How to Transform a Novel 2D Nanomaterial in '*Medical Grade*'

Neus Lozano,

Catalan Institute of Nanoscience and Nanotechnology (ICN2), CSIC and BIST, Campus UAB, Bellaterra, 08193 Barcelona, Spain

neus.lozano@icn2.cat

Graphene and its derivatives have been attracting tremendous attention for over a decade, since in 2004, a single sheet of graphene was isolated and characterized by Novoselov and Geim [1]. In particular, graphene oxide (GO) - the oxidized form of graphene - has become one the most investigated materials in the biomedical field due to its hydrophilicity and improved compatibility with biological systems. It is rapidly becoming the reference 2D nanomaterial for use in medical applications.

Determination of the opportunities and limitations that GO offers in biomedicine are particularly prone to inaccuracies due to the wide variability in the preparation methodologies for the synthesis of GO. Most of the methods used are based on oxidation of graphite following a modified Hummers' protocol [2], which involves the use of oxidizing reagents and acids. However, this method yields GO with different degrees of oxidation and impurities. Additional purification steps are required to enhance the purity of the material, by isolating the purest fraction of GO in the absence of by-products or contaminants [3]. Bacterial endotoxin contamination during the synthesis process and handling, can confound toxicological testing of the materials [4], and needs to be carefully and highly considered on the production of GO for biomedical applications.

To avoid some of the pitfalls encountered with commercial GO materials, we have made a systematic bottom-up effort during the last 10 years to generate '*medical grade'* GO suspensions. These water-based suspensions were produced from graphite flakes [5] following a modified Hummers' method further improved to ensure endotoxin-free [4] suspensions of single- to few-layer GO sheets of the highest chemical purity. These materials were produced in a range of different lateral dimensions [7] to assess the impact of this parameter with respect to biological impact [6].

Furthermore, a suite of characterization techniques has been established to confirm the quality, reproducibility, and low batch-to-batch variability of each synthesis [6]. In the last decade, these GO suspensions have been used for either hazard assessment or biomedical proof-of-concept studies, to reveal the relationship between the nanomaterial structure and either their toxicological limitations or their potential utility in biomedical applications.

This talk will describe the requirements needed to be fulfilled when a novel 2D nanomaterial, such as GO, should be produced for biological applications including their toxicological evaluation. As a general consideration, GO material must be fabricated as stable aqueous suspensions, with an exhaustive reproducibility and careful control of structural, chemical, and bacterial impurities, leading to what we define as '*medical grade'* quality requirement.

More broadly, biological studies of novel nanomaterials must be performed with such '*medical grade'* quality specifications, meaning very specific and thoroughly characterized types of materials, to allow accurate and reliable assessment of hazard or potential in healthcare applications.

References

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Figures

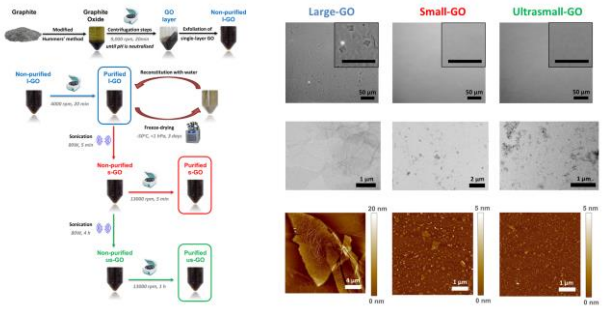

Figure 1. Synthesis and structural characterization of *'medical grade'* GO suspensions with three different lateral dimensions.