NANOTECHNOLOGY: FROM NANOTOXICOLOGY TO NANOMEDICINE

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Nanoparticles. New species in contact with biological systems. As society begins to use nanomaterials in greater quantities and in consumer products, interest in the broader implications of this emerging technology has grown together with unfounded "nanoeuphoria" and "nanoscares". The central question is whether the unknown risks of engineered nanoparticles (NP), in particular their impact on health and the environment, outweigh their established benefits for society. Therefore, for any application and future developments, a key issue is to accurately evaluate the utility of these materials and it is necessary to assess their potential toxicity –whether due to their inherent chemical composition (e.g., reactive metals), their physical size (e.g., Au_{55} attaching to DNA), their large and accessible inorganic surfaces (e.g., TiO_2 NP versus microparticles) or as a consequence of their particular nanoscale characteristics (e.g., carbon nanotubes that have reached the lungs appear significantly more toxic than carbon black and graphite). While there is a significant body of research on the effects of natural and incidental NP –those that occur as unintentional byproducts of other processes, such as combustion– only a few engineered nanomaterials have been studied in this way. In fact, some incidental NP are central to many natural processes, from marine aerosols to volcanoes and forest fires, and they do not have a great effect on health. Thus, it has been observed that nanomaterials, including fullerenes, are produced naturally in combustion processes, while burning paraffin and diesel produces carbon nanotubes (CNT). Nanomaterials can also be found perfectly integrated into biological structures. For example, biogenic magnetic NP occur naturally in many organisms ranging from bacteria through protozoa to animals. A biological model of coated nanomaterials also found in humans is ferritin, which is an iron storage protein, approximately 12-nm in diameter, that contains 5- to 7-nm-sized hydrous ferric oxide inside a protective protein shell. Obvious differences between natural, unintentional NP and intentional, anthropogenic NP are: i) the polydisperse and chemically complex nature of the former in contrast to the monodisperse and precise chemically engineered characteristics of the latter, and ii) particle morphology (often a branched structure from combustion particles versus spherical forms of engineered NPs, although other shapes, such as tubes, wires, rings and disks, are also manufactured). Despite these differences, the same toxicological principles are likely to apply for both types of NP.

If nanomaterials have received enormous attention it is because of their potential interaction with living systems. This gives rise to potential applications in biology and medicine, due to their ability to detect the state of biological systems and living organisms optically, electrically and magnetically, thanks to recent developments in materials physics and chemistry. Thus, NP can be designed with different properties, such as fluorescence or possessing a magnetic moment, and these properties can be harnessed and used as local nano-probes or nano-manipulators in biological and medical applications (e.g.: fluorescence labeling of cellular compartments; the use of fluorescent or magnetic particles as contrast agents; magnetic separation; and targeted drug delivery). Derivatization of NP with biological molecules has successfully been applied in materials science and biological research in recent years. Conjugates of NP biopolymers (like proteins or DNA) show great promise in both fields: biological diagnostics, where NP can provide unique detection signatures; and nanotechnology, where the information content of biomolecules can be harnessed for the spatial patterning of NP. There are many strategies available for bioconjugation of NP, including attachment to elastin, antisenses, biotin-avidin, antigen-antibodies, peptides, proteins, etc.

Thus, the characteristic biokinetic behavior of NP promises applications in diagnostic and therapeutic devices, and in tools to investigate and understand molecular processes and structures in living cells. However, precisely this unique biokinetic behavior of NPs (cellular endocytosis, transcytosis, neuronal, lymphatic and circulatory translocation and distribution, etc.) which makes them so attractive for medical applications, may be associated with potential toxicity. Not only bacteria, viruses and parasites, but also inorganic foreign bodies can be the cause of various pathologies: silicosis, asbestosis and inflammatory reactions to the debris from worn out prostheses or related to diesel exhaust fumes are only a few among many possible examples. Thus, for example, NP-facilitated drug delivery to the central nervous system (CNS) raises the question of the fate of the NP after their translocation to specific cell types or to sub-cellular structures in the brain. This and other aspects will be discussed in this presentation.

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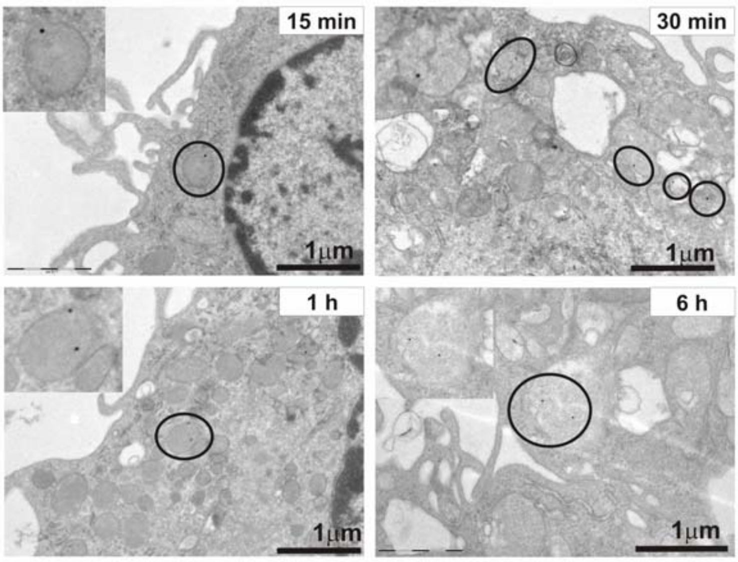

TEM image of Internalization of Au NPs conjugates in macrophages. Macrophages were incubated for a range of times: (A) 15 min, (B) 30 min, (C) 1 h and (D) 6 h with AuNPCysAGIP