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Graphene-Proceed with Caution: What We Know, what We don't

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Editorial

Graphene is the most important member of the nanostructured carbon family. The importance of this family of nanostructured materials made it the winner of Nobel Prize in chemistry in 1996. Surprisingly, in 2010, the high potential of the missing piece of the carbon nanostructures puzzle "graphene" has led it to win the Physics Nobel Prize [1]. This successful background will certainly stimulate much attention in graphene for the next few years, as reflected by a huge increase in the number of publications in this area during these years (Figure 1).

Graphene is composed of sp2-hybridized carbon atoms arranged in a two dimensional hexagonal structure, causing a large surface area on both sides. Compared to other members of nanostructured carbon family, graphene provides superior advantages in terms of mechanical strength, thermal conductivity, chemical inertly, optical transmittance, easy modification and larger surface area [2]. Graphene has been used in various technological applications ranging from very powerful super capacitors to biotechnology and medicine [3].

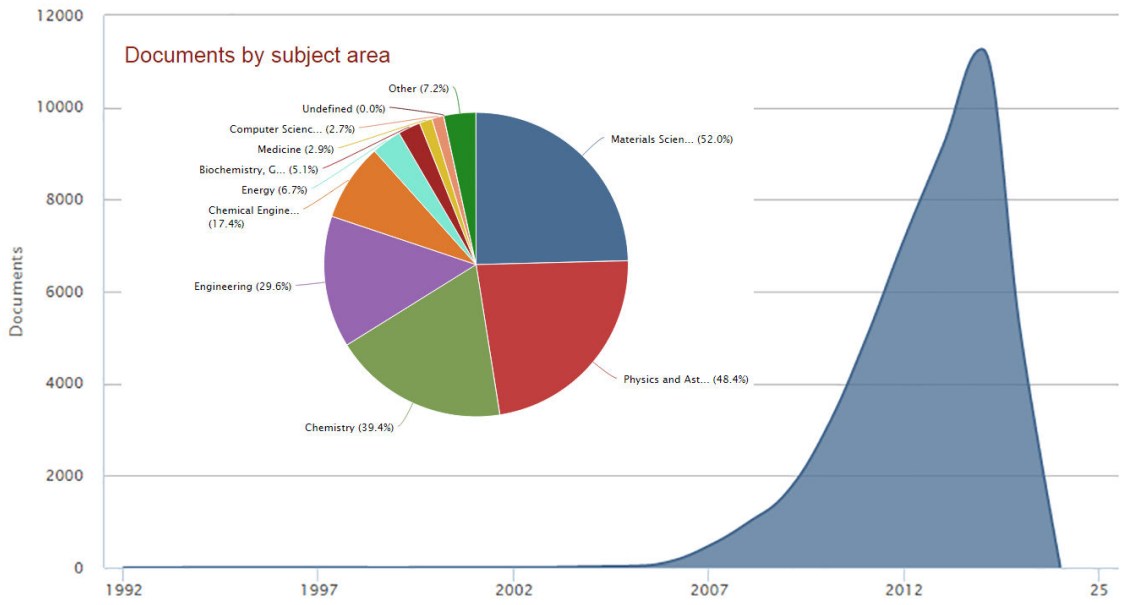

Figure 1: History of scientific publications on the papers having the term "graphene" in the title, extracted from Scopus database.

Although the applications of graphene can provide reliable advances and promising revolutions in biomedical applications, its usage is not without side effects for the human health [4]. Therefore, a complete evaluation on the nano toxicological aspects and human safety is necessary, and a number of critical challenges and opportunities have yet to be answered. Even though the use of this material seems to be a promising approach to enhance the general characteristics of biomaterials, more detailed analyses of the response of cells exposed to graphene are needed to confirm its exact effects on the human body. When working with graphene, various forms of this material must be considered since different types of graphene have specific physico-chemical characteristics inducing diverse toxicological effects (graphene oxide, few-layer graphene, and graphene nanosheets reduced graphene oxide). Generally, the risks of human health for graphene-family materials are determined by its chemical and physical behavior. Many studies have suggested that one of the mechanisms involved in the toxicity effects of this family of materials is oxidative stress [5]. In fact, the oxidative stress is triggered by the production of reactive oxygen species (ROS) in target cells. Another probable mechanism of graphene toxicity is cell membrane damage through

physical interaction with graphene's sharp edges. Also, graphene can considerably interact with cell membrane lipids and lead toxicity because of its hydrophobic surface. Toxicity also depends on the physico-chemical properties of graphene-family materials, such as density of the functional groups, size, conductivity, and chemical nature of the reducing agents, as well as the type exposed cells [6]. Different sizes of these nanostructured materials have significant effects in vivo. The increase in the uptake behavior of graphene to cells and the decrease in the circulation in blood stream is due to the increase in size. Some recent studies have shown that the smaller size and subsequently larger specific surface area of these materials can improve the generation of ROS [7]. Moreover, the particle size distribution of this family is critical to the pharmacokinetics and toxicity of graphene. The existence of a wide size distribution possibly makes inhomogeneous biological reactions. The cytotoxicity, subcellular localization, blood circulation, and cell uptake of these nanomaterials are highly affected by their particle size distribution. Indeed, the particle size distribution can affect the nanotoxicity as the dose of toxicity is associated with the mass and size of the exposed nanomaterials. The production of graphene with a high narrow size distribution is critical for a true assessment of the risks associated with the interaction of graphene with human body.

In recent years, graphene-family materials have shown satisfactory primary results for a wide range of biotechnological and biomedical applications, including tissue engineering, drug delivery, diagnosis and biosensors. However, the evaluation of safety and possible threats of graphene materials is obligatory to confirm their usage in biomedical applications. Now, incomplete information about the in vitro and in vivo toxicity of graphene is available. Furthermore, more systematic surveys are still highly required to completely understand the biological effects and address safety concerns before the clinical application of any graphene-based materials.

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