impact of graphene on human primary immune cells Orecchioni M, Bedognetti D, Newman L, Fuoco C, Spada F, Hendrickx W, Maricola FM, Sgarrella F, Rodrigues FA, Ménard-Moyon C, Cesarenì G, Kostarelos K, Bianco A and Delogu LG. *Nature Communication* 2017